### 1 **Title:**

- 2 Accuracy of Auto-Titrating CPAP to Estimate the Residual Apnea-Hypopnea Index in Patients
- 3 with Obstructive Sleep Apnea on Treatment with Auto-Titrating CPAP.

### 4 Authors:

- 5 Himanshu Desai M.D.<sup>1</sup>, Anil Patel M.D.<sup>2</sup>, Pinal Patel M.B.B.S.<sup>1</sup>, Brydon J.B. Grant M.D.<sup>1</sup> and
- 6 M. Jeffery Mador M.D.<sup>1, 3</sup>.

## 7 Institutions:

- 8 1. State University of New York at Buffalo, Buffalo, NY, USA
- 9 2. Faxton-St. Luke's Hospital, Utica, NY, USA
- 10 3. Veteran Affairs Medical Center, Buffalo, New York

# 11 **Corresponding Author:**

- 12 M. Jeffery Mador M.D.,
- 13 Division of Pulmonary, Critical Care and Sleep Medicine,
- 14 Section 111S
- 15 3495 Bailey Avenue,
- 16 Buffalo, New York 14215
- 17 Phone: 716-862-8635
- 18 Fax: 716-862-8632
- 19 Email: <u>mador@buffalo.edu</u>
- 20
- 21
- 22
- 23

#### 1 Abstract:

2 Objective:

3 Auto-titrating continuous positive airway pressure (Auto-CPAP) devices now have a smart card 4 (a pocket-sized card with embedded integrated circuits which records data from the CPAP machine such as CPAP usage, CPAP pressure, large leak, etc.) which can estimate the Apnea-5 6 Hypopnea Index (AHI) on therapy. The aim of this study was to determine the accuracy of auto-7 CPAP in estimating the residual AHI in patients with obstructive sleep apnea (OSA) who were 8 treated with auto-CPAP without a CPAP titration study. 9 Methods: 10 We studied 99 patients with OSA from 4/2005 to 5/2007 who underwent a repeat sleep study 11 using auto-CPAP. The estimated AHI from auto-CPAP was compared with the AHI from an 12 overnight polysomnogram (PSG) on auto-CPAP using Bland-Altman plot and likelihood ratio 13 analyses. A PSG AHI cutoff of 5 events per hour was used to differentiate patients optimally 14 treated with auto-CPAP from those with residual OSA on therapy. 15 Results: Bland and Altman analysis showed good agreement between auto CPAP AHI and PSG AHI. 16 17 There was no significant bias when smart card estimates of AHI at home were compared to smart 18 card estimates obtained in the sleep laboratory. An auto-CPAP cutoff for the AHI of 6 events per 19 hour was shown to be optimal for differentiating patients with and without residual OSA with a 20 sensitivity of 0.92 (95% CI: 0.76 to 0.98) and specificity of 0.90 (95% CI: 0.82 to 0.95) with a 21 positive likelihood ratio (LR) of 9.6 (95% CI: 5.1 to 21.5) and a negative likelihood ratio of 22 0.085 (95% CI: 0.02 to 0.25). Auto-CPAP AHI of 8 events per hour yielded the optimal 23 sensitivity (0.94, 95% CI: 0.73 to 0.99) and specificity (0.90, 95% CI: 0.82 to 0.95) with a

1	positive LR of 9.6 (95% CI: 5.23 to 20.31) and a negative LR of 0.065 (95%CI: 0.004 to 0.279)
2	to identify patients with a PSG $AHI \ge 10$ events per hour.
3	Conclusion:
4	Auto-CPAP estimate of AHI may be used to estimate residual AHI in patients with OSA of
5	varying severity treated with auto-CPAP.
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	

1	
2	
3	Keywords:
4	Auto-CPAP, Apnea-Hypopnea Index, Obstructive Sleep Apnea, Residual Apnea-Hypopnea
5	Index, Residual Obstructive Sleep Apnea, Smart Card
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	

1	
2	
3	Abbreviations:
4	AHI: Apnea-Hypopnea Index
5	AASM: American Academy of Sleep Medicine
6	BMI: Body Mass Index
7	CI: Confidence Interval
8	CSA: Central Sleep Apnea
9	CPAP: Continuous Positive Airway Pressure
10	CHF: Congestive Heart Failure
11	COPD: Chronic Obstructive Pulmonary Disease
12	ESS: Epworth Sleepiness Scale
13	OSA: Obstructive Sleep Apnea
14	PSG: Polysomnogram
15	RDI: Respiratory Disturbance Index
16	SD: Standard Deviation
17	

