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6 **Title: Comparison of empirical CPAP treatment versus initial portable**  
7 **sleep monitoring followed by CPAP treatment for patients with**  
8 **suspected Obstructive Sleep Apnea.**

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16 **Short title**

17 Alternative algorithms in managing OSA

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14 interpretation, and drafting of manuscript.

15 Ms Wing Chi Chan and Mr Tat On Chan were the registered polysomnographic  
16 technologists.

17 Dr Jenny Ngai, Dr Alvin Tung, Dr Susanna Ng and Dr Kah Lin Choo were co-  
18 investigators helping with patient recruitment.

19 Prof David S Hui was responsible for data interpretation and writing of final manuscript.

20

1 **ABSTRACT**

2

3 **Background**

4 Polysomnography (PSG) is labor-intensive for diagnosing obstructive sleep apnea (OSA).

5 We compared two algorithms for initiating continuous positive airway pressure (CPAP)

6 treatment for patients with suspected OSA.

7 **Methods**

8 Symptomatic OSA patients were randomized into either algorithm I or II. Algorithm I

9 consisted of an empirical CPAP trial whereas algorithm II utilized an Apnea Risk

10 Evaluation System (ARES), a wireless device applied on the forehead, for establishing a

11 diagnosis before a CPAP trial for 3 weeks. Primary outcome was success of CPAP trial,

12 defined as CPAP usage > 4 hours/night and willingness to continue CPAP. Subjective

13 usefulness of CPAP, accuracy of ARES versus PSG, and CPAP adherence at 6 months

14 were secondary end-points.

15 **Results**

16 Altogether 138 patients in algorithm I and 110 patients in algorithm II completed the

17 CPAP trial. There were no significant differences between these algorithms with respect

18 to the primary end-point. The sensitivity and specificity of algorithm I versus II as a

19 diagnostic test for OSA were 0.3, 0.8 versus 0.31, 1.00 respectively. In predicting CPAP

20 adherence at 6 months, the likelihood ratio positive for algorithm I and II was 2.7 and

21 5.27 respectively. The mean(SE) time taken from the first consultation to the end of

22 CPAP trial in algorithm I and algorithm II was 60(2) and 98(5) days respectively,  $p < 0.01$ .

23

1 **Conclusion**

2 An ambulatory approach with portable sleep monitoring for diagnosing OSA before a  
3 CPAP trial can identify more patients who would adhere to CPAP at 6 months than  
4 empirical CPAP treatment alone.

5

6 **Keywords**

7 Ambulatory Monitoring

8 Continuous Positive Airway Pressure

9 Diagnosis

10 Polysomnography

11 Sleep Apnea Syndromes

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## 1 INTRODUCTION

2 Obstructive sleep apnea syndrome (OSAS) causes disabling daytime sleepiness, impaired  
3 cognitive function and poor health status.<sup>1</sup> Untreated OSAS is associated with  
4 hypertension and other cardiovascular consequences,<sup>2-5</sup> with significant public health  
5 impact.<sup>6</sup> Conventionally, diagnosis of OSAS is based on an attended sleep study,<sup>7</sup> but the  
6 waiting time for polysomnography (PSG) is often lengthy especially in countries with  
7 limited healthcare resources.<sup>8,9</sup>

8 In recent years, 4 types of diagnostic devices have become available for managing  
9 patients suspected of OSAS, and these vary by the numbers of channels recording  
10 physiological parameters.<sup>10</sup> Several simple and portable monitoring devices have been  
11 validated as useful alternatives of PSG, with the advantage of reducing the waiting time  
12 and cost.<sup>11-15</sup> The established standard treatment of OSA is CPAP (continuous positive  
13 airway pressure),<sup>16</sup> which has also been used in the diagnostic mode as a diagnostic test  
14 bypassing PSG in some studies.<sup>17-19</sup> Changing the management algorithms of patients  
15 with OSAS has been discussed in a joint systematic review and practice parameters by  
16 the American Academy of Sleep Medicine (AASM), the American College of Chest  
17 Physicians and the American Thoracic Society.<sup>10,20</sup> This study aimed to investigate the  
18 feasibility of different management algorithms for initiating CPAP, diagnosing OSA, and  
19 identifying patients who might adhere to CPAP treatment.

## 1 **METHODS**

2

3 All patients in this prospective study were recruited from the Respiratory Clinic at the  
4 Prince of Wales Hospital, The Chinese University of Hong Kong (CUHK). Patients were  
5 referred by general practitioners and other specialists for assessment of suspected OSAS.

6 The inclusion criteria were either self-reported daytime sleepiness which interfered with  
7 daytime function or two of the following symptoms: choking or gasping during sleep,  
8 recurrent awakenings from sleep, unrefreshed sleep, daytime fatigue, and impaired  
9 concentration.<sup>21</sup> Patients who were either pregnant or unwilling to participate were  
10 excluded. Written informed consent was obtained from each subject in this study, which  
11 had received approval by the ethics committee of the CUHK. This study was registered in  
12 ClinicalTrials.gov, no. NCT00425659.

