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# Differential blood pressure response to CPAP treatment according to the circadian pattern in hypertensive patients with obstructive sleep apnea

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**"Differential blood pressure response to CPAP treatment according to the circadian pattern in hypertensive patients with obstructive sleep apnea"**

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**Take a message**

Only nondipper patients significantly benefited from CPAP treatment in terms of BP reduction. The study suggests that performing an ABPM before prescribing CPAP to hypertensive patients may be important in clinical practice to predict the blood pressure response.

**ABSTRACT**

**Introduction:** Continuous positive airway pressure (CPAP) has a heterogeneous effect on blood pressure (BP) in hypertensive patients. However, the effect of CPAP on BP in hypertensive subjects regarding to circadian BP pattern has never been explored. This study aimed to assess the effect of CPAP on BP considering the circadian BP pattern in untreated hypertensive patients.

**Methods:** This study is a post hoc analysis of the Spanish Cohort for the Study of the Effect of CPAP in Hypertension (CEPECTA), a multicentre, randomized trial of CPAP versus sham-CPAP in patients with new-onset systemic hypertension and an apnea/hypopnea index >15 events/h. We included patients for whom 24-h ambulatory BP monitoring (ABPM) data were available at baseline and 12 weeks after the intervention. Subjects were classified based on the dipping ratio (dipper/nondipper). We evaluated the effect of CPAP on ABPM parameters after 12 weeks of treatment.

**Results:** Overall, 272 hypertensive subjects were included in the analysis (113 dippers/159 nondippers). Baseline clinical and polysomnographic variables were similar between the groups. CPAP treatment in nondipper patients was associated with reductions in 24-h ambulatory BP variables and nighttime ambulatory BP measurements. However, a nonsignificant effect was reported in the dipper group. The differential effects of CPAP between the groups were -2·99 mmHg (-5·92 to -0·06) for the mean 24-h ambulatory BP and -5·35 mmHg (-9·01 to -1·69) for the mean nighttime ambulatory BP.

**Conclusions:** Our results show a differential effect of CPAP treatment on BP in hypertensive patients depending on the circadian pattern. Only nondipper patients benefited from CPAP treatment in terms of BP reduction.

## INTRODUCTION

Obstructive Sleep Apnea (OSA) is a common sleep disorder characterized by partial (hypopnea) or complete (apnea) episodes of collapse in the upper airway during sleep. This collapse causes intermittent hypoxia, hypercapnia, negative intrathoracic pressure and arousals, resulting in excessive daytime sleepiness and poor quality of life. OSA is associated with a higher cardiovascular risk due to several pathogenic factors, and hypertension has been established as one of the main causes of these cardiovascular complications [1–4]. Moreover, OSA can reportedly affect the circadian blood pressure (BP) pattern by increasing the prevalence of patients with a nondipper circadian BP pattern, which has been related to a poor cardiovascular prognosis [5–7].

Several randomized clinical trials and meta-analyses have indicated that continuous positive airway pressure (CPAP) can produce a modest but consistent reduction in BP, with greater reductions observed in resistant hypertension (RH) subjects [8–15]. Thus, severe OSA, hypersomnolence, higher BP values and adherence to CPAP are variables that have been associated with a greater improvement in BP in several studies [8,12,15]. Nevertheless, even in RH patients with moderate to severe OSA and good compliance, the effect of CPAP treatment on BP is highly variable [8].

Recently, our group published a study on office normotensive patients who showed a differential BP response to CPAP depending on the dipping ratio (DR) category. The results of this study indicate that several factors may contribute to modulating the effect of CPAP on BP [16] and highlight the importance of better characterizing OSA patients in terms of the BP response to CPAP treatment.

Therefore, due to the high variability of the results observed, using a precision medicine approach and identifying and differentiating subgroups of patients in whom BP could be reduced to a greater extent and who could benefit from CPAP treatment from those with low or no effects of CPAP on BP is necessary [8,17]. Determining which patients could benefit from this intervention could have important implications in clinical practice and for resource consumption.

The effects of CPAP treatment on BP in hypertensive subjects with respect to the circadian BP pattern have never been explored [18]. Thus, as previous results suggest, we hypothesize that the BP response in hypertensive patients could vary depending on the dipping ratio (DR) category. Therefore, the aim of the present study was to assess the effect of CPAP treatment on BP considering the baseline circadian BP pattern in untreated hypertensive patients.

## MATERIALS AND METHODS

### Design and study population

This study is a post hoc analysis of the Spanish Cohort for the Study of the Effect of CPAP in Hypertension (CEPECTA). This was a multicentre, randomized, prospective, double-blind and parallel study controlled by a placebo that evaluated the effect of CPAP treatment on BP in patients with OSA and untreated systemic hypertension diagnosed based on office BP measurements [19].

Briefly, patients aged between 18 and 75 years with untreated new-onset systemic hypertension were included between December 2004 and June 2007. Patients were excluded if they met any of the following criteria: had secondary hypertension, a BP greater than 180/100 mmHg, had cognitive impairment, were professional drivers or handled dangerous machinery, were shift workers, were pregnant, had severe chronic disease or were previously treated with CPAP, or had any contraindication for prescribing CPAP. Patients treated with antihypertensive, psychotropic, stimulant or antidepressant drugs and those consuming illicit drugs were also excluded.

All patients underwent polysomnography and 24-h ambulatory blood pressure monitoring (ABPM) (Spacelabs model 90207, EEUU) at baseline and after 6 and 12 weeks of treatment. Subjects with an apnea/hypopnea index (AHI) >15 events/hour were randomized to CPAP treatment or sham-CPAP and evaluated at 12 weeks.

Systemic hypertension was not treated with drugs during the study. More detailed information on the inclusion and exclusion criteria and the methodology of the CEPECTA study is published elsewhere [19].

The CEPECTA trial was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the ethics committee. All participants provided written informed consent. The trial is registered with ClinicalTrials.gov (NCT00202527).

For the present study, we selected 272 patients who completed CEPECTA trial and for whom 24-h ABPM data were available at baseline and after 12 weeks. The included patients were classified as dippers or nondippers based on the DR. (Figure 1)

**Procedures**

*Definition of hypertension*
Systemic hypertension was diagnosed according to standard criteria and defined as an office systolic blood pressure (SBP) ≥140 mmHg, a diastolic blood pressure (DBP) ≥90 mmHg, or both.

*Sleep evaluation*
All included subjects underwent polysomnography according to recommended guidelines. The sleep evaluation was considered valid if it lasted for >180 minutes of total sleep.