1

2

### 3 **INTRODUCTION**

4 Obstructive sleep apnea syndrome (OSA) is highly prevalent in middle age populations 5 and can interfere with quality of life and increase morbidity and mortality [1, 2]. Continuous 6 positive airway pressure (CPAP) is a standard, safe, and efficacious treatment for patients with 7 OSA [3]. Conventionally, the pressure applied during long term treatment is determined 8 manually by a technician during attended polysomnographic recording. This allows adjusting 9 pressures to find a setting that essentially eliminates apneas and hypopneas in all sleep stages and 10 body positions. In-lab CPAP titration also allows direct observation by trained technologists to 11 guide pressure selection, to adjust mask fit, to eliminate leak, and to help the patient adapt to the 12 initial CPAP experience [4]. However, there are some potential limitations associated with 13 polysomnogram (PSG)-directed CPAP determinations like the cost and inconvenience of repeat PSG, the potential bias of in-laboratory versus in-home environment, and the potential to 14 15 prescribe pressures that are not optimal due to results based on one night of study [5]. At home 16 auto-CPAP titration has been introduced as a practical strategy that can reduce the time to 17 effective treatment and reduce costs [6, 7]. The American Academy of Sleep Medicine 18 (AASM) has issued practice parameters for the use of auto-CPAP devices for treating patients 19 with OSA and have stated that auto-CPAP devices may be initiated and used in the self-adjusting 20 mode for unattended treatment of patients with moderate to severe OSA without significant co-21 morbidities (congestive heart failure, chronic obstructive pulmonary disease, central sleep apnea 22 syndromes or hypoventilation syndromes). This is an optional recommendation which implies 23 inconclusive or conflicting evidence or conflicting expert opinion [5]. The document also states

that certain auto-CPAP devices may be used in an unattended way to determine a fixed CPAP
treatment pressure for patients with moderate to severe OSA without significant co-morbidities
(optional recommendation).

4 AASM also recommended that patients being treated with auto-CPAP must have close 5 clinical follow up to determine treatment effectiveness and safety. A reevaluation or a standard 6 attended CPAP titration should be performed if symptoms do not resolve or if the auto-CPAP 7 treatment otherwise appears to lack efficacy [5]. Approximately two thirds of newly diagnosed 8 patients with OSA at our institution (Veterans Affairs Medical Center at Buffalo) are being 9 started on auto-CPAP treatment to avoid in-lab CPAP titration studies and to improve overall 10 access to sleep lab services. One potential way to determine efficacy of treatment objectively at 11 home is to follow the estimated residual AHI from the smart card which is a part of newer 12 generation auto-CPAP devices. A smart card is a pocket-sized card with embedded integrated 13 circuits which records data from the CPAP machine such as CPAP usage, CPAP pressure, large leak, etc. and can estimate the Apnea-Hypopnea Index (AHI) on therapy using machine specific 14 15 event detection algorithms. Sparse data exist to support the finding that the residual AHI 16 obtained from the auto-CPAP devices is a reliable marker of residual OSA [8].

17 The aim of our study was to determine the accuracy of auto-CPAP in estimating the 18 residual AHI in patients with OSA who are being treated with auto-CPAP without a CPAP 19 titration study.

20 PATIENTS AND METHODS

We analyzed data from 99 patients with OSA seen at Veterans Affairs (VA) Medical Center at Buffalo who were being treated with auto-CPAP and who returned for an attended inlab overnight sleep study using auto-CPAP from April, 2005 to May, 2007. All patients had

1 obstructive sleep apnea based on an in-lab attended diagnostic PSG. We excluded patients with 2 central sleep apnea (CSA) or combined sleep apnea with predominantly OSA but a central apnea 3 index of > 5 events per hour. The decision to treat the patient with auto-CPAP was made by the 4 treating physician. Patients without a history of snoring were not excluded. Epworth sleepiness scale (ESS) and body mass index (BMI) were recorded at the time of diagnostic PSG for each 5 6 patient. We also collected information about CPAP compliance, average AHI for the week prior 7 to the study night, mean auto-CPAP pressure, and average leak per minute from the auto-CPAP 8 smart card.

