PAP Adherence and Nasal Resistance: A Randomized Control Trial of $CPAP_{Flex}$ vs CPAP

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Abstract

Rationale: Continuous Positive Airway Pressure (CPAP) adherence is often poor in obstructive sleep apnea (OSA) and may be influenced by nasal resistance. CPAP with reduction of expiratory pressure ($CPAP_{Flex}$) may reduce discomfort in those with high nasal resistance and improve adherence in this subgroup.

Objectives: To evaluate the association of PAP adherence to nasal resistance and examine if $CPAP_{Flex}$ improves adherence over CPAP in subjects with high nasal resistance.

Methods: A randomized double-blind control cross-over trial of 4 weeks each of $CPAP_{Flex}$ versus CPAP in World Trade Center dust-exposed subjects with OSA stratified by nasal resistance measured by 4-Phase Rhinomanometry.

Results: 317 subjects with OSA (mean $AHI_{4\%}$=17±14/hr) were randomized. Overall, PAP adherence was poor, but adherence to CPAP (n=239, mean hours per night (95% CI)) = 1.97h (1.68, 2.26) was greater than to $CPAP_{Flex}$ (n=249, 1.65h (1.39, 1.91); difference 0.31h (0.03, 0.6); $p<0.05$). Contrary to our hypothesis there was no correlation between nasal resistance and adherence to CPAP ($r=0.098$, p=NS) or $CPAP_{Flex}$($r=0.056$, p=NS). There was no difference in adherence between CPAP and $CPAP_{Flex}$ (mean Δ hours (95% CI)) in subjects with low resistance (0.33h (-0.10, 0.76)) or high nasal resistance (0.26h (-0.14, 0.66)). No significant differences were observed in any of the secondary outcomes between PAP modes.

Conclusions: Contrary to expectations, our data do not show better adherence to $CPAP_{Flex}$ than to CPAP in subjects with high or low nasal resistance, and, show clinically insignificant better adherence overall with CPAP.

Clinical Trial registered with Clinicaltrials.gov (NCT01753999)

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Continuous Positive Airway Pressure (CPAP) is the primary form of treatment for obstructive sleep apnea (OSA) and has been demonstrated to normalize sleep disordered breathing and improve sleep continuity and daytime sleepiness. However, in most studies, adherence to CPAP (1-5) remains suboptimal. When defined by use for at least 4 hours per night, adherence rates have ranged from 50% to 83% (6-8).

Proposed explanations for the poor adherence to CPAP have included poor mask fit, excessive leak, and claustrophobia, but also the complaint of difficulty exhaling against high pressures (9-12). High nasal resistance has been associated with lower PAP adherence in some studies (13-15). Elevated nasal resistance increases expiratory pressures and may produce discomfort and increase mouth leaks (16). Technological strategies to mitigate this pressure increase include reducing mask pressure during expiration, which may be most relevant to patients with high nasal resistance. This pressure control strategy is employed in $CPAP_{Flex}$ (Respironics; Murraysville, PA), wherein pressure in the mask is reduced in proportion to expiratory flow only. Despite a few trials demonstrating a modest benefit for adherence of $CPAP_{Flex}$ over CPAP, (17) a meta-analysis did not show improved adherence (17-24). However, no studies have examined if an improved adherence to $CPAP_{Flex}$ might be related to selective effects in subjects with elevated nasal resistance.

The WTCSNORE cohort is composed of 9/11 World Trade Center (WTC) responders and rescue workers who were prospectively recruited to examine the relationship of nasal pathology to obstructive sleep apnea. Following exposure to massive quantities of large particle size dust and debris 43% of these subjects have experienced ongoing chronic rhinosinusitis (CRS) and 75% show new onset obstructive sleep apnea since 9/11(25, 26). This

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population with significant nasal complaints and those subjects with high nasal resistance provide an opportunity to examine the impact of reducing mask pressure using $CPAP_{Flex}$ on PAP adherence.

The aims of the present study were to 1) examine the correlation of PAP adherence to nasal resistance in WTCSNORE patients with OSA and 2) test in a randomized control trial stratified by nasal resistance whether reduction of expiratory pressure using $CPAP_{Flex}$ improved CPAP adherence preferentially in those with high nasal resistance. Our hypotheses were that 1) high nasal resistance is associated with decreased adherence to CPAP and 2) use of $CPAP_{Flex}$ improves adherence to CPAP in subjects with high nasal resistance but not in those with low nasal resistance.

Methods

Study Design and Population

We performed a double-blind randomized control trial with a cross over design in WTC responders with OSA comparing adherence to CPAP vs $CPAP_{Flex}$ (with a Flex setting of 3), with enrollment stratified by nasal resistance measured by 4-Phase Rhinomanometry. Methods have been previously published (27). Briefly, subjects were recruited at Rutgers-Robert Wood Johnson Medical School (RWJMS), NYU School of Medicine and Icahn School of Medicine at Mount Sinai (ISMMS) as part of the WTCSNORE study. The study protocol was approved by the Institutional Review Boards of Rutgers Biomedical Health Sciences (Pro2012002164), NYU School of Medicine (I12-02578) and the Icahn School of Medicine at Mount Sinai (HS#16-00511)

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and the Population Protection Committee of the WTC Health Program. All subjects signed informed consent. The trial was registered at the Clinicaltrials.gov website (NCT01753999). Recruitment for the study began in March of 2013 and continued until March 2017.

The inclusion criteria were diagnosis of OSA based on a 2-night home sleep study and being a member of the WTC General Responder Cohort at one of the trial sites. The exclusion criteria were: (i) gross anatomic alterations affecting the upper airway (e.g., micrognathia) (ii) unstable chronic medical conditions known to affect OSA (CHF, stroke) (iii) pregnancy or intent to become pregnant within the period of the protocol (iv) Inability to sign informed consent form (v) habitual snoring or diagnosis of OSA prior to 9/11/01.

Subjects underwent 2 nights of home monitoring using an ARES^{TM} Unicorder device (Watermark Medical/SleepMed, Inc., Columbia, SC). Data from the device was autoscored and then manually reviewed by a single trained sleep technician at NYU. Apneas were scored when there was a reduction in airflow to less than 10% of baseline. Hypopneas$_{4\%}$ were scored for >30% reduction in airflow associated with 4% or more decrease in oxygen saturation. AHI$_{4\%}$ was calculated as apneas+hypopneas$_{4\%}$ divided by total valid recording time. Hypopneas$_{AR}$ were scored for >30% reduction in airflow associated with only surrogates of arousal (head movement, changes in snoring, or changes in pulse rate; these were then edited for a disappearance of flow limitation and a marked (>150%) increase in flow amplitude at end of event). The RDI (Respiratory Disturbance Index) was calculated as apneas+hypopneas$_{4\%}$+ hypopneas$_{AR}$ divided by total valid recording time. The AHI$_{4\%}$ and RDI reported for each participant were the weighted average of each index for the two nights recorded, based on the

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duration of recording. Using these metrics, we defined OSA as present when $AHI_{4\%}$≥5/hr or when RDI≥15/hr.