*24-h ambulatory blood pressure monitoring*
Twenty-four-hour ABPM (Spacelabs model 90207, EEUU) was performed for all patients at baseline and after 6 and 12 weeks of treatment.
During ABPM, BP measurements were recorded every 20 minutes during the daytime (from 6 am to 10 pm) and every 30 minutes during the nighttime (between 10 pm and 6 am).
The diagnosis of true systemic hypertension was determined based on 24-h ABPM results following guidelines and standard criteria. The cut-off for systemic hypertension was defined as an SBP ≥135 mmHg, DBP ≥85 mmHg or both during the awake period [19].
Circadian patterns were defined based on the DR (nighttime/daytime BP ratio): non-dipper >0·9 and dipper ≤0·9.
The mean blood pressure was calculated using the formula (SBP + 2×DBP)/3.

*Office blood pressure measurements*
Office BP measurements were performed following guidelines. Before BP measurement, the patient should rest for at least 5 minutes in a seated position with the feet on the floor and the arm supported at the heart level. Caffeine, exercise, and smoking should be avoided for at least 30 minutes prior to measurement. The seated BP was recorded as the average of at least 2 replicate measurements [19,20].

*CPAP treatment*
Patients with CPAP treatment were titrated with an auto-CPAP (Autoset- T; ResMed, Sydney, Australia) according to a previously described protocol [19]. The optimal pressure was determined visually from the raw data, and the patient was treated with this pressure for 12 weeks. Furthermore, the patients receiving sham-CPAP also received the treatment at home for 12 weeks.

**Statistical analysis**
Baseline bivariate analysis was carried out using a t-test (or an equivalent nonparametric test) or $\chi^2$ test depending on whether the variables were quantitative or categorical, respectively. The differential CPAP effect on BP according to the circadian pattern was assessed using linear models. The models included the treatment (CPAP or Sham), circadian pattern (dipper or nondipper) and the interaction between them. All models were adjusted according to baseline measurements. Furthermore, the CPAP effect was evaluated using a linear model adjusted for age, sex, body mass index (BMI) and AHI. The assumptions of the model were assessed using residual analysis. All tests were two tailed, and p values <0.05 were considered indicative of statistical significance.

**RESULTS**

**Patient characteristics**
A total of 272 hypertensive subjects with untreated hypertension and an AHI>15/$h^{-1}$ events were included in the analysis. Of all the patients included, 113 (42%) were dippers, and 159 (58%) were nondippers.
The baseline characteristics of the enrolled subjects are shown in Table 1. No significant differences were observed in the baseline variables between the groups. Mainly, the subjects included were male with a median [IQR] age of 53·0 years [46·0; 60·0], a BMI of 30·8 kg/$m^2$ [28·1; 34·9], a median AHI of 38·0

[22·0; 58·0] events/h. No differences were observed in polysomnographic and sleep variables between the groups. The mean systolic and diastolic office blood pressures of the subjects were 150 (9·66) and 93.4 (6·60) mmHg, respectively

**Effect of CPAP treatment on BP by circadian pattern**

The mean CPAP compliance was 4·08 hours, without significant differences across the different groups. Changes in ABPM parameters after 12 weeks of treatment (CPAP or sham-CPAP) were evaluated in each circadian pattern group (dipper or nondipper). In the dipper group, we observed nonsignificant effects of CPAP on the mean 24-h ambulatory BP (0·11 mmHg; 95% CI -2·13 to 2·34), the mean daytime ambulatory BP (-0·21 mmHg; 95% CI -2·65 to 2·23) and the mean nighttime ambulatory BP (0·95 mmHg; 95% CI -1·84 to 3·73). In contrast, significant effects of CPAP were observed on the mean 24-h ambulatory BP (-2·88 mmHg; 95% CI -4·74 to -1·02) and the mean nighttime ambulatory BP (-4·40 mmHg; -6·73 to -2·08) in the nondipper group. The differential effects of CPAP between the circadian pattern groups revealed a better response in nondippers of -2·99 mmHg (-5·92 to -0·06) for the mean 24-h ambulatory BP and -5·35 mmHg (-9·01 to -1·69) for the mean nighttime ambulatory BP (see Figure 2 and Table 2). Moreover, more detailed information on absolute BP values and changes in each treatment and dipping category group is described in the supplemental material (e-Table 1). The model adjusted only for baseline measurements showed similar results (see e-Table 2).

When the analysis was performed only with patients diagnosed with systemic hypertension based on the results of 24-h ABPM, similar results were observed. A differential effect of CPAP was also observed between dippers and nondippers. Nondipper patients exhibited significantly reduced blood pressure, especially nighttime blood pressure (e-Table 3), while no significant changes were observed in the dipper group (e-Table 3).

## DISCUSSION

This study suggests that the BP response to CPAP treatment in hypertensive patients depends on the circadian blood pressure pattern. The results show significant reductions in the mean 24-h ambulatory BP, 24-h systolic BP, 24-h diastolic BP and nighttime ambulatory BP variables in nondipper patients, whereas no significant changes were observed in the dipper group after 12 weeks of CPAP treatment. Therefore, in relation to BP, only nondipper patients benefited from CPAP treatment.

Several studies have evaluated the effect of CPAP treatment on BP in hypertensive patients, and a reduction in BP has been described previously [19,21,22]. Data from a meta-analysis indicate a mild effect of CPAP treatment on BP in OSA patients, which has been reported to be approximately 2 mmHg [13–15,23,24], with greater reductions observed in subjects with RH [8–11]. Notably, the BP response to CPAP treatment has been found to be highly variable. Some authors noted that factors such as higher BP values, CPAP use or OSA severity could be related to a better BP response [10,12,25]; nevertheless, the causes of this variability have not been well established.

Therefore, this considerable variability in the BP response to CPAP treatment highlights the importance of differentiating patients who will effectively respond to CPAP treatment from those who will not. In recent years, some published studies have identified clinical and molecular profiles that may predict the BP response to CPAP treatment. Sanchez-de-la Torre et al. [17] reported a circulating miRNA profile that could predict BP responses to CPAP treatment in patients with RH and OSA. Moreover, in an observational study with severe OSA patients, Castro-Grattoni et al. [26] suggested that the circadian BP pattern, nocturnal hypertension and the nighttime heart rate could be predictors of the BP response to CPAP treatment. Furthermore, data from an observational study recently published by our group showed that in normotensive subjects, the BP circadian pattern may influence the BP response to CPAP treatment [16]. Although several authors have suggested that certain clinical characteristics may predict the BP response to treatment, no randomized studies have confirmed these findings, which could be very useful in clinical practice.

In our study, the decrease observed in the mean 24-h ambulatory BP was –2.99 mmHg. Moreover, when analysing nocturnal BP, the decrease was -5·35 mmHg in the mean nighttime ambulatory BP, -6·45 mmHg in the mean systolic ambulatory BP and -4·87 mmHg in the mean diastolic ambulatory BP.

In previous studies with systemic hypertension and RH patients, decreases in the mean 24-h ambulatory BP of approximately -1.5 mmHg [19] and -3 mmHg, respectively, were observed [8,9]. Our results show that blood pressure decreases are greater in nondipper patients than those in dipper patients, and nondipper patients would therefore benefit the most from CPAP treatment in terms of BP reduction.