9

#### 10 Polysomnography

11 Out of the 99 patients, 92 diagnostic PSGs were performed at the VA Medical Center at 12 Buffalo and 7 studies were done at different sleep labs with a scanned report in the patient's 13 electronic medical record. All PSGs done at the VA Medical Center were scored manually by 14 the same experienced, certified sleep technician and were reviewed and verified by one of two 15 certified sleep physicians (MJM or BJG). All patients underwent a second attended standard 16 nocturnal polysomnography using the auto-CPAP device in the sleep laboratory at the VA 17 medical center at Buffalo. The Auto CPAP device used by all patients was the Remstar Auto 18 with software version Encore Pro 1.6 (Respironics, Murrysville, PA). All PSG's were done 19 using the same polysomnography system (Sandman; Nellcor Puritan 20 Bennett:Ottawa,Ontario,Canada). The auto-CPAP device was used from lights off to lights on 21 with the smart card in place and the estimated AHI from the smart card was obtained without the 22 knowledge of the polysomnography scorer until after the manual scoring of the PSG had been 23 completed. Appear was defined as the absence of airflow for at least 10 seconds. If respiratory

1 effort was present during this apnea episode, it was defined as an obstructive apnea and when 2 respiratory effort was absent, it was termed a central apnea. Hypopnea was defined as a 3 reduction in airflow lasting at least 10 seconds and associated with either a 4 percent drop in 4 arterial oxyhemoglobin saturation or an electroencephalogram arousal. An arousal was defined according to the criteria proposed by the Atlas Task Force [9]. The severity of sleep apnea on 5 diagnostic PSG was classified as follows: mild, AHI > 5 to < 15 events per hour; moderate, AHI 6 7 >15 to < 30 events per hour; and severe, AHI > 30 events per hour. Residual OSA was defined as an AHI > 5 events per hour on PSG while using auto-CPAP. The estimated AHI from the smart 8 9 card was compared with the AHI from the overnight PSG. The average estimated AHI from the 10 week prior to the study from the smart card was also compared with the AHI from overnight 11 PSG and with the auto-CPAP AHI from the study night.

### 12 Statistical Analysis

Numeric variables are presented as arithmetic means  $\pm$  SD or medians (25<sup>th</sup>, 75<sup>th</sup>) 13 14 percentiles) when the data were not normally distributed. Statistical significance was considered 15 to be present when p < 0.05. The PSG from the study night was considered the gold standard for identifying and quantifying apneas and hypopneas during sleep. The accuracy of the auto-CPAP 16 17 smart card in detecting residual AHI was based on comparisons of the auto-CPAP AHI and the 18 PSG AHI which was evaluated by Spearman's coefficient of rank correlation (due to non normal 19 distribution of the data), agreement using the method of Bland and Altman [10] (MedCalc® 20 Statistical Software version 9.3.8), and by constructing receiver-operator characteristic (ROC) 21 curves [11] to determine optimal cutoff values for determining positive and negative likelihood 22 ratios. We log transformed the data to improve the scatter of the differences as the AHI 23 increased [10]. To avoid zero value problems with log transformation to base 10, we added 0.1 to

the AHI before log transformation (log 10[AHI+0.1]). The average estimated AHI from the week 1 2 prior to the study night from the smart card was also compared with PSG AHI and auto-CPAP AHI from the study night using Spearman's coefficient of rank correlation and Bland-Altman 3 4 analysis. The area under the receiver operating curve was estimated by the c index.[11]. We also analyzed the ability of auto-CPAP AHI to identify patients with residual OSA as likelihood 5 6 ratios (NCSS 2007 statistical software). Patients with and without residual OSA on auto-CPAP 7 were compared with t-test: two sample assuming unequal variances using Microsoft Office Excel 8 2003[12]. 9 The study protocol was approved by the institutional review board of the Western New

York Veteran Affairs Healthcare System, Buffalo, New York.

11

#### 12 **RESULTS**

13 We analyzed data from 99 patients. Patient characteristics are shown in Table 1. The mean age of patients was 56.7 years (range, 25-83) and the mean body mass index (BMI) was 14 15 35.0 (range, 22.4-52). Data for AHI and Epworth sleepiness scale (ESS) were available in 92/99 (93%) patients at the time of initial diagnostic PSG. 20 (22%) (19 male, 1 female) patients had 16 17 mild, 30 (33%) (29 male, 1 female) had moderate and 42 (45%) (41 male and 1 female) had 18 severe OSA as per diagnostic PSG. The mean ESS was 13.4±5.2 and median AHI was 26.3 19 (16.0, 63.2) events per hour at the time of diagnosis. Sixteen (16%) patients had COPD and five 20 (5%) patients had CHF. None of the patients had obesity hypoventilation syndrome. 21 Estimated AHI from the auto-CPAP smart card and PSG were obtained and analyzed for 22 all 99 patients. Spearman's coefficient of rank correlation was 0.74 (p<0.0001, 95% CI: 0.64 to 23 0.82) for the auto-CPAP AHI and PSG AHI (Figure 1). All residual apneas and hypopneas were