Rhinomanometry

We objectively assessed awake nasal resistance using 4-phase-rhinomanometery (RhinoLab GmbH, Rendsburg, Germany) which is a measurement of anterior nasal resistance (28). Subjects were fitted with a full face mask and flow through each nostril was measured while the differential pressure for its generation was measured through a pressure hose inserted into the sealed opposite nostril. Measurements were performed seated and in the supine position (before and 10 minutes after decongestion with 0.1% Xylometazoline solution) in a quiet procedure room with a constant temperature. Total nasal resistance was calculated 1/[1/Rleft + 1/Rright] and then log transformed. Total nasal resistance (TNR) measured supine (pre-nasal decongestant) was used to stratify resistance using the median value of our preliminary data (log[TNR]=0.8) as high or low.

Subjective nasal congestion was evaluated using a nasal symptom questionnaire for chronic rhinosinusitis (CRS) based on symptoms present for >8 weeks, Questions addressed nasal congestion or stuffy nose, sneezing, blocked nose, loss of smell, facial pain or sinus pressure, sore throat or hoarseness and postnasal drip. Presence of ≥3 symptoms was considered positive for CRS (25).

OSA patients were randomly allocated to receive a first period of treatment with CPAP or $CPAP_{Flex}$ (Flex setting of 3, Respironics AutoCPAP device).Randomization was stratified by site, nasal resistance (low=log[TNR]≤0.8 vs high=log[TNR]>0.8), gender and diagnostic $AHI_{4\%}$ (≤

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30 events/hour vs >30 events/hour) and performed by generating an allocation table of randomly permuted blocks of assignments to study condition (CPAP or $CPAP_{Flex}$) for each study site. Outcome of the randomized choice of treatment was provided to an unblinded individual who was not part of the analysis of the study data, and who remotely set the treatment mode via the modem. This setting (CPAP vs $CPAP_{Flex}$) was activated on the PAP device when the patient turned on the machine at home at the start of each treatment period. The unblinded individual maintained a master password protected file containing the serial number, patient ID and designation code for each treatment period and subject. PAP pressure was auto-titrated separately for each PAP mode, but then switched to constant pressure after titration. Details of PAP initiation are included in the online supplement. Subjects were crossed over to the other PAP mode after at least 4 weeks of the first PAP treatment and re-titrated. Devices were tracked by serial number. Subjects were blinded to the therapy type and no feedback was provided to subjects regarding the type of treatment. Objective adherence and efficacy of PAP treatment were monitored remotely. (See additional details in online supplement)

Outcomes

PAP usage was assessed with three metrics. The first metric and primary outcome of this study was hours of use per night (hrs/night) defined as the mean hours of nightly use over the last 2 weeks of the intervention period (see online supplement), as the first several weeks of use was felt to be influenced by adaptation and transient issues and not reflective of long term usage patterns. Secondary metrics of PAP usage were % subjects adherent (defined as $\geq$4 hours of use on $\geq$70% of nights), and % subjects rejecting the therapy (rejectors defined as average use <2

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hrs/night across all nights). Other secondary outcomes assessed were (i) the residual AHI derived from the PAP machine (ii) the influence of PAP treatment *sequence* on adherence, (iii) the change in Epworth Sleepiness Score (ESS) and Functional Outcomes of Sleep Questionnaire (FOSQ) between baseline and post-PAP, and (v) satisfaction with PAP therapy.

Statistical Methods

All statistical analyses were performed on a modified intention-to-treat basis (27) that required subjects to turn ON the PAP device in order to receive the treatment allocation. Thus, subjects who did not turn on the PAP device at home were excluded from analysis. Analysis of association between CPAP device type (CPAP or $CPAP_{Flex}$) and adherence was performed for the entire group and stratified by nasal resistance. Mean hours of PAP device use per night, adherence rates (≥4 hours use on 70% of nights) and device "rejection" rate (use<2hrs/night) were calculated as either mean ± SD, median (first quartile, Q1, third quartile, Q3), or counts and proportions, as appropriate. Correlation between nasal resistance and mean hours of use per night of each PAP mode were calculated with and without adjusting for AHI, age, gender and BMI. To account for intra-subject correlation due to cross-over design, the generalized estimating equations (GEE) models (29). were used to compare CPAP and $CPAP_{Flex}$, adjusted for randomization sequence (Period 1 CPAP followed by Period 2 $CPAP_{Flex}$, and Period 1 $CPAP_{Flex}$ followed by Period 2 CPAP). Whether the differences between CPAP and $CPAP_{Flex}$ would vary between randomization sequence were tested using treatment by randomization sequence interaction. Bootstrap method was used to derive the 95% confidence intervals (95% CIs) in PAP adherence and rejection rate comparisons (30). In addition to comparisons performed for

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all included subjects, we repeated all analyses in a subset defined as **non-rejectors** (subjects using PAP ≥2 hrs/night in either period), whom we felt were those who might have best experienced the differences between CPAP and $CPAP_{Flex}$. . Changes in ESS and FOSQ total and subscale scores from the baseline untreated condition were calculated and evaluated for each PAP treatment group and between CPAP and $CPAP_{Flex}$ using the GEE analysis, adjusting for age, gender and BMI. All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

Study Population

A CONSORT flowchart depicting this trial is presented in Figure 1. 317 subjects with OSA were randomized to receive PAP, with 155 allocated to CPAP and 162 to $CPAP_{Flex}$. 27 subjects in Period 1 and 30 subjects in Period 2 did not turn ON their PAP machine after taking it home, which is when the allocation is executed. Since they did not receive the treatment mode they were excluded from the analysis for that period.

Demographic data and baseline subject characteristics are shown in Table 1. Subjects were predominantly male, middle-aged, and obese. More than 40% had high nasal resistance and 84% had mild-moderate OSA. The average $AHI_{4\%}$ was 17/hr and the average RDI was 32/hr. There were no statistically significant differences in baseline characteristics between those assigned to the CPAP or $CPAP_{Flex}$ treatment arms in Period 1. Factors known to affect nasal resistance such as age, gender and BMI were well matched across treatment groups (31, 32)(Supplemental Tables E1)

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Correlation with Nasal Resistance

In the overall study population, (Figures 2A, 2B and 2C - CPAP (closed circles) or $CPAP_{Flex}$ (open circles), there was no correlation (r=0.098, p=NS for CPAP and r=0.056, p=NS for $CPAP_{Flex}$) between total nasal resistance (LogTNR) and hours/night of PAP use. Results were unchanged after adjusting for $AHI_{4\%}$, age, gender and BMI (data not shown). When we restricted the analysis to those subjects who were non-rejectors of PAP, i.e., who used PAP for at least 2 hours in either period, there was no correlation (r=0.16, p=0.14) for CPAP and a weak correlation (r=0.21, p=0.05) for $CPAP_{Flex}$) between nasal resistance and hours of PAP use (Figure 3), but in the opposite direction to our hypothesis: higher nasal resistance was associated with *greater* PAP use.

Primary Outcome

PAP adherence. Table 2 shows PAP usage data without stratification by nasal resistance. Overall, hours of PAP use (hours/night), excluding those who never turned on the machine in that period (mITT), averaged 1.97 hours on CPAP (95% CI= 1.68-2.26) and 1.65 hours (95% CI 1.39-1.91) on $CPAP_{Flex}$, with a statistically significant 0.31 h of *greater* use/night on CPAP (95%CI 0.03-0.6) and a greater % of subjects adherent to CPAP (17%) compared to $CPAP_{Flex}$ (11%). Similar results were found in the subgroup of non-rejectors (% subjects adherent=37% on CPAP vs 26% on $CPAP_{Flex;}$), although for this subgroup PAP use (hours/night) was not significantly different between PAP types.