Multiple studies have indicated that sleep alterations, such as duration changes, fragmentation or blunted BP declines, which are frequent in OSA, are associated with atherosclerosis, hypertension and an increased incidence of cardiovascular events [27,28].
Previous studies have highlighted the importance of reducing nighttime blood pressure and have suggested that decreasing nocturnal BP has higher prognostic value for reducing cardiovascular outcomes than reducing daytime blood pressure [29,30]. Furthermore, the fact that these reductions in BP are observed in nondipper subjects is especially important since this circadian pattern category has been related to a worse cardiovascular prognosis, a higher prevalence of organ damage and less favourable outcomes compared to the dipper category [31,32]. Moreover, international guidelines indicate even minimal reductions in BP levels may be clinically effective in reducing cardiovascular mortality [20].
Therefore, identification of bedtime chronotherapy strategies to reduce BP in hypertensive patients, especially at night, has received increasing interest [33], and some authors have even combined these strategies with CPAP treatment in hypertensive patients with OSA [34]. However, the results are not fully consistent, and more evidence is required to confirm the beneficial effect of combining both methods.

This study shows a differential BP response based on the circadian pattern category in hypertensive patients and demonstrated the importance of performing ABPM in hypertensive subjects before prescribing CPAP. The results support the recommendation of performing ABPM for the management of patients with office hypertension and suspected OSA. However, this recommendation was based on the assessment of the cardiovascular risk [35,36] whereas in our study is based on identifying patients who could benefit the most from CPAP treatment in terms of BP. Our study indicates that the BP circadian pattern at baseline may determine differences in the BP response to CPAP treatment. Therefore, performing ABPM may contribute to identify subgroups of hypertensive patients with OSA in whom blood pressure is expected to be reduced to a greater extent and highlights the utility of individual characteristics, such as the blood pressure circadian pattern, as factors to consider in the management of these patients.
In addition, the results suggest that the BP circadian pattern can be used when selecting the optimal therapeutic approach for each patient, and that CPAP treatment may be the first treatment approach in untreated hypertensive patients with OSA who are nondippers.
Future studies should determine the role of ABPM in managing these patients and clarify whether ABPM should be routinely performed for patients with hypertension and OSA before deciding to prescribe CPAP.

The main strength of this study is that to our knowledge, it is the first to confirm that the effect of CPAP on BP varies depending on the circadian pattern and to identify the dipping category as a clinical variable that allows differentiation between hypertensive OSA patients with a good BP response to CPAP treatment and those without a good response. Moreover, this study included a large sample size an implemented ABPM, and OSA was diagnosed by polysomnography. In addition, the included patients did not receive antihypertensive drugs and were treated only with conservative measures[19], thus enabling evaluation of the effects of CPAP without interference from changes in BP induced by pharmacological treatments. Nevertheless, the study presents several limitations that should be mentioned. This study encompasses the inherent limitations of a post hoc analysis. In our analysis, the included patients were classified according to the DR, which was not considered before randomization. However, dippers and nondippers were fully comparable at the baseline evaluation, and when we assessed the effect of CPAP, a fully adjusted model showed similar results. Second, the subjects presented moderate to severe OSA, and the results may not be generalizable to less severe OSA patients. Third, the included patients had recently been diagnosed with hypertension, exhibited mild hypertension, and were untreated. Thus, the results should be interpreted with caution when addressing patients receiving antihypertensive drugs. Fourth, the categorization of the circadian BP pattern with single 24-h ABPM is only moderately reproducible.

## CONCLUSIONS

In conclusion, our findings show that in patients with moderate to severe OSA who are newly diagnosed with hypertension, only those with a nondipper BP circadian pattern experience significant benefits for BP with CPAP treatment, especially nocturnal BP.

### Author contribution

ESB, GT, JD-C, CE, MST, FB, and MD participated in the study conception and design.
IB and FSM participated in the analysis of the data.
ESB, GT, IB, FSM, MST, FB, and MD participated in the interpretation of the data for the work.
All authors drafted the manuscript, revised it critically and provided final approval of the version to be published. MD is the guarantor.

### Declaration of interests

The authors have reported no conflicts of interest with organizations or companies to the European Respiratory Journal.

**REFERENCES**


1. Sapina E, Torres G, Barbe F, Sanchez-de-la-Torre M. The Use of Precision Medicine to Manage Obstructive Sleep Apnea Treatment in Patients with Resistant Hypertension: Current Evidence and Future Directions. Curr Hypertens Rep. 2018;20(7):60.
2. Pepin JL, Borel AL, Tamisier R, Baguet JP, Levy P, Dauvilliers Y. Hypertension and sleep: Overview of a tight relationship. Sleep Med Rev. 2014;18(6):509–19.
3. Sánchez-de-la-Torre M, Campos-Rodriguez F, Barbé F. Obstructive sleep apnoea and cardiovascular disease. Lancet Respir Med. 2013;1(1):61–72.
4. Lévy P, Kohler M, McNicholas WT, Barbé F, McEvoy RD, Somers VK, et al. Obstructive sleep apnoea syndrome. Nat Rev Dis Prim. 2015;1:1–20.
5. Pankow W, Nabe B, Lies A, Kohl F V, Lohmann FW. Influence of obstructive sleep apnoea on circadian blood pressure profile. J Sleep Res. 1995;4:102–6.
6. Suzuki T, Guilleminault C, Otsuka T, Shiomi T, Suzuki M. Blood Pressure "Dipping" and "Non-Dipping" Obstructive Sleep Apnea Syndrome Patients. Sleep. 2018;19(5):382–7.
7. Marrone O, Bonsignore MR. Nature and Science of Sleep Dovepress Blood-pressure variability in patients with obstructive sleep apnea: current perspectives. Nat Sci Sleep. 2018;10:229–42.
8. Martínez-García M-A, Capote F, Campos-Rodríguez F, Lloberes P, Josefa Díaz de Atauri M, Somoza M, et al. Effect of CPAP on Blood Pressure in Patients With Obstructive Sleep Apnea and Resistant Hypertension The HIPARCO Randomized Clinical Trial. JAMA. 2013;310(22):2407–15.
9. Pedrosa RP, Drager LF, De Paula LKG, Amaro ACS, Bortolotto LA, Lorenzi-Filho G. Effects of OSA treatment on BP in patients with resistant hypertension: A randomized trial. Chest. 2013;144(5):1487–94.
10. Lozano L, Tovar JL, Sampol G, Romero O, Jurado MJ, Segarra A, et al. Continuous positive airway pressure treatment in sleep apnea patients with resistant hypertension: a randomized, controlled trial. J Hypertens Wolters Kluwer Heal J Hypertens. 2010;28(28):2161–8.
11. Muxfeldt E, Margallo V, Costa LMS, Guimarães G, Cavalcante AH, Azevedo JCM, et al. Effects of Continuous Positive Airway Pressure Treatment on Clinic and Ambulatory Blood Pressures in Patients With Obstructive Sleep Apnea and Resistant Hypertension. Hypertension. 2015;65(4):736–42.
12. Dorigoni S, Dalle Vedove F, Danese PharmD E, Montagnana M, Cesare Guidi G, Narkiewicz K, et al. Effect of CPAP on Blood Pressure in Patients With OSA/Hypopnea: A Systematic Review and Meta-analysis. Chest. 2014;145:762–71.
13. Iftikhar IH, Valentine CW, Bittencourt LRA, Cohen DL, Fedson AC, Gíslason T, et al. Effects of continuous positive airway pressure on blood pressure in patients with resistant hypertension and obstructive sleep apnea: a meta-analysis. J Hypertens. 2014;32(12):2341–50.
14. Liu L, Cao Q, Guo Z, Dai Q. Continuous Positive Airway Pressure in Patients With Obstructive Sleep Apnea and Resistant Hypertension : A Meta-Analysis of Randomized Controlled Trials. J Clin Hypertens. 2016;18(2):153–8.
15. Montesi SB, Edwards BA, Ph D, Malhotra A, Bakker JP, Ph D. The Effect of Continuous