1 obstructive in nature on PSG study. A Bland-Altman plot of log values of auto-CPAP AHI and 2 PSG AHI is shown in Figure 2a. The scatter of AHI differences was non random. The smart 3 card estimate of AHI overestimated PSG AHI at low values of AHI and tended to underestimate 4 PSG AHI at higher AHI levels. A linear regression of the Bland Altman plot revealed an r-value of 0.69 (p<0.0001) as shown in figure 2b. We constructed ROC curves to assess the sensitivity 5 6 and specificity of different values of auto-CPAP AHI to identify patients with residual OSA, 7 defined as a PSG AHI  $\geq$  5 events per hour on auto-CPAP. The area under the ROC curve as 8 estimated by the c index was 0.958, 95% CI 0.920 to 0.997. An auto-CPAP AHI of 6 events per 9 hour yielded the optimal sensitivity (0.92, 95% CI: 0.76 to 0.98) and specificity (0.90, 95% CI: 10 0.82 to 0.95) with a positive likelihood ratio (LR) of 9.6 (95% CI: 5.1 to 21.5) and a negative 11 likelihood ratio of 0.085 (95% CI: 0.02 to 0.25) (Table 2). An auto-CPAP AHI of 8 events per 12 hour yielded the optimal sensitivity (0.94, 95% CI: 0.73 to 0.99) and specificity (0.90, 95% CI: 13 0.82 to 0.95) with a positive LR of 9.6 (95% CI: 5.23 to 20.31) and a negative LR of 0.065 (95%CI: 0.004 to 0.279) to identify patients with PSG AHI  $\geq$  10 events per hour on auto-CPAP 14 15 (Table 2). Auto-CPAP failed to identify one patient with residual OSA (auto-CPAP AHI 4, PSG AHI 5.1). 16

We also had data of average estimated AHI for one week prior to the study night from the auto-CPAP smart card on 88 (89%) patients. We compared average smart card AHI to PSG AHI and to auto-CPAP AHI from the study night. Spearman's coefficients of rank correlation were 0.67 (p<0.0001, 95% CI: 0.54 to 0.77) for average AHI and PSG AHI, and 0.86 (p<0.0001, 95% CI: 0.79 to 0.90) for average AHI and auto-CPAP AHI during the study night. Bland-Altman plots of log values of average AHI comparing with PSG AHI, and average AHI comparing with auto-CPAP AHI during the study night are shown in Figure 3a and 3b respectively. The

1 comparison of the average AHI and PSG AHI also revealed a non random scatter of AHI 2 differences. The average AHI overestimated PSG AHI at low values of AHI and tended to 3 underestimate PSG AHI at higher AHI values. A linear regression of the Bland-Altman plot 4 revealed an r-value of 0.64 (p<0.0001). Comparing the average AHI and study night AHI from 5 the smart card, there was no significant bias and the scatter of the differences was random. 6 Table 3 shows mean AHI at the time of diagnosis and on auto-CPAP treatment for 7 patients with mild, moderate and severe OSA. 26 (26%) of 99 patients had residual OSA (PSG 8 AHI > 5 events per hour) on auto-CPAP treatment. We compared age, BMI, diagnostic AHI data 9 and auto- CPAP smart card compliance data from patients with residual OSA with those from 10 without residual OSA using t-test: two sample assuming unequal variances (Table 4). Patients 11 without residual OSA were younger (p=0.02) and had lower BMI (p=0.04) compared to patients 12 with residual OSA. Patients without residual OSA tended to have better compliance (% of days 13 with device use, % of days with >4 hours use) than those with residual OSA, which did not quite 14 reach statistical significance. Average leak per minute was higher in patients with residual OSA 15 compared to those without residual OSA (p=0.04). Seventeen patients (17%) had a residual AHI 16 of  $\geq 10$  events per hour on auto-CPAP treatment.