When stratified by high versus low nasal resistance there was no difference in PAP hours of use per night between CPAP and $CPAP_{Flex}$ either in subjects with high or with low nasal

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resistance, for all outcomes (Table 3A). In the subset of non-rejectors (Table 3B) of PAP, for **both** CPAP and $CPAP_{Flex}$ groups, subjects with high nasal resistance showed a trend towards greater adherence (% subjects adherent) compared to those with low nasal resistance although the hours per night did not show a significant difference. Similar to all users, the subset of non-rejectors showed no preference towards CPAP or $CPAP_{Flex}$ whether they had high or low nasal resistance.

Secondary Outcomes

PAP therapy was equally effective in the two PAP modes (PAP device measured AHI <5/hr on treatment). There were no differences in the titration pressure that was identified by the PAP device during the titration period. There was no effect of treatment sequence on the difference between CPAP and $CPAP_{Flex}$ in adherence (Chi-Square 0.24, P=NS).(Table 2)

When comparing subjects with subjective symptoms for chronic rhinosinusitis (CRS) versus those without, there was no difference in adherence outcomes in subjects with congestion symptoms of chronic rhinosinusitis (CRS+) versus those without (CRS-). (Supplemental Table E2)

Overall effect of PAP on ESS, FOSQ and FOSQ subdomains, compared to the untreated baseline is shown in Table 4. There were no differences in ESS or FOSQ between the ***end of period*** values in all treated subjects or in the subgroup of non-rejectors of PAP unadjusted or adjusted (data not shown). Compared to baseline untreated measures there were minimal ***changes*** seen in these outcomes on PAP. There were no differences in these outcomes between subjects with high vs low nasal resistance (data not shown) except for a 1.4point

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reduction in ESS on $CPAP_{Flex}$ in subjects with high resistance (p value =0.006) that was not observed in those with low resistance.

No differences in satisfaction with therapy were observed between PAP modes (Supplement Table E3). Of note, subjects with high nasal resistance did not express greater difficulty exhaling on PAP therapy. (See Supplemental Table E4) However subjects with low nasal resistance reported that it was easier to inhale with $CPAP_{Flex}$ compared to CPAP, although neither group reported significant difficulty inhaling (I.e scores were low for this question).

Other Factors Influencing PAP Adherence

Supplemental Table E5 compares PAP adherence in sub-groups based on demographic, OSA severity and co-morbid conditions. CPAP use was greater in older subjects, more severe OSA and those with higher therapeutic pressure. These group differences were not observed with $CPAP_{Flex}$. When comparing PAP use within subjects (cross-over data) adherence to CPAP was greater than adherence to $CPAP_{Flex}$ in older subjects, and in subjects without anxiety and PTSD.

63% of subjects used a nasal mask or nasal prongs; 27% used an oronasal mask and no differences in mask choice were observed between subjects with high versus low resistance. We did not observe differences in adherence based on mask choice. (data not shown)

Discussion

In this study we did not see the expected correlation of PAP adherence to nasal resistance that prompted our RCT evaluating the impact of $CPAP_{Flex}$ on treatment adherence in subjects with

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OSA. While we specifically examined the effect of $CPAP_{Flex}$ in subjects stratified by nasal resistance, our data do not show better adherence to $CPAP_{Flex}$ than to CPAP, and, in fact, shows slightly better adherence overall (approximately 20 mins of use) when patients used CPAP compared to $CPAP_{Flex}$. The clinical significance of this advantage of CPAP is unclear because there were no differences in the patient-reported sleep parameters between the two PAP interventions. Our data do suggest that $CPAP_{Flex}$ should not be considered an intrinsically superior therapy for OSA. Our data also show that $CPAP_{Flex}$ should not be considered a reliable "rescue" for poor CPAP adherence without FLEX, even in those with chronic nasal symptoms and reported "difficulty exhaling" on CPAP. Our study also showed no difference in adherence between subjects with high versus low nasal resistance.

In addition to the early observational study (17) only one RCT study by Chihara et al (23) has shown a significant difference in adherence between CPAP and $CPAP_{Flex}$. This cross over trial of APAP vs APAP+ $CPAP_{Flex}$ versus APAP +$APAP_{Flex}$ showed higher PAP adherence in subjects using APAP+ $CPAP_{Flex,}$ compared to APAP, and switching PAP modes did not have a significant effect on adherence in any group. In contrast, and similar to our data, Kushida et al,(21) did not report differences in adherence to either APAP+A_{Flex} compared to APAP or CPAP. Similarly, Pepin et al. showed no difference between CPAP and $CPAP_{Flex}$ overall but reported improved adherence on $CPAP_{Flex.}$ in the subset of subjects who demonstrated low adherence on CPAP(19).

Reduction of pressure during exhalation ($CPAP_{Flex}$) was developed with the goal of alleviating the common complaint of difficulty exhaling against a fixed pressure. Our prior work (16) had suggested that subjects with high nasal resistance may experience greater discomfort

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from exhalation pressure on CPAP, which we postulated could result in lower adherence. A previous study observed lower CPAP adherence among patients with higher nasal resistance (15), and an improvement in PAP adherence following nasal surgery (14). Additionally, small nasal volume has been associated with poor PAP adherence (33, 34). However, in contrast to our *a-priori* hypothesis based on these observations, we found that high nasal resistance was not associated with low PAP adherence. The large sample size of our study makes it unlikely that this result was a chance finding. Furthermore, a secondary analysis of our data comparing subjects with CRS symptoms versus those without symptoms also shows no difference in adherence between groups, consistent with our primary finding. We speculate that since our subjects had a high prevalence of chronic rhinosinusitis, the higher nasal resistance could have been mediated by nasal mucosal edema rather than anatomical factors such as a deviated septum or interior turbinate hypertrophy that have been suggested to play a role in CPAP non-adherence (35). Nasal edema and the resultant increase in nasal resistance lead to a subjective but intermittent or reversible sensation of nasal congestion. A recent study with longer-term follow up of patients on CPAP showed a small improvement in subjective nasal stuffiness and objective obstruction with CPAP at 2 years (34) . We did not measure nasal resistance at the end of the treatment period and therefore cannot comment on whether greater PAP use was a result of improvement in nasal symptoms.

Paradoxically, and contrary to our expectation, in the subset of non-rejectors of PAP, there was a trend for subjects with higher nasal resistance to have a ***higher*** adherence to PAP. Because of post hoc nature of this analysis as well as multiple comparisons performed, this finding needs to be confirmed in future studies.

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Adherence to PAP was significantly lower in our study than in other published studies. A recent review of over 80 articles published on CPAP adherence estimated the nonadherence prevalence at 34.1%, and the mean nightly CPAP use at 4.7 hours (8). The possible reasons for the very poor adherence observed in our study compared to published literature include that our subjects were not a sleep lab referral population. Adherence may have been lower as this was not a population specifically seeking evaluation and treatment of OSA (i.e., it is closer to a screening population than a sleep clinic population). We also note that our study had a predominance of subjects with mild-moderate OSA severity, which has been associated with lower adherence than severe/symptomatic subjects in some studies. Of note, our subjects with severe OSA had higher adherence to CPAP compared to those with mild and moderate OSA. Furthermore, in our WTC Responder cohort there is a high prevalence of comorbidities such as chronic rhinosinusitis, post-traumatic stress disorder (PTSD), anxiety and depression and these may also be associated with lower PAP adherence, (36, 37). However, we did not see statistically differences in adherence between subjects with and without these conditions; because this was a secondary analysis and may not have sufficient number of subjects we do not consider this to be conclusive.