Positive Airway Pressure Treatment on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Clin Sleep Med. 2012;8(5):587–96.

16. Sapiña-Beltrán E, Santamaria-Martos F, Benítez I, Torres G, Masa JF, Sá Nchez-De-La-Torre M, et al. Normotensive patients with obstructive sleep apnoea: changes in 24-h ambulatory blood pressure monitoring with continuous positive airway pressure treatment. J Hypertens. 2019;37(4):720–7.
17. Sánchez-De-La-Torre M, Khalyfa A, Sánchez-De-La-Torre A, Martinez-Alonso M, Martinez-García MA, Barceló A, et al. Precision Medicine in Patients With Resistant Hypertension and Obstructive Sleep Apnea Blood Pressure Response to Continuous Positive Airway Pressure Treatment. J Am Coll Cardiol. 2015;66(9):1023–32.
18. Akashiba T, Minemura H, Yamamoto H, Kosaka N, Saito O, Horie T. Nasal continuous positive airway pressure changes blood pressure "non-dippers" to "dippers" in patients with obstructive sleep apnea. Sleep. 1999;22(7):849–53.
19. Duran-Cantolla J, Aizpuru F, Montserrat JM, Ballester E, Teran-Santos J, Aguirregomoscorta JI, et al. Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial. BMJ. 2010;(341):c5991.
20. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003;289(19):2560–72.
21. Campos-Rodriguez F, Perez-Ronchel J, Grilo-Reina A, Lima-Alvarez J, Benitez MA, Almeida-Gonzalez C. Long-term Effect of Continuous Positive Airway Pressure on BP in Patients With Hypertension and Sleep Apnea. Chest. 2007;132(6):1847–52.
22. Barbe F, Duran-Cantolla J, Capote F, de la Pena M, Chiner E, Masa JF, et al. Long-term Effect of Continuous Positive Airway Pressure in Hypertensive Patients with Sleep Apnea. Am J Resp Crit Care Med. 2010;181(7):718–26.
23. Bazzano LA, Khan Z, Reynolds K, He J. Effect of nocturnal nasal continuous positive airway pressure on blood pressure in obstructive sleep apnea. Hypertension. 2007;50(2):417–23.
24. Bratton DJ, Stradling JR, Barbé F, Kohler M. Effect of CPAP on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: A meta-analysis using individual patient data from four randomised controlled trials. Thorax. 2014;69(12):1128–35.
25. Wolf J, Hering D, Narkiewicz K. Non-dipping pattern of hypertension and obstructive sleep apnea syndrome. Hypertens Res. 2010;33(9):867–71.
26. Castro-Grattoni AL, Torres G, Martínez-Alonso M, Barbé F, Turino C, Sánchez-de-la-Torre A, et al. Blood pressure response to CPAP treatment in subjects with obstructive sleep apnoea: The predictive value of 24-h ambulatory blood pressure monitoring. Eu RespirJ. 2017;50(4).
27. Hermida RC, Ayala DE, Mojón A, Fernández JR. Decreasing sleep-time blood pressure determined by ambulatory monitoring reduces cardiovascular risk. J Am Coll Cardiol. 2011 Sep;58(11):1165–73.
28. Domínguez F, Fuster V, Fernández-Alvira JM, Fernández-Friera L, López-Melgar B, Blanco-Rojo R, et al. Association of Sleep Duration and Quality With Subclinical Atherosclerosis. J Am

Coll Cardiol. 2019;73(2):134–44.

29. Roush GC, Fagard RH, Salles GF, Pierdomenico SD, Reboldi G, Verdecchiaf P, et al. Prognostic impact from clinic, daytime, and nighttime systolic blood pressure in nine cohorts of 13844 patients with hypertension. J Hypertens. 2014;32(12):2332–40.
30. Brien EO, Parati G, George Stergiou, Asmar R, Beilin L, Bilo G, et al. European Society of Hypertension Position Paper on Ambulatory Blood Pressure Monitoring. J Hypertens. 2013;31(9):1731–68.
31. Konecny T, Kara T, Somers VK. Obstructive sleep apnea and hypertension: an update. Hypertens . 2014;63(2):203–9.
32. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC / ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Cardiology ( ESC ) and the European Society of. J Hypertens. 2018;36(10):1953–2041.
33. Hermida RC, Ayala DE, Fernández JR, Mojón A, Crespo JJ, Ríos MT, et al. Bedtime Blood Pressure Chronotherapy Significantly Improves Hypertension Management. Heart Fail Clin. 2017;13(4):759–73.
34. Serinel Y, Yee BJ, Grunstein RR, Wong KH, Cistulli PA, Arima H, et al. Chronotherapy for hypertension in obstructive sleep apnoea (CHOSA): a randomised, double-blind, placebo-controlled crossover trial. Thorax. 2017;72(6):550–8.
35. Parati G, Lombardi C, Hedner J, Bonsignore MR, Grote L, Tkacova R, et al. Recommendations for the management of patients with obstructive sleep apnoea and hypertension. Eur Respir J. 2013;41(3):523–38.
36. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013;34(28):2159–219.