#### 17 **DISCUSSION**

In this study, we assessed the accuracy of auto-CPAP to estimate residual AHI in patients with OSA being treated with auto-CPAP without a CPAP titration study. This is the first reasonably large study (n=99) conducted to address this question to the best of our knowledge. Woodson et al [8] (n=24 of which only 8 patients had simultaneous attended PSG) compared auto-CPAP AHI with PSG AHI in patients undergoing unattended home auto-CPAP titration and found that auto CPAP overestimated AHI by an average of 1.4 events per hour when compared

1 to PSG AHI. The results of our study showed that there is reasonable clinical agreement between 2 auto-CPAP AHI and PSG AHI and auto CPAP cutoffs can be determined which predict with 3 accuracy which patients have residual disease on therapy as defined by either a PSG AHI of > 54 events per hour or  $\geq$  10 events per hour. Bland and Altman plots demonstrate that the difference between auto-CPAP AHI and PSG AHI was not uniform with auto-CPAP overestimating the 5 AHI at lower values of AHI and underestimating the AHI at higher values of AHI. There was a 6 7 marked underestimation of AHI by auto-CPAP when compared to PSG in two patients. One 8 patient had an auto-CPAP AHI of 9 events per hour and PSG AHI of 41.1 events per hour, the 9 other had auto-CPAP and PSG AHIs of 29 events per hour and 52.7 events per hour, respectively. The first patient had an unsatisfactory PSG study as he slept poorly during the study 10 night. Auto-CPAP identified a similar number of events during the night but since it cannot 11 12 differentiate between sleep and wakefulness, it assumed a longer sleep time than was actually present, leading to the discrepancy in AHI. In the other patient, no factors were identified that 13 14 would explain why the auto-CPAP underestimated the actual AHI. Our study showed that an 15 auto-CPAP AHI of 6 identified patients with residual OSA (AHI  $\geq$  5 events per hour) with strong positive and negative likelihood ratios [13]. This suggests that the auto-CPAP device can be used 16 to assess the adequacy of therapy with a reasonable level of accuracy. 17

Our study also showed good clinical agreement between the average smart card AHI from the week prior to the study night and PSG AHI as well as auto-CPAP AHI from the study night. The average AHI from the prior week gives perhaps a better estimate of effectiveness of treatment as it measures the AHI at home and over a period of seven days instead of a one night value obtained in lab. It also replicates the way clinicians will use this modality in the real world. Authors would like to emphasize that in-lab PSG titration has some advantages over home strategies like pressure selection under direct observation by a trained technician, adjusting mask
 fit, eliminating leak and educating patients; and confirming effectiveness during supine or REM
 sleep.

Though no widely-accepted definition of residual OSA exists, we used the traditional 4 5 cutoff point of  $AHI \ge 5$  events per hour on PSG [2]. The positive airway pressure titration task 6 force of the AASM defines an optimal CPAP titration as an RDI < 5 events per hour for at least 7 15 minutes which should include supine REM sleep [14]. In this study, we found that almost one 8 in four patients (26%) on auto-CPAP treatment had residual OSA. Although the prevalence of 9 residual OSA in our study may seem high, our findings are consistent with prior investigations. 10 Torre-Bouscoulet et al [15] reported a prevalence of 29% in 279 patients with residual OSA 11 defined as a residual RDI >10 events per hour using an auto-CPAP device. Stammitz et al [16] 12 also reported a residual OSA prevalence of 17% in a small number of patients, but he defined 13 residual OSA as RDI > 5 events per hour from the auto-CPAP device. Baltzan et al [17] reported a prevalence of 17% using a cut off of  $AHI \ge 10$  events per hour on PSG in patients treated with 14 15 fixed pressure CPAP after a CPAP titration study and who had persistent resolution of symptoms. Another study showed that almost one in five patients with good CPAP compliance 16 had residual moderate to severe OSA on their prescribed setting [18]. The long term effects of 17 18 residual OSA are not fully understood. One study showed that subtherapeutic CPAP did not 19 result in a decrease in mean blood pressure [19]. Peker et al [20] reported that incomplete 20 treatment was not found to be associated with a reduction in the incidence of cardiovascular 21 complications. This high prevalence of residual OSA in patients treated with auto-CPAP or 22 fixed-pressure CPAP after a CPAP titration study stresses the importance of follow-up to 23 determine treatment effectiveness. Clinical follow up alone may not be enough as prevalence of

residual OSA was found to be high even in patients without symptoms [17, 18]. Thus, institution
of auto CPAP with no further evaluation if symptoms improve will not be sufficient if the
therapeutic goal is to avoid residual OSA. However, evaluation of residual AHI by smart card
estimate may be a satisfactory method to avoid residual OSA in treated patients.

5 In this study, we have not excluded patients with OSA who also had other co morbidities 6 like CHF, COPD or hypoventilation syndromes. The AASM does not recommend use of auto 7 CPAP in patients with such co morbidities [5]. None of our patients in this study had 8 hypoventilation syndromes likely because sleep physicians at our institution did not start 9 autoCPAP in such patients. Sixteen (16%) patients had COPD and 5 (5%) patients had CHF. 10 Since patients with central events and/or Cheynes-Stokes breathing during the diagnostic study 11 were excluded from the study, it is perhaps not surprising that smart card estimates of AHI in the 12 small number of patients with CHF were reasonably accurate. It is interesting that smart card 13 estimates of AHI were no less accurate in patients with COPD than in the rest of the study group. 14 However, the small number of such patients precludes definitive conclusions and further study is 15 required in this patient population.