Only minimal changes in subjective outcomes of sleepiness and quality of life (ESS and FOSQ) were seen following either CPAP or $CPAP_{Flex}$ therapy, perhaps due to the poor overall adherence to any PAP therapy or due to the short follow-up period. Furthermore, subjects had an average ESS that was not elevated (mean ESS=8.1) at baseline, leaving little room for improvement. This was also true for the FOSQ, that was not reduced at baseline. (mean FOSQ=17.2)

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The strengths of this study include a large sample size with adequate power, double blind randomized study methodology with uniform PAP education, devices with heated humidification, and adequate follow-up and assessments of efficacy. In addition, nasal resistance was assessed using an objective measure that was performed in the supine position, mimicking the sleep position. The choice of nasal resistance measurement technique requires discussion as it can be performed using anterior or posterior rhinomanometry that are known not to be well correlated (38). In the present study we chose to use anterior rhinomanometry as it is non-invasive and well tolerated by subjects and correlates with subjective nasal symptoms of congestion. (38, 39)

Our results were in the WTC general responder cohort and this could raise questions about generalizability of the very poor overall PAP adherence. However, we have shown that while the WTC responders have a high prevalence of OSA (27), their risk factors (40), and their sleep disorder diagnoses are quite similar to those of the general population (41). We had a significant loss to follow-up with 30% of the subjects dropping out of Period 2 of the protocol. Analysis of Period 1 data alone (Table E6 in Supplement) showed findings similar to the cross-over data analysis with CPAP adherence higher than $CPAP_{Flex}$ but the differences are not statistically significant (possibly due to the smaller sample size).

While nasal obstruction is a common complaint is OSA, there is limited data on objective measurement of nasal resistance in OSA cohorts. The Icelandic cohort reported 35% prevalence of significant nocturnal nasal obstruction complaints. (42) Other small laboratory studies report a prevalence from 20-60% of elevated nasal resistance in OSA subjects. (43-45) Terry Young measured nasal resistance in the Wisconsin cohort but did not report its prevalence. (46)

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A limitation of our data is that we assessed adherence to therapy after only one month of therapy and did not assess longer term adherence. However, short-term adherence has been consistently shown to correlate with long-term PAP adherence, suggesting that 1-month adherence reflects long-term usage (8, 47). We chose not to use a PAP washout period between arms of the study as withdrawal of therapy for OSA was not deemed appropriate, and our primary goals were not to demonstrate the effect of CPAP itself, but rather to show the effect of $CPAP_{Flex}$ on adherence. While the implication of not using a wash-out period between the two periods is unclear we are not aware of any carry-over effect on our primary outcome measure (adherence). It is however possible that lack of a washout period could have impacted secondary outcome measures such as sleepiness, but this should have appeared as an "order effect" if significant and was not present in our data.

In conclusion, we did not find the expected relationship of high nasal resistance to poor PAP adherence. Furthermore, our RCT shows that adherence to PAP was not greater with $CPAP_{Flex}$ compared to CPAP, but rather that CPAP use exceeded $CPAP_{Flex}$ use by about 20 min. While this increase in adherence approached the 30 min considered to be potentially clinically significant (24, 48), the lack of improvement in symptoms attributed to OSA does not support the latter. In a population with significant nasal complaints and overall poor adherence to PAP, our data certainly does not support the assertion that $CPAP_{Flex}$ is superior to CPAP.

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Figure Legends:

Figure 1: Consort Diagram of RCT.

Figure 2: Scatter plot showing relationship between Total Nasal Resistance (Log TNR) and adherence to CPAP (closed circles) and $CPAP_{Flex}$ (open circles) in all subjects.(Figure 2A). Figures 2B and 2C show the same data separated by CPAP and CPAP. No relationship was observed between nasal resistance and PAP adherence.

Figure 3: Scatter plot of nasal resistance (Log TNR) and adherence in non-rejectors (i.e. after excluding rejectors) of PAP. CPAP (closed circles) and $CPAP_{FLEX}$ (open circles) Higher TNR shows a trend for greater adherence/use for CPAP (r=0.16, p=0.14) and $CPAP_{FLEX}$ (r=0.21, P=0.05).

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Table 1. Demographic data and baseline characteristics of subjects.

		Period 1 CPAP N=144	Period 1 $CPAP_{FLEX}$ N=146
		Mean ± SD	Mean ± SD
Age (Yrs)		53.4 ± 8.4	53.2 ± 7.9
Sex (%Female)		9.1	13.0
BMI (Kg/m^2)		30.9 ± 5.5	30.6 ± 5.8
Snoring (%)		88.7	92.4
AHI4% (/hr)		17.0 ±13.8	17.4 ± 15.3
RDI (/hr)		32.4 ±15.6	32.5 ± 17.3
LogTNR (n=274)		0.7 ± 0.4	0.7 ± 0.4
% High Resistance		44.1	41.1
CRS Score (n=280)		2.6 ± 2.3	2.3 ± 2.2
CRS (y/n)		50.4	38.3
ESS (n=286)		8.8 ± 5.0	8.4 ± 4.9
FOSQ (n=269)		17.3 ± 2.4	17.1 ± 3.0
Current Smoking status			
Yes (%) (n=29)		11.2	8.9
No (%) (n=260)		88.8	91.1
Alcohol			
Regular (%), n=97		36.4	31
Intermittent (%), n=148		52.4	50.4
Never (%),n=43		11.2	18.6
Sedatives (%)		23.4	21.1
Stimulants (%)		16.1	17.6
Oral steroids (%)		1.4	2.1
Nasal Steroids (%)		13.3	10.3
OAD (%)		23.8	24
Hypertension (%)		26.6	32.6
Diabetes (%)		9.8	11.8
Anxiety and Panic Disorder (%)		11.2	11.6
Depression (%)		9.1	12.3

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PTSD (%)		16.8	14.4
GERD (%)		39.9	36.3

There were no significant differences between the two groups for any of the measures. OAD: obstructive airways disease; CRS: Chronic rhinosinusitis; GERD: Gastroesophageal reflux disease; PTSD: Post Traumatic Stress Disorder; BMI: Body Mass Index; TNR: Total Nasal Resistance; $AHI_{4\%}$ Apnea+Hypopnea Index with 4% O2 desaturation for hypopnea; RDI: Respiratory Disturbance Index; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcome of Sleep Questionnaire.

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Table 2: Modified Intention To Treat analysis comparing CPAP vs $CPAP_{Flex}$ adherence in all subjects receiving exposure to the PAP intervention.