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# TABLES

## Table 1. Baseline characteristics of the studied groups

| | Global N = 272 | Dipper | | Nondipper | | p value |
|---|---|---|---|---|---|---|
| | | Sham N=62 | CPAP N=51 | Sham N=73 | CPAP N=86 | |
| Demographic and Clinical variables | | | | | | |
| Age (years) -median [IQR]- | 53·0 [46·0;60·0] | 51·5 [46·0;59·8] | 50·0 [45·0;57·0] | 55·0 [46·0;60·0] | 54·0 [49·0;61·8] | 0·108 |
| Male: -n (%)- | 223 (82·0%) | 50 (80·6%) | 42 (82·4%) | 64 (87·7%) | 67 (77·9%) | 0·544 |
| BMI (kg/m2) -median [IQR]- | 30·8 [28·1;34·9] | 30·4 [28·4;33·4] | 32·4 [28·4;34·9] | 31·8 [28·7;35·2] | 30·5 [27·4;34·6] | 0·356 |
| Smoking status: -n(%)- | | | | | | 0·607 |
| Non smoker | 90 (34·2%) | 25 (41·7%) | 15 (29·4%) | 25 (35·7%) | 25 (30·5%) | |
| Former smoker | 103 (39·2%) | 21 (35·0%) | 23 (45·1%) | 29 (41·4%) | 30 (36·6%) | |
| Smoker | 70 (26·6%) | 14 (23·3%) | 13 (25·5%) | 16 (22·9%) | 27 (32·9%) | |
| Alcohol consumption (g/day) -median [IQR]- | 15·0 [0·00;32·0] | 15·0 [0·00;30·0] | 15·0 [0·00;35·0] | 12·5 [0·00;30·0] | 15·0 [0·00;40·0] | 0·867 |
| Polysomnographic and sleep parameters | | | | | | |
| Stage 1 (min) -median [IQR]- | 32·0 [13·0;60·0] | 32·0 [19·8;53·5] | 36·5 [11·5;80·0] | 29·0 [13·0;39·0] | 31·5 [12·5;83·8] | 0·557 |
| Stage 2 (min) -median [IQR]- | 216 [166;257] | 224 [177;285] | 224 [166;254] | 200 [149;255] | 212 [170;252] | 0·432 |
| Stage 3 (min) -median [IQR]- | 31·5 [13·0;58·0] | 30·0 [13·0;53·0] | 34·0 [11·0;77·5] | 30·0 [13·0;51·0] | 29·5 [10·0;63·2] | 0·351 |
| REM Stage (min) -median [IQR]- | 50·5 [33·0;70·0] | 51·0 [41·5;70·2] | 47·0 [21·2;71·2] | 48·5 [30·8;68·8] | 51·0 [39·2;70·5] | 0·783 |
| Total sleep time (min) -median [IQR]- | 357 [314;400] | 390 [337;411] | 358 [316;415] | 353 [303;390] | 354 [314;382] | 0·152 |
| AHI (events/h) -median [IQR]- | 38·0 [22·0;58·0] | 41·0 [25·2;58·0] | 48·0 [22·5;67·0] | 35·0 [20·0;56·0] | 31·0 [22·0;52·0] | 0·245 |
| Mean saturation (%) -median [IQR]- | 93·5 [92·0;95·0] | 94·0 [92·0;95·0] | 94·0 [92·0;95·0] | 93·0 [92·0;94·0] | 93·0 [92·0;95·0] | 0·137 |
| TSat90 (%) -median [IQR]- | 3·00 [1·00;16·8] | 3·00 [0·00;18·5] | 2·50 [1·00;15·5] | 2·00 [0·00;13·0] | 3·50 [1·00;13·8] | 0·754 |
| Arousals Index (events/h) -median [IQR]- | 31·5 [19·0;49·8] | 32·0 [21·0;45·0] | 41·5 [25·0;54·0] | 26·0 [18·5;49·0] | 29·5 [19·0;48·0] | 0·374 |
| ESS (0-24) -median [IQR]- | 10·0 [8·00;13·0] | 9·50 [6·50;13·0] | 10·0 [7·50;13·0] | 10·0 [8·00;12·0] | 10·0 [8·00;12·0] | 0·699 |
| CPAP compliance (h/night) -median [IQR]- | 4·08 [4·02;5·09] | 4·08 [3·07;5·07] | 4·40 [4·02;6·05] | 4·07 [4·03;5·02] | 4·17 [4·02;6·00] | 0·289 |
| Blood pressure (mmHg) -mean(SD)- | | | | | | |
| Office SBP | 150 (9·66) | 151 (10·3) | 150 (8·55) | 150 (10·2) | 150 (9·38) | 0·821 |
| Office DBP | 93·4 (6·60) | 93·1 (7·97) | 93·8 (7·83) | 94·2 (5·15) | 92·8 (5·82) | 0·527 |
| Mean 24-h ambulatory BP | 98·2 (8·12) | 95·9 (9·56) | 98·5 (8·94) | 99·6 (7·37) | 98·5 (6·77) | 0·060 |
| Mean daytime ambulatory BP | 101 (8·41) | 101 (9·96) | 104 (9·53) | 101 (7·28) | 100 (6·99) | 0·037 |
| Mean nighttime ambulatory BP | 91·8 (9·87) | 85·2 (9·66) | 86·8 (8·83) | 96·9 (8·96) | 95·3 (7·02) | <0·001 |

Statistically significant p values (p values less than 0·05) are shown in bold. Abbreviations: BMI = Body Mass Index; AHI =Apnoea-Hypoapnoea Index; TSat90 = nighttime with oxygen saturation less than 90%; CPAP = Continuous Positive Airway Pressure; ESS= Epworth Sleepiness Scale; REM= Rapid Eye Movement; SBP= Systolic Blood Pressure; DBP= Diastolic Blood Pressure; BP= Blood Pressure

**Table 2. Changes in blood pressure by circadian pattern groups adjusted by confounding factors**

| | Dipper (Sham=62/CPAP=51) | | Nondipper (Sham=73/CPAP=86) | | Difference | |
|---|---|---|---|---|---|---|
| Blood Pressure | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* |
| 24h- ABPM (mmHg) | | | | | | |
| Mean | 0·11 (-2·13 to 2·34) | 0·9997 | -2·88 (-4·74 to -1·02) | **0·0139** | -2·99 (-5·92 to -0·06) | **0·0458** |
| Systolic | -0·11 (-3·22 to 2·99) | 0·9999 | -3·63 (-6·21 to -1·04) | **0·032** | -3·52 (-7·58 to 0·55) | 0·0898 |
| Diastolic | 0·16 (-1·92 to 2·25) | 0·9987 | -2·49 (-4·23 to -0·76) | **0·0267** | -2·66 (-5·4 to 0·08) | 0·0573 |
| Daytime- ABPM (mmHg) | | | | | | |
| Mean | -0·21 (-2·65 to 2·23) | 0·9982 | -2·16 (-4·18 to -0·14) | 0·1574 | -1·95 (-5·14 to 1·25) | 0·2308 |
| Systolic | -0·3 (-3·55 to 2·95) | 0·9979 | -2·45 (-5·15 to 0·25) | 0·2846 | -2·15 (-6·4 to 2·1) | 0·3195 |
| Diastolic | -0·24 (-2·56 to 2·09) | 0·9971 | -2·01 (-3·93 to -0·08) | 0·1762 | -1·77 (-4·81 to 1·28) | 0·2538 |
| Nighttime- ABPM (mmHg) | | | | | | |
| Mean | 0·95 (-1·84 to 3·73) | 0·9097 | -4·4 (-6·73 to -2·08) | **0·0014** | -5·35 (-9·01 to -1·69) | **0·0043** |
| Systolic | 0·48 (-3·5 to 4·45) | 0·9955 | -5·97 (-9·29 to -2·65) | **0·0028** | -6·45 (-11·66 to -1·23) | **0·0155** |
| Diastolic | 1·21 (-1·33 to 3·74) | 0·788 | -3·66 (-5·78 to -1·54) | **0·0046** | -4·87 (-8·2 to -1·53) | **0·0044** |