16 A limitation of our study is that only one manufacturer's auto-CPAP device was used for the study. Different auto CPAP devices use different algorithms to detect AHI and they may 17 18 have different detection rates [21,22]. The CPAP device employed in this study adjusts pressure 19 based on analysis of flow (looking for flow limitation) and presence of snoring [22]. Some 20 devices also measure upper airway resistance using the forced oscillation technique [21,22]. 21 Thus, the results of this study may only be applicable to the auto-CPAP device employed in this 22 study. Another limitation is that the smart card only provides an estimate of the AHI on therapy. 23 There is no assessment of oxygen saturation levels. If hypoxemia was prominent in the

diagnostic study, further assessment may be required to ensure that hypoxemia has been resolved
 with therapy.

3	In conclusion, auto-CPAP AHI may be used to estimate residual AHI in patients with
4	varying severity of OSA being treated with auto-CPAP without a CPAP titration study provided
5	its limitations in accuracy are understood. Average auto-CPAP AHI from prior week's use at
6	home was not less accurate than the estimate of AHI obtained from auto-CPAP during the
7	overnight sleep study. Based on the likelihood ratios, auto CPAP yielded a large increase in the
8	probability of residual OSA (PSG AHI $\geq$ 5 events per hour) when the auto CPAP AHI was $\geq$ 6
9	events per hour and a large reduction in the probability of residual OSA when the auto CPAP
10	AHI was < 6 events per hour [13]. Thus, auto-CPAP AHI can be used to assess the adequacy of
11	therapy in patients with OSA with reasonable level of accuracy.
12	
13	
14	
15	
16	
17	
18	ACKNOWLEDGEMENTS
19	Funding: None
20	
21	Work was performed at: Western New York Veteran Affairs Healthcare System, Buffalo, New
22	York
23	

1	Himanshu Desai, M.D., has no financial or personal conflict of interest in presenting this
2	manuscript.
3	Anil Patel, M.D., has no financial or personal conflict of interest in presenting this manuscript
4	Pinal Patel, M.B.B.S., has no financial or personal conflict of interest in presenting this
5	manuscript
6	Brydon J. B. Grant, M.D., has no financial or personal conflict of interest in presenting this
7	manuscript
8	M Jeffrey Mador, M.D., has no financial or personal conflict of interest in presenting this
9	manuscript
10	
11	
12	
13	
14	
15	
16	
17	
18	References
19 20	1. Young, T., et al., <i>Sleep disordered breathing and mortality: eighteen-year follow-</i>
20	<ol> <li>Young, T., et al., <i>The occurrence of sleep-disordered breathing among middle-</i></li> <li>a static static black and the static static</li></ol>
22 23 24	<ol> <li>aged adults. N Engl J Med, 1993. 328(17): p. 1230-5.</li> <li>Kushida, C.A., et al., Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related.</li> </ol>
25	breathing disorders. Sleep, 2006. <b>29</b> (3): p. 375-80.
26 27 28	<ul> <li>LITINER, WI.R., et al., Practice parameters for clinical use of the multiple sleep latency test and the maintenance of wakefulness test. Sleep, 2005. 28(1): p. 113-21.</li> </ul>