	CPAP (n=239) Period 1 n=144 Period 2 n=95		**$CPAP_{Flex}$ (n=249) Period 1 n=146 Period 2, n=103**		**Within subject difference (CPAP-$CPAP_{Flex}$)**	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Hours per night	1.97	1.68, 2.26	1.65	1.39, 1.91	**0.31**	**0.03, 0.60**
% subjects adherent	17%	12%, 22%	11%	7%, 16%	**5%**	**1%, 10%**
% rejectors (< 2hr/night use)	65%	64%, 68%	68%	64%, 68%	-3%	-3%, 2%
Residual AHI from PAP device (/hr)	2.71	2.28, 3.14	2.94	2.51, 3.37	-0.23	-0.75, 0.28
Pressure (cmH2O)	7.92	7.58, 8.25	8.09	7.77, 8.41	-0.17	-0.51, 0.16
Non-Rejectors of PAP	**CPAP (n=103)**		**$CPAP_{Flex}$ (n=102)**			
Hours per night	3.63	3.18, 4.08	3.21	2.78, 3.65	0.42	-0.13, 0.96
% subjects adherent	37%	26%, 44%	26%	18%, 34%	**10%**	**1%, 19%**
Residual AHI from PAP device (/hr)	3.83	3.37,4.28	3.40	2.96, 3.84	0.43	-0.11, 0.97
Pressure (cmH2O)	8.24	7.79, 8.68	8.36	7.96, 8.77	-0.13	-0.53, 0.28

Adherence was evaluated as hours/night, % subjects adherent (subjects who used PAP ≥4 hours for ≥70% of nights) and % rejectors (defined as average use <2hours/night). Residual apneas and hypopneas on treatment was obtained from the PAP device. Non-rejectors ≥2 hours of use per night in either period.
Bolded values are $p<0.05$

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Table 3A: CPAP vs $CPAP_{Flex}$ use in all subjects stratified by nasal resistance.

High Nasal Resistance	**CPAP N=105**		**$CPAP_{Flex}$ N=110**		**Difference (CPAP-$CPAP_{Flex}$)**	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Hours per night	2.08	1.60, 2.55	1.75	1.31,2.20	0.33	-0.10, 0.76
% subjects adherent	21%	14%, 29%	16%	9%, 23%	5%	-1%, 12%
% rejecting therapy	67%	58%, 76%	67%	58%, 76%	0%	-9%, 9%
Low Nasal Resistance		**N=126**		**N=131**		
Hours per night	1.81	1.44, 2.18	1.55	1.22, 1.88	0.26	-0.14, 0.66
% subjects adherent	14%	7%, 20%	8%	4%, 13%	**6%**	**0%, 12%**
% rejecting therapy	64%	55%, 72%	69%	61%, 77%	-5%	-16%, 5%
Difference High vs. Low nasal resistance						
Hours per night	0.27	-0.34,0.87	0.20	-0.35,0.75	0.07	-0.52, 0.65
% subjects adherent	8%	-2%, 17%	8%	0%,17%	0%	-10%, 8%
% rejecting therapy	3%	-10%, 15%	-2%	-14%,10%	5%	-8%, 19%

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Table 3B: CPAP vs $CPAP_{FLEX}$ use in non-rejectors only.

High Nasal Resistance	**CPAP N=41**		**$CPAP_{Flex}$ N=40**		**Difference (CPAP-$CPAP_{Flex}$)**	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Hours per night	4.13	3.43, 4.84	3.83	3.07,4.59	0.30	-0.60, 1.20
% subjects adherent	48%	35%, 64%	41%	25%, 55%	6%	-4%, 25%
Low Nasal Resistance		**N=49**		**N=49**		
Hours per night	3.30	2.69, 3.91	2.83	2.31, 3.36	0.47	-0.26, 1.20
% subjects adherent	32%	18%, 42%	17%	8%, 28%	15%	-1%, 25%
Difference High vs. Low nasal resistance						
Hours per night	0.83	-0.10, 1.76	1.0	0.02, 1.92	-0.16	-1.33, 1.00
% subjects adherent	**16%**	**1%, 39%**	**25%**	**5%,39%**	-9%	-20%, 17%

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Table 4: Change in Sleepiness and FOSQ variables with therapy (mean (SE))

Variable	Baseline	CPAP (end of period)	CPAP vs Baseline p-value	$CPAP_{FLEX}$ (end of period)	$CPAP_{FLEX}$ vs Baseline p-value	CPAP vs $CPAP_{FLEX}$ P-value
ESS	8. 59 (0.29)	7.99 (0.42)	0.1	7.84 (0.41)	**0.04***	0.64
FOSQ (Total)	17.21 (0.17)	17.3 (0.38)	0.9	17.45 (0.26)	0.4	0.60
FOSQ Subdomains						
Activity Level	3.3 (0.04)	3.1 (0.04)	0.1	3.3 (0.08)	0.8	0.09
Vigilance	3.3 (0.04)	3.4 (0.04)	0.2	3.4 (0.07)	0.5	0.53
Intimacy	3.3 (0.06)	3.1 (0.04)	0.4	3.3 (0.12)	1.0	0.37
General Productivity	3.5 (0.04)	3.6 (0.04	0.3	3.6 (0.07)	0.3	0.79
Social Outcome	3.5 (0.05)	3.7 (0.04)	**0.04***	3.6 (0.07))	0.3	0.31

ESS= Epworth sleepiness Scale; FOSQ- Functional outcomes of sleep questionnaire.

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Figure 1

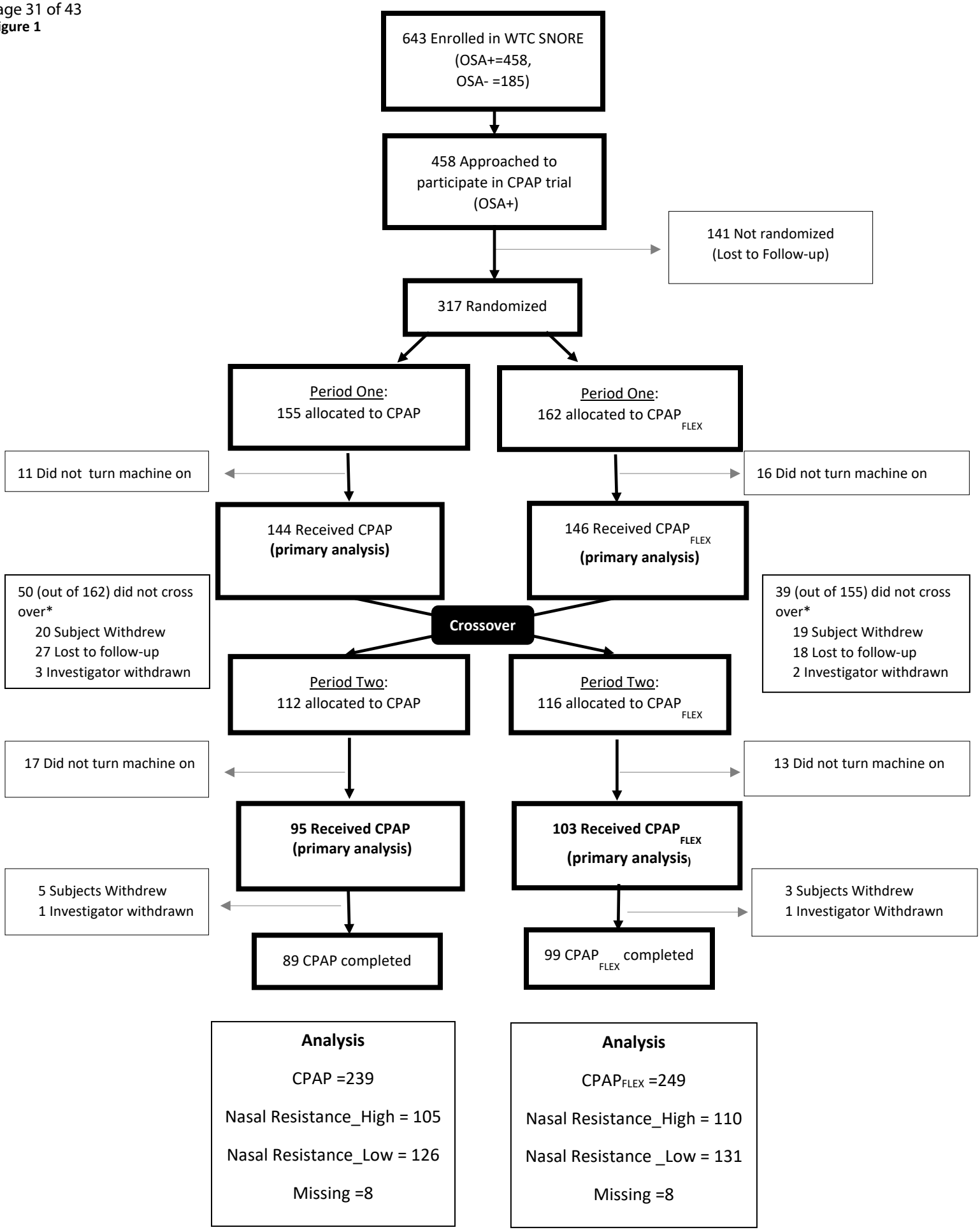

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Figure 2:

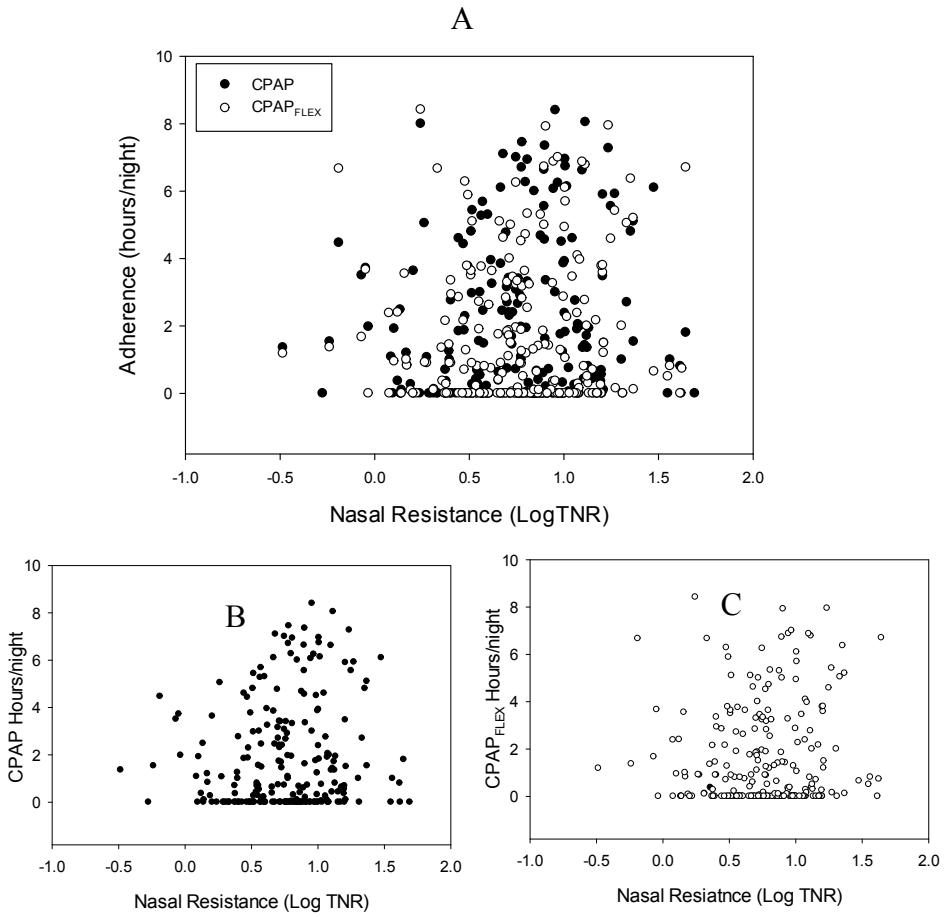

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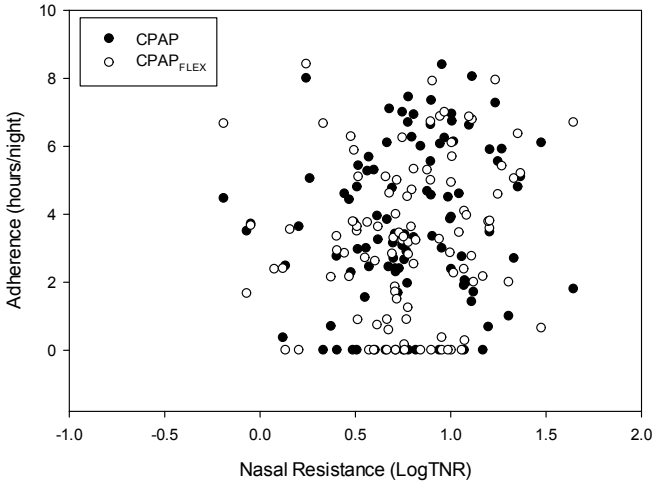
Figure 3:



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ON LINE SUPPLEMENT

PAP Adherence and Nasal Resistance: A Randomized Control Trial of $CPAP_{Flex}$ vs CPAP

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METHODS

PAP Initiation

From the ambulatory ARES studies, we identified 458 subjects with OSA. Of these subjects 141 subjects either declined to participate or were unable to be contacted. Participants who consented for the trial underwent mask fitting and desensitization and PAP education and were assigned to CPAP or $CPAP_{Flex}$ with an auto-CPAP or auto-$CPAP_{Flex}$ as a first treatment and crossed over to the other after completing the first arm of the protocol. The treatment allocation was delivered remotely via modem when the subject turned on the device in the home. Titration of the assigned therapy was at home with AutoCPAP setting of 5-15 cm H_2O pressure (Respironics AutoCPAP device) with CPAP or $CPAP_{Flex}$ over 5 days. Prescribed therapy was set at the 90%ile of autotitration pressure after this period if the subject used the machine for more than 4 hours a night on each of those nights. If fixed pressures were not achieved by the end of the first week due to insufficient use, the subject was left in the autotitration mode for the 4 week period.

During the first week, the research co-coordinator called the subject twice (day 3 and day 7) to discuss any mask or CPAP related issues. Subjects were brought in to have their mask

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switched if masks were an issue. Period 1 of the intervention began subsequent to this break-in week and lasted for 4 weeks. Treatment was switched remotely and period 2 of the intervention began subsequent to that and lasted 4 weeks. All subjects were provided heated humidification.

Trial Assessments

Adherence was monitored continuously from the CPAP machine for 1 month with first intervention, then switched to the alternate intervention and adherence monitored for another month. Data from last 2 weeks of each period were used for objective adherence comparisons between interventions. The metrics calculated were average hrs/night, % adherent (≥4 hours of use on 70% or more of nights).

At enrollment and at the end of each intervention period subjects filled out Epworth Sleepiness Scale (ESS), Functional Outcome of Sleep Questionnaire (FOSQ) and a satisfaction questionnaire. (21)

Monitoring of CPAP Efficacy and Adherence

Efficacy was evaluated by (i) reviewing residual AHI and inspiratory flow limitation at optimal pressure as recorded on the device and (ii) review of raw airflow signal. Nightly adherence at the optimal pressure was recorded on the device and also transmitted to the sleep center.