13 While the patients were waiting for routine in-patient PSG, they were randomized by a  
14 random table into one of the two algorithms of CPAP initiation: I) empirical CPAP trial  
15 or II) performance of home sleep study using a level III device, the ARES, (Advanced  
16 Brain Monitoring; Carlsbad, CA, USA), followed by a CPAP trial. The ARES was a  
17 wireless physiological recorder applied on the forehead and it has been shown to have  
18 reasonable sensitivity and specificity versus in-patient PSG for diagnosing severe OSA in  
19 symptomatic patients in Hong Kong.<sup>22</sup>

20 In algorithm I, an overnight home autoCPAP titration (ResMed, AutoSet spirit, Australia)  
21 was performed to determine the 95<sup>th</sup> centile pressure for abolishing OSA. CPAP  
22 (Respironics, REMstar, USA) was then loaned to the patients for 3 weeks based on the  
23 95<sup>th</sup> centile pressure. In algorithm II, home sleep study was performed with the ARES

1 followed by an autoCPAP titration in a similar manner as in algorithm I for patients with  
2 an ARES RDI  $\geq 10$ /hr during the home sleep study. CPAP was then loaned for 3 weeks  
3 as in algorithm I. CPAP trial was omitted for those patients with ARES RDI  $< 10$ /hr in  
4 this study as they were less likely to comply with CPAP in view of the mild degree of  
5 OSA.<sup>23</sup> All patients received basic CPAP education via video and written information  
6 given by nurses experienced in managing OSAS, followed by acclimatization with CPAP  
7 for 30 minutes during daytime.<sup>24</sup> Patients were provided with a telephone number for  
8 advice if there were problems using CPAP. Patients were reassessed after completion of  
9 CPAP trial. All recruited patients eventually underwent routine PSG for definitive  
10 diagnosis at the end of the study.

11 The primary outcome was CPAP adherence and willingness to continue CPAP after the  
12 CPAP trial for 3 weeks. CPAP adherence was defined as CPAP usage  $> 4$  hours/night  
13 during the CPAP trial. The willingness of continuing CPAP was assessed by a  
14 questionnaire on side effects, subjective improvement in symptoms, and usefulness of the  
15 machine. A CPAP trial was regarded as unsuccessful when either one or both conditions  
16 not fulfilled. CPAP usage was assessed objectively by the hour meter of the CPAP device.  
17 Secondary outcomes included subjective usefulness of CPAP, accuracy of ARES versus  
18 PSG, the amount of waiting time shortened, and CPAP adherence at 6 months with CPAP  
19 usage  $> 4$  hours/night after commencement of the study.

20 PSG (Siesta, Compumedics, Australia) was performed for all recruited patients for  
21 definitive diagnosis at either the North District Hospital or Prince of Wales Hospital after  
22 completion of CPAP trial. The raw data were manually staged according to the AASM by

1 registered polysomnographic technologists who were blinded to the randomization  
2 status.<sup>25</sup> Obstructive apnea was defined as cessation of airflow for as least 10 seconds  
3 with continuous inspiratory effort. Central apnea was defined as cessation of airflow for  
4 as least 10 seconds without respiratory effort throughout the entire period of the event.  
5 Mixed apnea was defined as cessation of airflow of as least 10 seconds, with absent  
6 respiratory effort in the initial portion of the event followed by resumption of the effort in  
7 the subsequent portion of the event.

8

### 9 **Data analysis and statistics**

10 Statistical analyses were undertaken using SPSS 16 for Windows (SPSS, Chicago,  
11 Illinois, USA). A planned per protocol analysis was conducted comparing outcomes of  
12 patients in the two algorithms. A 10-12% of arbitrary difference in response after CPAP  
13 trial between the 2 algorithms was taken as a conservative estimate of effect size. An  
14 estimated minimal sample size of 273 patients was required to give a power of 0.8 with  
15 an alpha error at 5% and 95% confidence intervals. Paired t test and Chi square test were  
16 used where appropriate. Agreement between ARES RDI and PSG AHI was analyzed  
17 using the Bland and Altman method.

18

19

### 20 **Apnea Risk Evaluation System**

21 The ARES is a level III sleep monitoring device,<sup>12</sup> and has been validated in the HK  
22 Chinese population.<sup>18</sup> It was a wireless physiological recorder that measured blood  
23 oxygen saturation, pulse rate, airflow, respiratory effort, snoring levels, head movement

1 and head position.<sup>12, 26</sup> Raw data were analysed by the ARES Insight software, which  
2 applied pattern recognition algorithms to quantify obstructive respiratory events,  
3 followed by manual editing by the service provider. The ARES raw data were not  
4 accessible to the investigators for editing.