1 5. Morgenthaler, T.I., et al., Practice parameters for the use of autotitrating 2 continuous positive airway pressure devices for titrating pressures and treating 3 adult patients with obstructive sleep apnea syndrome: an update for 2007. An 4 American Academy of Sleep Medicine report. Sleep, 2008. 31(1): p. 141-7. 5 Cross, M.D., et al., Comparison of CPAP titration at home or the sleep laboratory 6. 6 in the sleep apnea hypopnea syndrome. Sleep, 2006. 29(11): p. 1451-5. 7 7. Masa, J.F., et al., Alternative methods of titrating continuous positive airway 8 pressure: a large multicenter study. Am J Respir Crit Care Med, 2004. 170(11): p. 9 1218-24. 10 Woodson, B.T., et al., Nonattended home automated continuous positive airway 8. 11 pressure titration: comparison with polysomnography. Otolaryngol Head Neck 12 Surg, 2003. **128**(3): p. 353-7. 13 9. EEG arousals: scoring rules and examples: a preliminary report from the Sleep 14 Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep, 15 1992. 15(2): p. 173-84. 16 10. Bland, J.M. and D.G. Altman, Statistical methods for assessing agreement 17 between two methods of clinical measurement. Lancet, 1986. 1(8476): p. 307-10. 18 11. Hanley, J.A. and B.J. McNeil, The meaning and use of the area under a receiver 19 operating characteristic (ROC) curve. Radiology, 1982. 143(1): p. 29-36. 20 Ruxton, G.D., *The unequal variance t-test is an underused* 12. 21 alternative to Student's t-test and the 22 Mann-Whitney U test. Behavioral Ecology, 2006: p. 688-690. 23 Katz, D., Odds and Probabilities: Bayes Theorem and Likelihood Ratios, in Clinical 13. 24 Epidemiology and Evidence-based Medicine: A Primer for the Clinician. 2001, 25 SAGE. p. 57-62. 26 14. Kushida, C.A., et al., Clinical guidelines for the manual titration of positive airway 27 pressure in patients with obstructive sleep apnea. J Clin Sleep Med, 2008. 4(2): p. 28 157-71. 29 15. Torre-Bouscoulet, L., et al., Autoadjusting positive pressure trial in adults with sleep 30 apnea assessed by a simplified diagnostic approach. J Clin Sleep Med, 2008. 31 **4**(4): p. 341-7. 32 16. Stammnitz, A., et al., Automatic CPAP titration with different self-setting devices in 33 patients with obstructive sleep apnoea. Eur Respir J, 2004. 24(2): p. 273-8. 34 17. Baltzan, M.A., et al., Prevalence of persistent sleep apnea in patients treated 35 with continuous positive airway pressure. Sleep, 2006. 29(4): p. 557-63. 36 18. Pittman, S.D., et al., Follow-up assessment of CPAP efficacy in patients with 37 obstructive sleep apnea using an ambulatory device based on peripheral 38 arterial tonometry. Sleep Breath, 2006. 10(3): p. 123-31. 39 19. Becker, H.F., et al., Effect of nasal continuous positive airway pressure treatment 40 on blood pressure in patients with obstructive sleep apnea. Circulation, 2003. 41 **107**(1): p. 68-73. 42 Peker, Y., et al., Increased incidence of cardiovascular disease in middle-aged 20. 43 men with obstructive sleep apnea: a 7-year follow-up. Am J Respir Crit Care 44 Med, 2002. 166(2): p. 159-65. 45 Series, F., et al. Reliability of home CPAP tiration with dfferent automatic CPAP 21. 46 devices. Respiratory Research. 2008. July 24;9:56.

1 2 3 4 5	22.	Rigau J. et al. <i>Bench model to simulate upper airwauy obstruction for analyzing automatic continuous positve airway pressure devices.</i> Chest. 2006. 130: p. 350-361.
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28		
29 30		
31		
32		
33		
34 25	<b>T</b> 11	
35	Table	1. Characteristics of the Study Population

	Mild	Moderate	Severe	Total
Number of Patients*	20	30	42	99
Male	19	29	41	96
Female	1	1	1	3
Age at Diagnostic PSG	$54.4 \pm 11.4$	$56.3 \pm 13.9$	57.4 ± 9.7	$56.7 \pm 11.3$

BMI at Diagnostic PSG	33.0 ± 5.1	33.1 ± 5.4	$36.8 \pm 6.7$	$35.0 \pm 6.3$
ESS at Diagnostic PSG	$13.2 \pm 4.9$	$13.0 \pm 5.4$	$13.8 \pm 5.2$	13.4±5.2†
AHI at Diagnosis	$11.0 \pm 2.5$	$20.3 \pm 4.3$	66.1 ± 25.2	26.3 (16.0, 63.2)
Hypertension	13 (65%)	24 (80%)	32 (76%)	74 (75%)
Diabetes Mellitus	6 (30%)	13 (43%)	17 (40%)	40 (40%)
CAD	5 (25%)	6 (20%)	12 (29%)	24 (24%)
COPD	3 (15%)	4 (13%)	8 (19%)	16 (16%)
Hypothyroidism	2 (10%)	1 (3%)	5 (12%)	10 (10%)
Obesity	9 (45%)	9 (30%)	26 (62%)	45 (45%)
CHF	0 (0%)	1 (3%)	4 (10%)	5 (5%)

2 PSG (Polysomnogram), BMI (Body Mass Index), ESS (Epworth Sleepiness Scale), CAD (Coronary Artery

3 Disease), COPD (Chronic Obstructive Pulmonary Disease), CHF (Congestive Heart Failure)

4 Age, BMI and ESS passed normality test and are presented as means  $\pm$  1SD. AHI for mild, moderate and severe

5 OSA passed normality test, but total AHI did not and hence presented as median with 25<sup>th</sup> and 75<sup>th</sup> percentiles.