Estimated CPAP effects using a linear model adjusted for baseline measurements, age, sex, BMI, and AHI. The model includes treatment, circadian pattern and their interaction. Statistically significant p values (p values less than 0·05) are shown in bold.
Abbreviations: CPAP = Continuous Positive Airway Pressure; ABPM= Ambulatory Blood Pressure Monitoring.

**e-Table 1. Changes in blood pressure at twelve weeks according to the circadian pattern**

## e-Table 2. Changes in blood pressure by circadian pattern group

| | Dipper | | Nondipper | |
|---|---|---|---|---|
| | Sham N=62 | CPAP N=51 | Sham N=73 | CPAP N=86 |
| 24h- ABPM | | | | |
| Mean (mmHg) | | | | |
| Baseline | 95·9 (93·47 to 98·33) | 98·51 (95·99 to 101·02) | 99·62 (97·9 to 101·34) | 98·5 (97·05 to 99·95) |
| 3 months | 95·24 (92·74 to 97·75) | 97·41 (94·62 to 100·2) | 99·36 (97·47 to 101·24) | 95·38 (93·73 to 97·02) |
| Change | -0·66 (-2·13 to 0·81) | -1·1 (-2·78 to 0·57) | -0·26 (-1·61 to 1·08) | **-3·12 (-4·53 to -1·71)** |
| Systolic (mmHg) | | | | |
| Baseline | 127·65 (124·42 to 130·88) | 130·67 (127·03 to 134·31) | 130·83 (128·68 to 132·97) | 130·84 (128·98 to 132·71) |
| 3 months | 126·51 (123·24 to 129·78) | 128·9 (125·12 to 132·68) | 130·48 (127·77 to 133·19) | 126·6 (124·34 to 128·86) |
| Change | -1·14 (-3·01 to 0·73) | -1·77 (-4·23 to 0·69) | -0·35 (-2·08 to 1·38) | **-4·24 (-6·31 to -2·17)** |
| Diastolic (mmHg) | | | | |
| Baseline | 80·03 (77·78 to 82·27) | 82·42 (80·21 to 84·64) | 84·02 (82·25 to 85·79) | 82·33 (80·77 to 83·88) |
| 3 months | 79·61 (77·08 to 82·13) | 81·66 (79·08 to 84·24) | 83·79 (82·1 to 85·49) | 79·76 (78·08 to 81·45) |
| Change | -0·42 (-2·01 to 1·17) | -0·76 (-2·26 to 0·73) | -0·22 (-1·46 to 1·01) | **-2·56 (-3·77 to -1·35)** |
| Daytime- ABPM | | | | |
| Mean (mmHg) | | | | |
| Baseline | 101·24 (98·71 to 103·77) | 104·34 (101·66 to 107·02) | 100·99 (99·29 to 102·69) | 100·11 (98·61 to 101·61) |
| 3 months | 100·06 (97·28 to 102·84) | 102·27 (99·42 to 105·13) | 101·54 (99·71 to 103·37) | 98·34 (96·54 to 100·15) |
| Change | -1·18 (-2·94 to 0·58) | **-2·07 (-3·89 to -0·25)** | 0·55 (-0·8 to 1·89) | **-1·76 (-3·32 to -0·21)** |
| Systolic (mmHg) | | | | |
| Baseline | 133·76 (130·43 to 137·08) | 137·57 (133·72 to 141·42) | 132·4 (130·47 to 134·33) | 132·49 (130·64 to 134·33) |
| 3 months | 131·98 (128·35 to 135·62) | 134·75 (130·9 to 138·59) | 132·7 (130·25 to 135·14) | 129·9 (127·59 to 132·21) |
| Change | -1·77 (-3·95 to 0·4) | **-2·82 (-5·43 to -0·22)** | 0·3 (-1·42 to 2·02) | **-2·59 (-4·73 to -0·46)** |
| Diastolic (mmHg) | | | | |
| Baseline | 84·98 (82·6 to 87·37) | 87·73 (85·34 to 90·11) | 85·29 (83·48 to 87·1) | 83·92 (82·3 to 85·54) |
| 3 months | 84·1 (81·33 to 86·87) | 86·04 (83·39 to 88·69) | 85·96 (84·24 to 87·68) | 82·57 (80·69 to 84·45) |
| Change | -0·89 (-2·75 to 0·97) | **-1·69 (-3·32 to -0·05)** | 0·67 (-0·59 to 1·93) | -1·35 (-2·74 to 0·05) |
| Nighttime- ABPM | | | | |
| Mean (mmHg) | | | | |
| Baseline | 85·22 (82·77 to 87·67) | 86·84 (84·36 to 89·33) | 96·88 (94·79 to 98·97) | 95·28 (93·77 to 96·78) |
| 3 months | 85·61 (83·27 to 87·95) | 87·67 (84·53 to 90·81) | 94·99 (92·66 to 97·32) | 89·44 (87·59 to 91·28) |
| Change | 0·39 (-1·1 to 1·87) | 0·83 (-1·41 to 3·07) | **-1·89 (-3·73 to -0·05)** | **-5·84 (-7·63 to -4·06)** |
| Systolic (mmHg) | | | | |
| Baseline | 115·44 (112·16 to 118·71) | 116·88 (113·29 to 120·48) | 127·68 (124·78 to 130·59) | 127·56 (125·43 to 129·68) |
| 3 months | 115·56 (112·57 to 118·56) | 117·22 (112·92 to 121·51) | 126·04 (122·34 to 129·74) | 120·01 (117·38 to 122·64) |
| Change | 0·13 (-1·84 to 2·1) | 0·33 (-3·01 to 3·68) | -1·64 (-4·17 to 0·89) | **-7·55 (-10·12 to -4·97)** |
| Diastolic (mmHg) | | | | |
| Baseline | 70·11 (67·89 to 72·33) | 71·82 (69·65 to 74) | 81·48 (79·36 to 83·6) | 79·14 (77·59 to 80·69) |
| 3 months | 70·63 (68·25 to 73) | 72·9 (70·06 to 75·74) | 79·47 (77·49 to 81·44) | 74·15 (72·39 to 75·91) |
| Change | 0·52 (-1·05 to 2·08) | 1·08 (-0·86 to 3·02) | **-2·01 (-3·82 to -0·21)** | **-4·99 (-6·52 to -3·46)** |