5 Patients had to answer an ARES questionnaire which assessed the risk factors for OSA.  
6 The final analysis required the combination of physiologic signal data with the results of  
7 the ARES questionnaire to generate an overall risk level for OSA. Accordingly, apnea  
8 was defined as cessation of airflow  $\geq 10$  seconds. Hypopnea was defined as  $\geq 50\%$   
9 reduction in airflow with  $\geq 3\%$  desaturation from the baseline. An ARES RDI between 0-  
10 5/hr, 6-20/hr, 21-40/hr, 41-60/hr, over 61/hr were defined as normal, mild, moderate,  
11 severe and very severe OSA respectively by the manufacturer.<sup>12</sup>

12

## 1 **RESULTS**

2 Between July 2007 and December 2008, 399 patients were referred to our respiratory  
3 clinic with suspected OSA and among these, 28 were excluded. Altogether 371 patients  
4 were randomized. Details of enrollment are shown in Figure 1. The age, BMI, and  
5 baseline ESS of the patients were similar between the two algorithms (table 1). About  
6 86% of patients receiving CPAP completed the 3-week CPAP trial. There was no  
7 significant difference between the 2 algorithms in the proportion of patients with a  
8 successful CPAP trial (algorithm II 38.1% vs. algorithm I 28.9%,  $p = 0.17$ , table 2).  
9 There was no significant relationship between the severity of OSA and the proportion of  
10 successful or unsuccessful CPAP trial within each algorithm ( $p=0.25$ ).

### 11 **An empirical CPAP trial versus ARES as a diagnostic tool for OSA**

12 Considering algorithm I as a diagnostic test for confirming OSA, the sensitivity and  
13 specificity were 0.3 and 0.8 respectively. As only patients with ARES RDI  $> 10$ /hr were  
14 offered CPAP in algorithm II, the specificity and likelihood ratios were undetermined  
15 because all cases suffered from OSA (Table 2).

16 If ARES alone was used as a diagnostic tool, the sensitivity was 0.89 and the specificity  
17 was 0.5. The likelihood ratio for a successful trial (LR+) and the likelihood ratio for an  
18 unsuccessful trial (LR-) were 1.78 and 0.22 respectively. The area under the curve (AUC)  
19 was 0.89 (Fig 2). The agreement between ARES and PSG was moderate ( $\kappa=0.31$ ,  
20 figure 3).

1 **Secondary outcomes and prediction of CPAP adherence at 6 months between the 2**  
2 **algorithms**

3 Concerning the subjective usefulness of CPAP, 64.5 % (71/110) of the patients in  
4 algorithm II considered the therapy good or very good versus 54.3% (75/138) of patients  
5 in algorithm I feeling the same way ( $p=0.33$ ). Likewise, 53.6% (59/110) of patients in  
6 algorithm II were willing to use CPAP after the CPAP trial compared to 42.0% (58/138)  
7 in algorithm I. Patients in both algorithms showed improvement in ESS and Calgary  
8 Sleep Apnea Quality of Life Index (SAQLI) after CPAP trial, although the improvement  
9 in ESS was slightly greater in algorithm I. Residual AHI while using CPAP was also  
10 similar between the 2 groups (Table 3). The mean(SE) time taken from the first  
11 consultation to the end of CPAP trial in algorithm I and algorithm II was 60(2) and 98(5)  
12 days respectively. ( $p<0.01$ , table 1).

13 At 6 months of the study after routine PSG had been performed, 202 patients were further  
14 followed up. Half of the patients with an unsuccessful trial in algorithm I switched to  
15 CPAP whereas 37% (20/54) of patients with an unsuccessful trial in algorithm II used  
16 CPAP at 6 months after PSG ( $p=0.17$ ). Compared to algorithm I, algorithm II had a  
17 relatively higher LR+ (5.27 vs 2.7). Table 4 summarizes the results.

## 1 **DISCUSSION**

2 This study compared 2 models for initiating CPAP with an empirical CPAP trial at a  
3 fixed pressure following a home titration study versus a level 3 portable home monitoring  
4 before a CPAP trial in CPAP naïve patients referred to a tertiary referral center with  
5 suspected OSAS. There were no significant differences between the 2 approaches in  
6 terms of achieving a successful CPAP trial, CPAP usage, perceived usefulness of CPAP,  
7 and willingness to use CPAP in the future. However, the combination of an initial  
8 portable sleep monitoring to detect those with RDI at least 10/hr and a subsequent CPAP  
9 trial appeared superior for predicting CPAP adherence at 6 months in comparisons with  
10 empirical CPAP treatment alone. The waiting time for completion of CPAP trial from the  
11 first consultation was shortened by 72% and 64% in algorithm I and algorithm II  
12 respectively compared to usual practice with PSG.

13 Several studies have examined different models of care involving initial ambulatory  
14 home diagnosis in diagnosing OSA, identifying patients who benefit from CPAP, and  
15 reducing the need for PSG.<sup>27-30</sup> Senn et al<sup>27</sup> conducted a 2-week CPAP trial as an initial  
16 diagnostic test in comparisons with PSG for 76 patients with suspected OSAS. Their  
17 CPAP trial predicted OSA (AHI>10/hr) with a sensitivity of 80%, a specificity of 97%,  
18 and positive and negative predictive values of 97% and 78%, respectively. In 35 of 76  
19 OSA patients (46%) with positive CPAP trial results, these patients were prescribed long-  
20 term CPAP therapy whereas 33 of 35 patients (94%) still used CPAP after 4 months and  
21 their symptoms remained improved. These patients were identified by the CPAP trial  
22 with positive and negative predictive values of 92% and 100%, respectively.<sup>27</sup> Our study