6 † Missing data of ESS in 7 patients, \* the AHI of patients with outside diagnostic studies not included in Table..

- 7
- ~
- 8

9

- 10
- 11
- 12
- 13

## 14 Table 2.Sensitivity, Specificity, and Likelihood ratios

PSG AHI	APAP AHI	Sens	Spec	+ LR	Lower CI	Upper CI	- LR	Lower CI	Upper CI
5	6	0.92	0.90	9.6	5.1	21.5	0.085	0.02	0.25
10	8	0.94	0.90	9.6	5.23	20.31	0.065	0.004	0.279

1	APAP (auto-CPAP), Sens (sensitivity), Spec (specificity), + LR (positive likelihood ratio), - LR (negative likelihood
2	ratio), Lower CI (lower 95% confidence interval), Upper CI (upper 95% confidence interval).
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	

# 21 Table 3.AHI at Diagnosis and on Auto-CPAP Treatment

	Mild	Moderate	Severe	Total*
AHI at Diagnosis	11.0±2.5	21.0±4.3	66.0±25.2	26.3(16.0, 63.2)

	AHI on auto-CPAP	5.9±6.1	6.4±6.7	7.3±6.9	4.1(3.0, 8.5)
	from smart card	25-20	4 8+10 2	6 64 10 2	1 6(0 2 6 1)
	from PSG	2.3±3.9	4.8±10.3	0.0±10.3	1.0(0.3, 0.1)
1	Presented as mean $\pm$ SD for mild	d, moderate and se	vere; median (25 <sup>th</sup> , 7	<sup>75<sup>th</sup> percentile) for tota</sup>	l
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19	Table 4. Characteristics of	f Patients With	n and Without R	esidual OSA on A	Auto-CPAP

	Patients with residual	Patients without residual OSA.	t Critical two-tail	P value
	OSA, AHI ≥	AHI <5 on auto-		
	5 on auto-	CPAP (n=73,		
	CPAP (n=26, 269/)	74%)		
<b>A</b> = -	<b>2070</b> )	55 22 + 12 02	2.00	0.02
Age	58.92±12.13	55.32±12.03	2.00	0.02
BMI	37±6.6	34±6.1	2.02	0.04
AHI at Diagnosis	38.67±24.56	37.6±31.36	2.01	0.29
PLMI at Diagnosis	17.44±27.03	20.56±31.17	2.01	0.52
% of Days with Device	73.63±29.29	83.73±24.2	2.04	0.07
Use				
Average use for days	298.83±129.0	384.45±309.49	1.99	0.08
used in Min.	9			
Average Leak (	38.06±55.1	16.47±31.82	2.06	0.04
milliliters per Minute)				
Mean Auto CPAP	8.34±2.32	7.94±2.14	2.09	0.56
pressure from prior				
week (cm H2O)				
% of Days with >4 Hrs.	49.91±36.32	64.79±31.15	2.04	0.06
Use				

<sup>1</sup> Characteristics Presented as means ± SD. AHI: Apnea-Hypopnea Index, BMI: Body Mass Index, PSG:

2 Polysomnogram, PLMI: Periodic Leg Movement Index



# 2 Figure 1.Scatter plot of PSG AHI and auto-CPAP AHI



4 Spearman's coefficient of rank correlation is 0.74 (p<0.0001, 95% CI 0.64 to 0.82) for PSG AHI and auto-CPAP

5 AHI.

#### Figure 2a.Bland-Altman plot of auto-CPAP AHI and PSG AHI (Logarithmic



#### transformation)

Log 10(AHI+0.1) values used. The scatter of the differences was non random.



Log 10(AHI+0.1) values used. r=0.69 (p<0.0001)

# 1 Figure 3a.Bland-Altman plot of average smart card AHI and PSG AHI (Logarithmic



**transformation**)

Log 10(AHI+0.1) values used. The scatter of the differences was non random The difference between auto-CPAP AHI and PSG AHI was significantly correlated with the average of auto-CPAP AHI and PSG AHI (r=0.64, p<0.0001)

# 1 Figure 3b.Bland-Altman plot of average smart card AHI and auto-CPAP AHI



2 (Logarithmic transformation)

Log 10(AHI+0.1) values used. Mean difference (bias) of 0.2 (95% CI: 0.17 to 0.25). The scatter of the differences was random (r=0.15, p=0.15)