Sample Size calculation

The details of the study protocol have been previously published. (27) To first determine if high nasal resistance is associated with decreased CPAP adherence, we based our power analysis on the method of Fisher's Z test (35) for correlation coefficients. With 317 participants and setting alpha at 0.05 (two-sided), there was a 80% power to test a small (negative) correlation of -0.14. The sample size was estimated using the effect size from the Aloia trial. (49) In this study $CPAP_{Flex}$ significantly improved adherence by 1.7h per night (from 3.5±2.8h for CPAP to 4.7±2.2h for $CPAP_{Flex}$ corresponding to Cohen's d of 0.48). We assumed that the effect size of $CPAP_{Flex}$

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improvement between high vs. low nasal resistance would be 80% of the effect seen in Aloia et al., Cohen's d=0.40. To test an effect size d=0.40 with 80% power and alpha= 5% (2-sided), we needed 100 subjects each with high and low nasal resistance, based on the method of two-sample t-test with equal variance. With a total of 317 subjects, we have enough power to test this hypothesis.

To determine if the benefit of $CPAP_{Flex}$ on adherence will be greatest if it is offered at CPAP initiation rather than as a "rescue" therapy in subjects with high nasal resistance, we expected that 150 subjects will have high nasal resistance and half of them will receive $CPAP_{Flex}$ at the initiation of treatment per randomization. Using the method of two sample t-test, we expected to have 80% power (alpha=0.05, 2-sided) to test an effect size of Cohen's d= 0.46 in the improvement between $CPAP_{Flex}$ vs CPAP at initiation in subjects with high nasal resistance. After accounting for 40% CPAP/$CPAP_{Flex}$ rejection, we expected to be able to test a difference of Cohen's d of 0.60.

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RESULTS

Table E1 Demographic and baseline variables among treatment groups stratified by nasal resistance.

	Low Nasal Resistance				High Nasal Resistance			
	Period I CPAP (n=80)		Period I $CPAP_{Flex}$ (n=86)		Period I CPAP (n=64)		Period I $CPAP_{Flex}$ (n=60)	
	n	%	n	%	n	%	n	%
Gender								
Female	4	5.0	8	9.3	9	14.3	11	18.3
Male	76	95.0	78	90.7	54	85.7	49	81.7
Comorbidities								
Snoring	67	85.9	80	94.1	58	92.1	54	90.0
Diabetes	8	10.0	12	14.3	6	9.5	5	8.3
Hypertension	24	30.0	26	31.0	14	22.2	21	35.0
OAD	18	22.5	18	20.9	16	25.4	17	28.3
CRS	34	43.6	39	47.0	36	58.1	27	46.6
GERD	31	38.8	34	39.5	26	41.3	19	31.7
PTSD	11	13.8	14	16.3	13	20.6	7	11.7
Medications								
Nasal Steroids	11	13.8	8	9.3	8	12.7	7	11.7
Oral Steroids	2	2.5	1	1.2	0	0.0	2	3.3
Stimulants	10	13.2	13	15.9	12	19.7	12	20.0
Sedatives	18	23.7	12	14.6	14	23.0	18	30.0
Smoking								
Never	69	86.3	75	87.2	58	92.1	58	96.7
Current	11	13.8	11	12.8	5	7.9	2	3.3
Alcohol								
Never	10	12.5	17	20.0	6	9.5	10	16.7
Intermittent	41	51.3	42	49.4	34	54.0	31	51.7
Regular	29	36.3	26	30.6	23	36.5	19	31.7

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	Low Nasal Resistance		High Nasal Resistance	
	Period I CPAP (n=80)	**Period I CPAP $_{FLEX}$ (n=86)**	**Period I CPAP (n=64)**	**Period I CPAP $_{FLEX}$ (n=60)**
	mean ± SD	mean ± SD	mean ± SD	mean ±SD
Age	54.7 ± 9.0	52.9 ± 8.6	51.6 ± 7.2	53.7 ± 6.9
BMI	31.2 ± 5.8	30.5 ± 6.1	30.5 ± 5.0	30.6 ± 5.5
CRS Score	3.0 ± 2.2	2.4 ± 2.3	2.1 ± 2.3	2.1 ± 2.2
Log TNR	0.5 ± 0.2	0.5 ± 0.3	1.0 ± 0.2	1.1 ± 0.2
AHI	17.2 ± 13.5	17.9 ± 17.7	16.7 ± 14.2	16.7 ± 11.1
RDI	32.5 ± 16.4	32.6 ± 19.3	32.3 ± 14.7	32.4 ± 14.0
ESS	8.8 ± 4.7	9.0 ± 5.3	8.8 ± 5.3	7.5 ± 4.2
FOSQ	17.3 ± 2.3	16.9 ± 3.2	17.2 ± 2.5	17.5 ± 2.8

OAD: obstructive airways disease; CRS: Chronic rhinosinusitis; GERD: Gastroesophageal reflux disease; PTSD: Post traumatic Stress Disorder; BMI: Body Mass Index; TNR: Total Nasal Resistance; AHI: Apnea+Hypopnea Index; RDI: Respiratory Disturbance Index; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcome of Sleep Questionnaire.

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Table E2: Adherence to CPAP vs $CPAP_{Flex}$ in all subjects stratified by nasal symptoms for chronic rhinosinusitis (CRS+ vs CRS-).

CRS+	**CPAP N=106**			**$CPAP_{Flex}$ N=108**			**Difference (CPAP-$CPAP_{Flex}$)**	
	Mean	**95% CI**		**Mean**	**95% CI**		**Mean**	**95% CI**
Hours per night	1.96	1.52, 2.41		1.72	1.34, 2.11		0.24	-0.14, 0.61
% subjects adherent	15%	9%, 22%		12%	6%, 18%		3%	-2%, 8%
% rejecting therapy	66%	57%, 75%		66%	57%, 75%		1%	-9%, 10%
CRS-	**N=132**			**N=134**				
Hours per night	2.01	1.62, 2.40		1.58	1.22, 1.94		**0.43**	**0.00, 0.86**
% subjects adherent	18%	11%, 25%		11%	5%, 16%		**7%**	**1%, 14%**
% rejecting therapy	62%	54%, 71%		70%	62%, 78%		-8%	-18%, 2%
Difference CRS+ vs. CRS-								
Hours per night	-0.05	-0.64,0.55		0.14	-0.38,0.67		-0.19	-0.77, 0.38
% subjects adherent	-2%	-1%, 7%		2%	-6%, 10%		-4%	-13%, 4%
% rejecting therapy	4%	-8%, 17%		-4%	-16%, 8%		9%	-5%, 23%

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Table E3
Satisfaction with Therapy

Questionnaire	**Range (0-100)**
Q1 How well did you sleep	poor to very well
Q2 How do you like your therapy	very unlikable to very likable
Q3 Did you have trouble breathing in	none to a lot
Q4 Did you have trouble breathing out	none to a lot
Q5 Comfort with mask	Very uncomfortable to very comfortable
Q6 Benefit of therapy	No benefit-large benefit

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	CPAP n=192		**CFLEX n=202**		**Difference**		
	Mean	**StdError**	**Mean**	**StdErr**	**Mean**	**StdErr**	**p-value**
How well did you sleep	62.56	1.88	63.21	1.61	-0.65	1.89	0.73
How do you like your therapy	59.90	2.12	59.25	1.94	0.65	1.94	0.74
Did you have trouble breathing in	22.41	2.16	22.87	2.06	-0.46	2.65	0.86
Did you have trouble breathing out	22.64	2.11	20.05	2.02	2.60	2.40	0.28
Comfort with mask	52.87	2.11	54.59	1.89	-1.72	2.03	0.40
Benefit of therapy	60.50	2.38	63.44	2.13	-2.94	1.99	0.14

Sequence effect

dep	**Source**	**DF**	**ChiSq**	**p-value**	**Method**
How well did you sleep	Period*tx	1	0.01	0.9033	Score
How do you like your therapy	Period*tx	1	0.99	0.3188	Score
Did you have trouble breathing in	phase*tx	1	0	0.9899	Score
Did you have trouble breathing out	Period*tx	1	1.44	0.2301	Score
Comfort with mask	Period*tx	1	2.38	0.1232	Score
Benefit of therapy	Period*tx	1	0.09	0.7603	Score

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Table E4: Satisfaction with therapy stratified by nasal resistance.