1 has shown similar findings. The positive LR+ values of both algorithms suggested that a  
2 successful CPAP trial implied a higher likelihood of adhering to CPAP at 6 months. The  
3 relatively higher LR+ value of algorithm II at 6 months implied that patients would have  
4 an even higher probability continuing CPAP in the long run, if they had a successful  
5 CPAP trial after portable monitoring with the ARES device. The PSG AHI and the ESS  
6 of the successful group of the 2 algorithms were similar in severity. This suggests that the  
7 presence of an objective test might improve CPAP adherence by supporting the clinical  
8 diagnosis. Furthermore, in algorithm I, many patients with unsuccessful CPAP trial were  
9 using CPAP at 6 months after PSG. It is possible that undergoing an objective test  
10 provided more convincing evidence to patients for accepting CPAP as treatment of OSA  
11 than just a provisional clinical diagnosis made by the doctors. Thus this highlights the  
12 importance of undergoing a diagnostic test by either a validated portable home sleep  
13 study or PSG before a CPAP trial.

14 As a diagnostic tool for OSA, neither algorithm I nor II provided clinically useful  
15 diagnostic values in this study because of a substantial number of false negative  
16 responses in both algorithms. This implies an unsuccessful CPAP trial in algorithm I  
17 cannot rule out OSA. This was different from the study by Senn et al in which the  
18 number of false negative cases was small. Although we had adopted the conventional 4  
19 hours cut-off as the definition of a successful CPAP trial, the results were still similar  
20 even if a hypothetical analysis was performed using 2 hours as the cut-off as in the study  
21 by Senn et al.<sup>24</sup> Moreover, PSG AHI > 10/hr was considered true positive in Senn et al's  
22 study while we took the conventional cut off of 5/hr. The differences in cut-off values

1 might explain the difference in results.

2 In a randomized control trial (RCT) by Skomro et al<sup>28</sup> comparing a similar ambulatory  
3 approach (home-based level 3 testing followed by one week of autoCPAP and then fixed-  
4 pressure CPAP based on 95<sup>th</sup> centile pressure) versus in-lab PSG and CPAP titration,  
5 diagnosis and treatment of OSA in the sleep laboratory did not lead to superior four-week  
6 outcomes in sleepiness scores, sleep quality, quality of life, blood pressure, and CPAP  
7 adherence.<sup>28</sup> Another RCT, comparing portable monitoring and autotitration versus PSG  
8 for the diagnosis and treatment of OSA, has shown that the former approach resulted in  
9 CPAP adherence and clinical outcomes similar to one using PSG.<sup>29</sup> In a RCT that  
10 compared standard PSG against ambulatory CPAP titration (autoCPAP titration followed  
11 by CPAP set at 95<sup>th</sup> centile pressure) in high-risk patients identified by a diagnostic  
12 algorithm involving symptom score and a level 3 portable sleep diagnostic device,  
13 Mulgrew et al<sup>30</sup> have shown that PSG confers no advantage over the ambulatory  
14 approach in terms of diagnosis, CPAP titration (AHI on CPAP), ESS score, and SAQLI  
15 over 3 months. Adherence to CPAP therapy was better in the ambulatory group than in  
16 the PSG group.<sup>30</sup>

17 It should be pointed out that the various ambulatory methods of determining CPAP  
18 pressure (autotitration, autotitration for 1 week followed by fixed pressure, and fixed  
19 pressure determined by algorithm based on predictive formula, arbitrary pressure based  
20 on BMI) for treatment of moderate to severe OSA have made no significant difference to  
21 clinical outcome measures vs PSG-guided CPAP titration study.<sup>31-33</sup> More recently, a  
22 nurse-led model of care using home auto-adjusting device to set therapeutic CPAP has

1 demonstrated non-inferior results (change in ESS, CPAP adherence at 3 months) to  
2 physician-directed care involving two laboratory PSG to diagnose and treat symptomatic  
3 patients with moderate to severe OSA.<sup>34</sup>

4 Using an economic model to ascertain the potential role of portable studies in the  
5 diagnosis of patients with suspected OSA with focus on ruling in disease in symptomatic  
6 patients, Ayas et al<sup>35</sup> have shown that the pre-test probability threshold of patients in  
7 which portable studies would be useful was fairly modest (47–68% depending on  
8 diagnostic vs. split studies), suggesting that they may be potentially useful in a broad  
9 range of patients. A previous study by Krieger et al<sup>36</sup> has suggested that there is a risk  
10 that ambulatory diagnostic procedures alter the relationship of patients to their disease  
11 and/or the medical staff so that subsequent compliance with CPAP treatment may be  
12 decreased. Further studies are needed to assess whether application of the ambulatory  
13 approach for management of OSA may compromise CPAP usage.