Note: statistically significant p values (p values less than 0·05) are shown in bold. Abbreviations: ABPM=Ambulatory Blood Pressure Monitoring

| Blood Pressure | Dipper (Sham=62/CPAP=51) | | Nondipper (Sham=73/CPAP=86) | | Difference | |
|---|---|---|---|---|---|---|
| | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* |
| 24h- ABPM (mmHg) | | | | | | |
| Mean | 0·06 (-2·13 to 2·25) | 0·9999 | -3·08 (-4·91 to -1·24) | **0·0064** | -3·14 (-6·02 to -0·26) | **0·0328** |
| Systolic | -0·07 (-3·12 to 2·98) | 1 | -3·89 (-6·45 to -1·34) | **0·0163** | -3·83 (-7·82 to 0·17) | 0·0606 |
| Diastolic | 0·07 (-1·97 to 2·11) | 0·9999 | -2·63 (-4·35 to -0·92) | **0·0152** | -2·71 (-5·4 to -0·02) | **0·0486** |
| Daytime- ABPM (mmHg) | | | | | | |
| Mean | -0·25 (-2·66 to 2·16) | 0·9969 | -2·49 (-4·51 to -0·48) | 0·0754 | -2·24 (-5·4 to 0·93) | 0·1648 |
| Systolic | -0·28 (-3·49 to 2·93) | 0·9982 | -2·88 (-5·56 to -0·19) | 0·1568 | -2·6 (-6·8 to 1·61) | 0·2257 |
| Diastolic | -0·3 (-2·58 to 1·99) | 0·9942 | -2·27 (-4·19 to -0·35) | 0·0959 | -1·97 (-4·98 to 1·03) | 0·1974 |
| Nighttime- ABPM (mmHg) | | | | | | |
| Mean | 0·87 (-1·84 to 3·58) | 0·9229 | -4·37 (-6·66 to -2·09) | **0·0012** | -5·24 (-8·81 to -1·67) | **0·0042** |
| Systolic | 0·55 (-3·33 to 4·44) | 0·9923 | -5·93 (-9·2 to -2·67) | **0·0025** | -6·49 (-11·58 to -1·39) | **0·0128** |
| Diastolic | 1·04 (-1·44 to 3·52) | 0·8447 | -3·63 (-5·73 to -1·53) | **0·0045** | -4·67 (-7·94 to -1·39) | **0·0054** |

Estimated CPAP effects using a linear model adjusted for baseline measurements. The model includes treatment, circadian pattern and their interaction. Statistically significant p values (p values less than 0·05) are shown in bold. Abbreviations: ABPM= Ambulatory Blood Pressure Monitoring; CPAP= Continuous Positive Airway Pressure.

**e-Table 3. CPAP effect on blood pressure according to the circadian pattern in true hypertensive subjects adjusted by confounding factors**

| Blood Pressure | Dipper (Sham=33/CPAP=43) | | Nondipper (Sham =58/CPAP=62) | | Difference | |
|---|---|---|---|---|---|---|
| | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* | *CPAP effect mean (95% CI)* | *p value* |
| 24h- ABPM (mmHg) | | | | | | |
| Mean | 0·01 (-2·86 to 2·88) | 0·9999 | -3·27 (-5·4 to -1·14) | **0·016** | -3·28 (-6·88 to 0·33) | 0·0745 |
| Systolic | 0·78 (-3·17 to 4·72) | 0·9804 | -4·8 (-7·72 to -1·88) | **0·0083** | -5·58 (-10·54 to -0·62) | **0·0277** |
| Diastolic | -0·32 (-3·1 to 2·45) | 0·9957 | -2·52 (-4·58 to -0·46) | 0·0821 | -2·19 (-5·68 to 1·29) | 0·2162 |
| Daytime- ABPM (mmHg) | | | | | | |
| Mean | -0·98 (-4·13 to 2·17) | 0·9294 | -2·7 (-5·04 to -0·36) | 0·1115 | -1·72 (-5·68 to 2·24) | 0·3924 |
| Systolic | -0·32 (-4·45 to 3·8) | 0·9987 | -3·72 (-6·79 to -0·66) | 0·0841 | -3·4 (-8·59 to 1·79) | 0·1977 |
| Diastolic | -1·3 (-4·4 to 1·8) | 0·8445 | -2·19 (-4·49 to 0·11) | 0·2459 | -0·89 (-4·79 to 3) | 0·6516 |
| Nighttime - ABPM (mmHg) | | | | | | |
| Mean | 1·8 (-1·7 to 5·31) | 0·7441 | -4·55 (-7·15 to -1·95) | **0·0042** | -6·35 (-10·74 to -1·97) | **0·0048** |
| Systolic | 2·61 (-2·57 to 7·79) | 0·7572 | -6·92 (-10·75 to -3·09) | **0·0028** | -9·53 (-16·02 to -3·04) | **0·0042** |
| Diastolic | 1·44 (-1·78 to 4·66) | 0·8164 | -3·51 (-5·91 to -1·1) | **0·0242** | -4·95 (-8·99 to -0·91) | **0·0167** |

Estimated CPAP effects using a linear model adjusted for baseline measurements, age, sex, BMI, and AHI. The model includes treatment, circadian pattern and their interaction. Statistically significant p values (p values less than 0.05) are shown in bold.
Abbreviations: ABPM= Ambulatory Blood Pressure Monitoring; CPAP= Continuous Positive Airway Pressure

**Figure 1. Flow diagram of the study**

Abbreviations: CPAP=Continuous Positive Airway Pressure

**Figure 2. Changes in BP parameters at twelve weeks according to the circadian pattern**

The figure shows the means (95% CIs) of the observed values for 24-h ambulatory BP, daytime BP and nighttime BP at baseline and after 12 weeks of treatment according to the circadian pattern. In the nondipper group, the figure shows a greater reduction in BP in patients with CPAP compared with those receiving sham-CPAP treatment. In the dipper group, no differential effect was observed.