	CPAP n=86			CFLEX n=95			Difference		
High Nasal Resistance	**Mean**	**StdErr**		**Mean**	**StdErr**		**Mean**	**StdErr**	**p-value**
How well did you sleep	64.40	2.59		61.47	2.47		2.93	2.76	0.289
How do you like your therapy	60.32	3.16		58.97	2.83		1.35	2.86	0.637
Did you have trouble breathing in	20.48	3.05		25.30	3.10		-4.82	3.44	0.162
Did you have trouble breathing out	22.68	3.18		22.60	3.06		0.08	3.23	0.981
Comfort with mask	50.69	3.04		51.34	2.78		-0.65	2.85	0.820
Benefit of therapy	61.39	3.46		63.61	2.97		-2.22	2.89	0.443
	CPAP n=95			**CFLEX n=100**					
Low Nasal Resistance	**Mean**	**StdErr**		**Mean**	**StdErr**		**Mean**	**StdErr**	**p-value**
How well did you sleep	61.93	2.74		64.40	2.25		-2.46	2.53	0.330
How do you like your therapy	60.50	2.96		59.05	2.83		1.45	2.56	0.571
Did you have trouble breathing in	26.29	3.27		17.87	2.59		**8.42**	**3.76**	**0.025**
Did you have trouble breathing out	22.75	2.98		17.48	2.83		5.28	3.67	0.151
Comfort with mask	56.93	3.01		57.35	2.65		-0.42	2.75	0.877
Benefit of therapy	60.66	3.47		64.66	3.00		-4.00	2.63	0.128
High vs. Low Nasal Resistance	**Mean**	**StdErr**	**p-value**	**Mean**	**StdErr**	**p-value**	**Mean**	**StdErr**	**p-value**
How well did you sleep	2.47	3.77	0.512	-2.92	3.34	0.382	5.39	3.75	0.150
How do you like your therapy	-0.18	4.33	0.967	-0.07	4.00	0.985	-0.11	3.84	0.978
Did you have trouble breathing in	-5.81	4.47	0.194	7.43	4.04	0.066	**-13.24**	**5.10**	**0.009**
Did you have trouble breathing out	-0.07	4.35	0.987	5.13	4.17	0.218	-5.20	4.89	0.287
Comfort with mask	-6.24	4.28	0.145	-6.01	3.84	0.117	-0.22	3.96	0.955
Benefit of therapy	0.72	4.90	0.883	-1.05	4.22	0.803	1.78	3.91	0.650

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Table E5: Comparison of adherence between groups.

		CPAP (hrs/night)					$CPAP_{Flex}$ (hours/night)					Difference (CPAP-Cflex)		
var		**Period 1**	**Period 2**	**Mean**	**StdErr**	**p-value**	**Period 1**	**Period 2**	**Mean**	**StdErr**	**p-value**	**Mean**	**StdErr**	**p-value**
Age	<50	52	30	1.6	0.2		54	35	1.4	0.2		0.2	0.2	NS
	>=50	92	60	2.2	0.2		92	64	1.8	0.2		**0.4**	**0.2**	**0.045**
	Difference			**0.6**	**0.3**	**0.05**			0.4	0.3	NS	0.2	0.3	NS
Gender	Female	13	14	2.1	0.5		19	7	1.9	0.4		0.2	0.6	NS
	Male	131	76	1.9	0.2		127	92	1.6	0.1		**0.3**	**0.1**	**0.02**
	Difference			-0.2	0.5	NS			-0.3	0.5	NS	0.1	0.6	NS
OSA	Mild	76	49	1.8	0.2		79	53	1.7	0.2		0.1	0.2	NS
severity	Moderate	46	27	1.8	0.3		40	28	1.5	0.2		0.3	0.2	NS
	Severe	21	14	2.9	0.4		25	17	1.8	0.3		1.0	0.4	0.007
	Difference	Mild -Mod		0.0	0.3	NS			-0.2	0.3	NS	0.1	0.3	NS
	Difference	Mild-Severe		1.0	0.4	0.015			0.2	0.4	NS	**0.9**	**0.4**	**0.04**
	Difference	Mod-Severe		1.1	0.5	0.017			0.3	0.4	NS	0.8	0.5	0.09
ESS	<10	86	49	1.9	0.2		89	56	1.6	0.2		0.3	0.2	NS
	>=10	56	40	2.2	0.2		56	42	1.8	0.2		0.4	0.2	NS
	Difference			0.3	0.3	NS			0.2	0.3	NS	0.1	0.3	NS
Pressure	<8	56	43	2.2	0.2		51	43	2.1	0.2		0.1	0.2	NS
cmH2O	≥8	54	24	3.1	0.3		54	23	2.7	0.2		0.5	0.3	NS
	Difference			**1.0**	**0.3**	**0.005**			0.5	0.3	NS	0.4	0.4	NS
PTSD	No	114	71	2.1	0.2		111	77	1.7	0.2		**0.4**	**0.2**	**0.02**
	Yes	22	16	1.7	0.3		28	17	1.5	0.3		0.3	0.3	NS
	Difference			-0.3	0.4	NS			-0.2	0.3	NS	-0.1	0.3	NS

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Table E6: Period 1 data only comparing CPAP and $CPAP_{Flex}$.

	CPAP N=144		$CPAP_{Flex}$ N=146		Difference (CPAP-$CPAP_{Flex}$)	
	Mean	**95%CI**	**Mean**	**95%CI**	**Mean**	**95%CI**
Hours per night	1.94	1.58, 2.31	1.75	1.41, 2.09	0.20	-0.30, 0.70
% subjects adherent	0.15	0.09, 0.21	0.12	0.06, 0.17	0.04	-0.04, 0.11
% rejectors (< 2hr/night use)	0.63	0.55,0.71	0.67	0.60, 0.75	-0.04	-0.15, 0.07
Pressure (cmH2O)	8.02	7.61, 8.44	8.37	7.97, 8.78	-0.35	-0.93, 0.23
Residual AHI from PAP device (/hr)	2.89	2.28, 3.49	3.12	2.52, 3.71	-0.23	-1.08, 0.62
Non-Rejectors of PAP	N=53		N=48			
Hours per night	4.50	4.05, 4.95	4.35	3.90, 4.80	0.15	-0.48, 0.78
% subjects adherent	0.42	0.28, 0.55	0.35	0.22, 0.49	0.06	-0.13, 0.25
Pressure (cmH2O)	8.45	7.90, 8.99	8.43	7.91, 8.95	0.02	-0.73, 0.77
Residual AHI from PAP device (/hr)	2.18	1.67, 2.69	2.35	1.73, 2.96	-0.16	-0.96, 0.63

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