14

15 There were several limitations in this study. Firstly, the study population consisted of  
16 symptomatic patients with a high clinical pretest probability of OSAS and therefore the  
17 results of this study might not be applicable to the general population. However, the  
18 ambulatory approach may be useful for referral centers which attract lots of symptomatic  
19 OSA patients. Secondly, the free loan of CPAP might have encouraged some patients to  
20 participate in the study and increased the response rate. Lastly, our study did not include  
21 the conventional approach of diagnosing OSA with PSG for comparisons, as this was  
22 adequately addressed by numerous studies before.<sup>27-35</sup>

1 In summary, this RCT has shown that an initial ambulatory management approach  
2 consisting of a level 3 portable sleep monitoring followed by a CPAP trial was more  
3 useful for predicting future CPAP adherence in patients with a high clinical probability of  
4 OSAS than empirical CPAP treatment alone, but not very useful as a diagnostic test.  
5 Patients with a high likelihood of OSAS should be offered a CPAP trial after detection of  
6 OSAS with a portable sleep monitoring device as this approach may improve subsequent  
7 CPAP adherence. For those with either a negative home sleep study or a failed CPAP  
8 trial, further investigation with PSG is mandatory. This ambulatory approach may  
9 facilitate the management of symptomatic OSA patients in countries with limited access  
10 to PSG.

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13

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## 1   **References**

2

3   1       Engleman HM, Douglas NJ. Sleep. 4: Sleepiness, cognitive function, and quality  
4 of life in obstructive sleep apnoea/hypopnoea syndrome. *Thorax* 2004; **59**: 618-22.

5   2       Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular  
6 consequences. *Lancet* 2009; **373**: 82-93.

7   3       Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, *et al.* Sleep  
8 disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep  
9 cohort. *Sleep* 2008; **31**: 1071-8.

10  4       Marshall NS, Wong KKH, Liu PY, Cullen SRJ, Knuiman MW, Grunstein RR.  
11 Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health  
12 Study. *Sleep* 2008; **31**: 1079-85.

13  5       Valham F, Mooe T, Rabben T, Stenlund H, Wiklund U, Franklin KA. Increased  
14 risk of stroke in patients with coronary artery disease and sleep apnea: a 10-year follow-  
15 up. *Circulation* 2008; **118**: 955-60.

16  6       Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a  
17 population health perspective. *Am J Respir Crit Care Med* 2002; **165**: 1217-39.

18  7       Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, Jr., *et*  
19 *al.* Practice parameters for the indications for polysomnography and related procedures:  
20 an update for 2005. *Sleep* 2005; **28**: 499-521.

21  8       Ng DK, Kwok K-L, Chow P-Y, Cheung M-Y. Diagnostic access for sleep apnea  
22 in Hong Kong.[comment]. *Am J Respir Crit Care Med* 2004; **170**: 196; discussion 96-7.

- 1 9 Flemons WW, Douglas NJ, Kuna ST, Rodenstein DO, Wheatley J. Access to  
2 diagnosis and treatment of patients with suspected sleep apnea. *Am J Respir Crit Care*  
3 *Med* 2004; **169**: 668-72.
- 4 10 Chesson ALJ, Berry RB, Pack A. Practice parameters for the use of portable  
5 monitoring devices in the investigation of suspected obstructive sleep apnea in adults.  
6 *Sleep* 2003; **26**: 907-13.
- 7 11 Zou D, Grote L, Peker Y, Lindblad U, Hedner J. Validation a portable monitoring  
8 device for sleep apnea diagnosis in a population based cohort using synchronized home  
9 polysomnography. *Sleep* 2006; **29**: 367-74.
- 10 12 Westbrook PR, Levendowski DJ, Cvetinovic M, Zavora T, Velimirovic V,  
11 Henninger D, *et al.* Description and validation of the apnea risk evaluation system: a  
12 novel method to diagnose sleep apnea-hypopnea in the home. *Chest* 2005; **128**: 2166-75.
- 13 13 Liesching TN, Carlisle C, Marte A, Bonitati A, Millman RP. Evaluation of the  
14 accuracy of SNAP technology sleep sonography in detecting obstructive sleep apnea in  
15 adults compared to standard polysomnography. *Chest* 2004; **125**: 886-91.
- 16 14 Quintana-Gallego E, Villa-Gil M, Carmona-Bernal C, Botebol-Benhamou G,  
17 Martinez-Martinez A, Sanchez-Armengol A, *et al.* Home respiratory polygraphy for  
18 diagnosis of sleep-disordered breathing in heart failure. *Eur Respir J* 2004; **24**: 443-8.
- 19 15 Golpe R, Jimenez A, Carpizo R. Home sleep studies in the assessment of sleep  
20 apnea/hypopnea syndrome. *Chest* 2002; **122**: 1156-61.

- 1 16 Sullivan C, Issa F, Berthon JM, Falkner B, A C, Sforza E, *et al.* Reversal of  
2 obstructive sleep apnea by continuous positive airway pressure applied through the nares  
3 *Lancet* 1981; **1**: 862-65.
- 4 17 Gugger M. Comparison of ResMed AutoSet (version 3.03) with  
5 polysomnography in the diagnosis of the sleep apnoea/hypopnoea syndrome. *Eur Respir*  
6 *J* 1997; **10**: 587-91.
- 7 18 Rees K, Wraith PK, Berthon-Jones M, Douglas NJ. Detection of apnoeas,  
8 hypopnoeas and arousals by the AutoSet in the sleep apnoea/hypopnoea syndrome. *Eur*  
9 *Respir J* 1998; **12**: 764-9.
- 10 19 Kiely JL, Delahunty C, Matthews S, McNicholas WT. Comparison of a limited  
11 computerized diagnostic system (ResCare Autoset) with polysomnography in the  
12 diagnosis of obstructive sleep apnoea syndrome. *Eur Respir J* 1996; **9**: 2360-4.
- 13 20 Flemons WW, Littner MR, Rowley JA, Gay P, Anderson WM, Hudgel DW, *et al.*  
14 Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review  
15 cosponsored by the American Academy of Sleep Medicine, the American College of  
16 Chest Physicians, and the American Thoracic Society.[see comment]. *Chest* 2003; **124**:  
17 1543-79.
- 18 21 Sleep-related breathing disorders in adults: recommendations for syndrome  
19 definition and measurement techniques in clinical research. The Report of an American  
20 Academy of Sleep Medicine Task Force. *Sleep* 1999; **22**: 667-89.