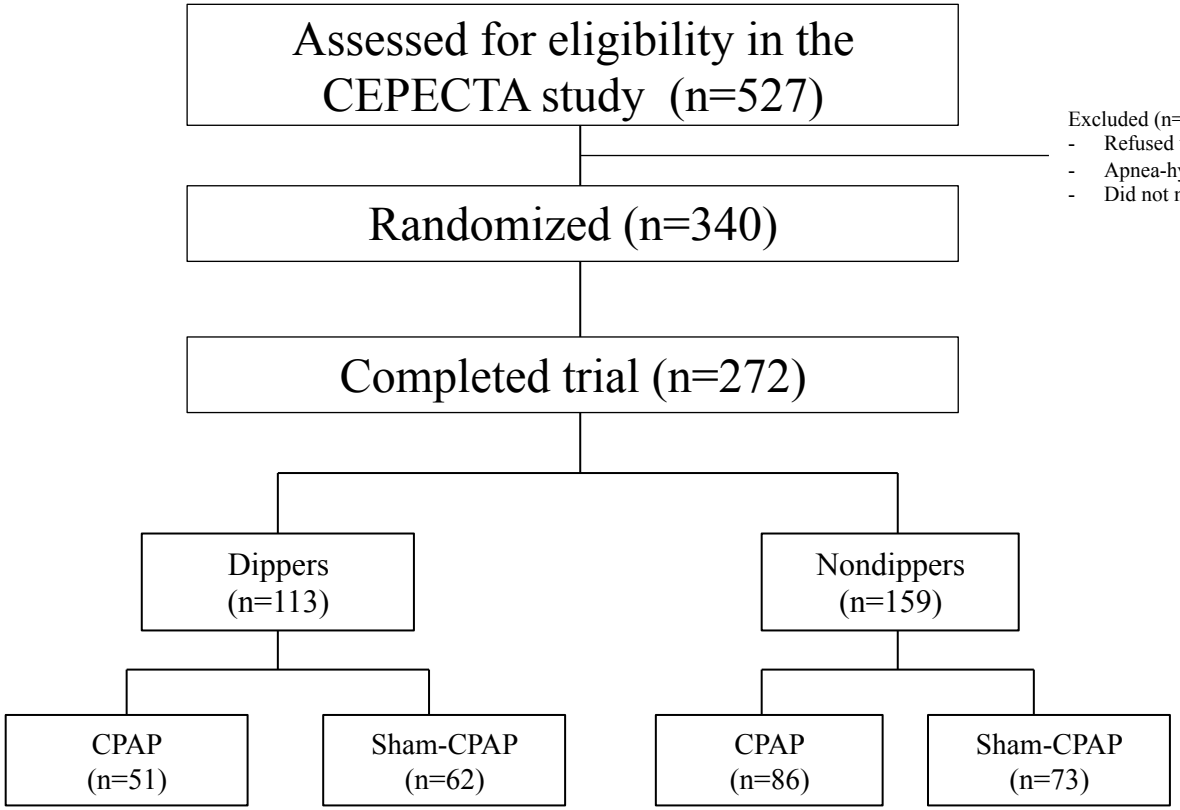
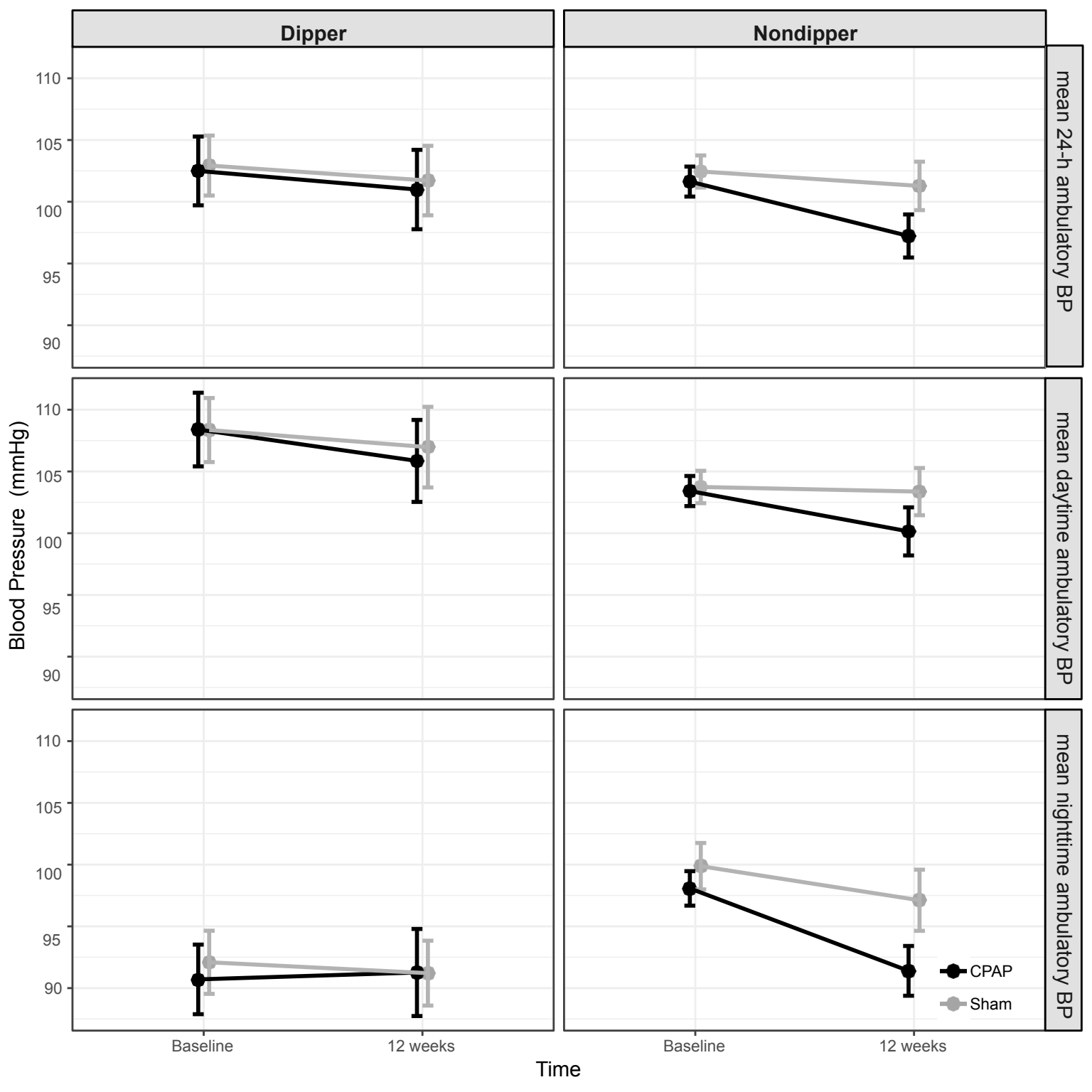



**Figure 1: Flow diagram of study**
Abbreviations: CPAP=continuous positive airway pressure


Dipper
Nondipper
mean 24-h ambulatory BP
mean daytime ambulatory BP
mean nighttime ambulatory BP
Blood Pressure (mmHg)
110
105
100
95
90
Baseline
12 weeks
Time
CPAP
Sham