- 1 22 To KW, Chan WC, Chan TO, Tung A, Ngai J, Ng S, *et al.* Validation study of a  
2 portable monitoring device for identifying OSA in a symptomatic patient population.  
3 *Respirology* 2009; **14**: 270-75.
- 4 23 McArdle N, Devereux G, Heidarnejad H, Engleman H, Mackay T, Douglas N.  
5 Long-term Use of CPAP Therapy for Sleep Apnea/Hypopnea Syndrome. *Am J Respir*  
6 *Crit Care Med* 1999; **159**: 1108-14.
- 7 24 Hui DS, Chan JK, Choy DK, Ko FW, Li TS, Leung RC, *et al.* Effects of  
8 augmented continuous positive airway pressure education and support on compliance and  
9 outcome in a Chinese population. *Chest* 2000; **117**: 1410-6.
- 10 25 Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM Manual for the Scoring  
11 of Sleep and Associated Events: Rules, Terminology and Technical Specification. 1st edn.  
12 Westchester, Illinois: American Academy of Sleep Medicine 2007.
- 13 26 Ayappa I, Norman RG, Seelall V, Rapoport DM. Validation of a self-applied  
14 unattended monitor for sleep disordered breathing. *J Clin Sleep Med* 2008; **4**: 26-37.
- 15 27 Senn O, Brack T, Russi EW, Bloch KE. A continuous positive airway pressure  
16 trial as a novel approach to the diagnosis of the obstructive sleep apnea syndrome. *Chest*  
17 2006; **129**: 67-75.
- 18 28 Skomro RP, Gjevre J, Reid J, McNab B, Ghosh S, Stiles M, *et al.* Outcomes of  
19 home-based diagnosis and treatment of obstructive sleep apnea. *Chest* 2010; **138**: 257-63.
- 20 29 Berry RB, Hill G, Thompson L, McLaurin V. Portable monitoring and  
21 autotitration versus polysomnography for the diagnosis and treatment of sleep apnea.  
22 *Sleep* 2008; **31**: 1423-31.

- 1 30 Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of  
2 obstructive sleep apnea without polysomnography: a randomized validation study. *Ann*  
3 *Intern Med* 2007; **146**: 157-66.
- 4 31 West SD, Jones DR, Stradling JR. Comparison of three ways to determine and  
5 deliver pressure during nasal CPAP therapy for obstructive sleep apnoea. *Thorax* 2006;  
6 **61**: 226-31.
- 7 32 Masa JF, Jimenez A, Duran J, Capote F, Monasterio C, Mayos M, *et al.*  
8 Alternative methods of titrating continuous positive airway pressure: a large multicenter  
9 study. *Am J Respir Crit Care Med* 2004; **170**: 1218-24.
- 10 33 Hukins CA. Arbitrary-pressure continuous positive airway pressure for  
11 obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2005; **171**: 500-5.
- 12 34 Antic NA, Buchan C, Esterman A, Hensley M, Naughton MT, Rowland S, *et al.*  
13 A randomized controlled trial of nurse-led care for symptomatic moderate-severe  
14 obstructive sleep apnea. *Am J Respir Crit Care Med* 2009; **179**: 501-8.
- 15 35 Ayas NT, Fox J, Epstein L, Ryan CF, Fleetham JA. Initial use of portable  
16 monitoring versus polysomnography to confirm obstructive sleep apnea in symptomatic  
17 patients: An economic decision model. *Sleep Medicine*; **11**: 320-24.
- 18 36 Krieger J, Sforza E, Petiau C, Weiss T. Simplified diagnostic procedure for  
19 obstructive sleep apnoea syndrome: lower subsequent compliance with CPAP. *Eur Respir*  
20 *J* 1998; **12**: 776-9.
- 21
- 22

1 **FIGURE LEGEND**

2

3

4 **Figure 1:** Flow of participants through different algorithms of managing patients with a  
5 high probability of OSAS. Altogether 138 and 110 patients in algorithm I and II  
6 respectively completed the CPAP trial and were available for data analysis.

7

8 **Figure 2:** ROC showing the performance of ARES in diagnosing OSAS in patients with  
9 a high probability of OSAS under unattended setting.

10

11 **Figure 3:** Bland-Altman plot of differences between PSG AHI and ARES RDI

12

	Algorithm I (n = 187)	Algorithm II (n = 184)	p-value
Male / Female	138 / 49	136 / 48	0.87
Age (yrs)	50.87 (0.80)	49.76 (0.78)	0.21
BMI (kg/m <sup>2</sup> )	29.05 (0.32)	28.90 (0.30)	0.12
ESS at baseline	14.47 (0.29)	13.85 (0.30)	0.05
Time from 1st consultation to completion of CPAP trial (days)	60 (2)	98 (5)	<0.01
Waiting Time for PSG after finishing CPAP trial (days)	153 (14)	171(18)	0.45

1

2 Table 1. Demographic characteristics of all patients, values expressed in mean (SE)

3

	Algorithm I (n=138)		Algorithm II (n=110)	
	successful CPAP trial	unsuccessful CPAP trial	successful CPAP trial	unsuccessful CPAP trial
Confirmed OSAS by PSG	38	90	42	68
No evidence of OSAS by PSG	2	8	0	0
Sensitivity (95% CI)	0.30 (0.27, 0.34)		0.38	
Specificity (95% CI)	0.80 (0.62, 0.71)		n/a	
PPV	0.95		n/a	
NPV	0.08		n/a	
LR+	1.5		n/a	
LR-	0.8		n/a	

1

2 Table 2. Diagnostic accuracy of CPAP trials vs PSG. LR+ = sensitivity / (1 -specificity),

3 LR- = (1 – sensitivity) / specificity

1

	Algorithm I (n = 138)	Algorithm II (n = 110)	p-value (t-test)
Number of patients completed CPAP trial			
successful	40	52	0.17
unsuccessful	98	58	
Number of days using CPAP	16.68 (0.72)	18.10 (0.93)	0.22
Compliance (hrs / day)	4.28 (0.19)	4.65 (0.20)	0.10
Usefulness of CPAP			
Very bad	6	3	
Bad	10	5	0.33
Not useful	47	31	
Good	69	60	
Very good	6	11	
Willing to use CPAP in the future (Yes / No)	59 / 51	58 / 80	0.11
Improvement of ESS after CPAP	5.22 (0.46)	3.96 (0.42)	0.04
95% CI of improvement	4.32-6.12	3.12-4.8	
Mean(SE) AHI	36(2)	30(1.8)	0.04
Severity of OSA			
Normal	11	0	
Mild	26	16	
moderate	30	34	
Severe	71	60	
Residual AHI	8.56 (0.67)	8.31 (0.66)	0.801
Changes in SAQLI	0.09 (0.08)	0.29 (0.09)	0.109

2

3 Table 3. Secondary outcomes of patients undergone and completed CPAP trial, values  
4 expressed in mean (SE)

1

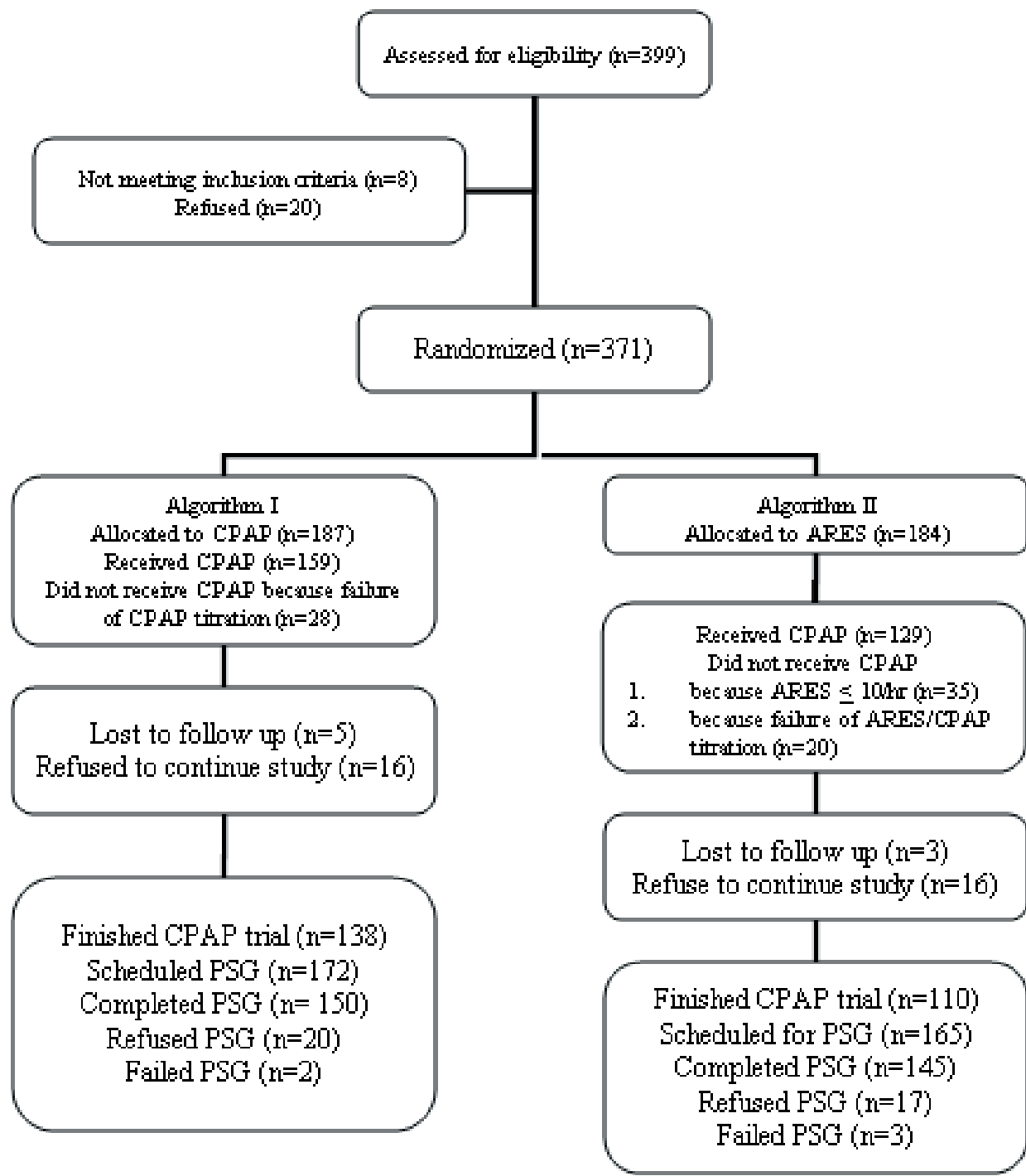
	Algorithm I (n=116)		Algorithm II (n=86)	
	Using CPAP at 6 months	Not using CPAP at 6 months	Using CPAP at 6 months	Not using CPAP at 6 months
successful CPAP trial	28	7	28	4
unsuccessful CPAP trial	41	40	20	34
ESS at 6 <sup>th</sup> month	9.80 (0.45)	14.41 (0.32)	10.02 (0.55)	14.15 (0.35)
PSG AHI Mean (SE)	40.6(2.8)*	29.5(2.9)	36.4(2.5)*	28.3(2.8)
LR+		2.7		5.27
LR-		0.69		0.47

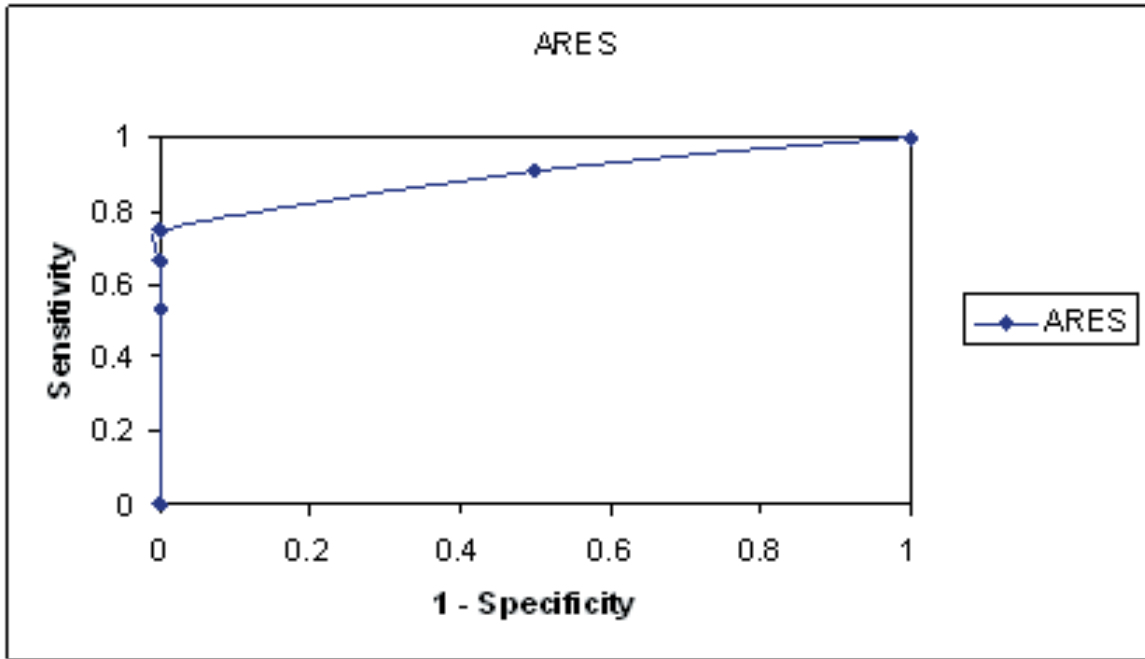
2 \*P=0.26

3

4 Table 4. CPAP adherence at 6 months

5





<b>Parameters</b>	<b>Values</b>	<b>95% C.I</b>
<b>AUC</b>	<b>0.89</b>	<b>(0.81, 0.98)</b>
<b>Sensitivity</b>	<b>0.89</b>	<b>(0.84, 0.94)</b>
<b>Specificity</b>	<b>0.50</b>	<b>(0.42, 0.59)</b>
<b>PPV</b>	<b>0.98</b>	--
<b>NPV</b>	<b>0.12</b>	--
<b>LR+</b>	<b>1.78</b>	--
<b>LR-</b>	<b>0.22</b>	--

