PIMA1-JO-PR

Adherence and quality of life of CPAP for obstructive sleep apnea: a randomized controlled trial

Protocol ID: PIMA1-3450

Secondary IDs: 3450

Date of the protocol: 14 February 2018

Date of submission to the Ethics and Clinical Research Committee of the Hospital Universitario de La Princesa: March 12, 2018

Research project report

TITLE: *Study on the individualization of a plan to improve adherence based on stratification and the use of telemonitoring for sleep apnea with CPAP.*

Main researcher: Dr David Rudilla, Dr Pedro Landete, Dr Enrique Zamora.
Project type: Individual
Duration: 6 months

Summary (Objetives and Methodology)
Aim: 1 Improve the adherence of patients diagnosed with OSA to CPAP treatment; 2 Follow adhesion; 3 Optimize resources; 4 Comply with SEPAR regulations; Develop experience in telemonitoring along with stratification.
Methodology: Patients with OSA (referral cohort) will be included. All participants will have a diagnosis of OSA with objective tests and a comprehensive evaluation. A follow-up will be carried out with objective evaluation questionnaires and compliance results will be obtained with the measurement of the CPAP hour meter.

List of acronyms in this report

- CPAP- Continuous Positive Airway Pressure (English). Positive Pressure in the Airways (Spanish)
- COPD- Chronic Obstructive Pulmonary Disease
- FEV - Forced Expiratory Volume
- AHI- apnea-hypopnea index
- CHF - Congestive Heart Failure
- mMRC - Modified Medical Research Council. Dyspnoea scale
- PIMA - Individualized Adhesion Improvement Plan
- OSA - sleep apnea-hypopnea syndrome
- SEPAR- Spanish Society of Pneumology
- TM: Telemonitoring

Background section and current status of the issue

OSA is characterized by the appearance of repetitive episodes of obstructive apnea and hypopnea during sleep associated with daytime sleepiness. The severity of OSA is evaluated and classified according to the number of apneas and hypopneas per hour of sleep (apnea-hypopnea index-AHI). In our country, in a prevalence study carried out more than 10 years ago, it was estimated that 15-20% of the population suffered from OSA. The natural history of OSA is still poorly understood, but longitudinal studies show that untreated OSA is associated with increased risk of accidents, loss of quality of life, and increased cardiovascular mortality.
There are few studies on adherence understood as compliance maintained over time and in relation to an awareness of disease and a change in healthy lifestyles; Furthermore, no work has been carried out to address these aspects together with technological advances such as telemonitoring. Of the studies reviewed, the most important conclusions regarding treatment with CPAP are the following:
- Park et al. (2012). This work analyzes the influence of anatomical differences on adherence, which is why they suggest that the examination be incorporated before prescribing. In any case, there is no great impact on adherence as it is the education part, etc.

- Budhiraja et al (2007) and Aloia et al (2007). Long-term adherence is determined by how the results are in the first two weeks.
- Batool-Anwar et al. (2017) studied the influence of the couple, finding that in the first 6 months it is important, although not so much in the long term. It is important to take into account the immediate social support of the patient in order to improve adherence to CPAP.
- Balachandran et al (2013). They found that the patients with the best adherence were those who had a better predisposition and perception of being able to carry out the therapy and its benefits, measured through a simple 6-item questionnaire. The statistical analyzes were regression, and the most important derived result is that the adherence of the patient can be "predicted" based on certain characteristics.
- Hwang et al. (2018) recently carried out a randomized study in which they found that the use of CPAP telemonitoring with automated feedback messages improved 90-day adherence in patients with OSA.

Regarding the educational and training aspects, Olsen et al. Found scientific evidence applying an educational program for new patients. The methodology used was the motivational interview. The detailed contents of each session of said intervention are based on the work of Miller and his colleagues (Miller, Zweben, DiClemente, and Rychtarik, 1995) but with modifications directed to sleep apnea pointed out by Aloia, et al., 2004) .

VitalAire has developed a stratification procedure based on this evidence from which an individualized adherence improvement plan is developed. Said stratification procedure has been registered in the Territorial Registry of Intellectual Property of the Community of Madrid (Spain). Therefore, Air Liquide Medicina S.L.U, as the owner of the VitalAire activity, has the authorship of the rights derived from the exploitation of PIMA. However, scientific exploitation in oral communication format, poster, publication, will be recognized by the signatories of the same.

References included in the previous section: Background and current status

1. Grupo Español de Sueño. Documento consenso español sobre el síndrome de apneas-hipopneas del sueño. Arch Bronc 2005; 41: 4
2. Nogueira F, Nigro C, Cambursano H, Borsini E, Silio J, Avila J. Practical guidelines for the diagnosis and treatment of obstructive sleep apnea síndrome. Medicina 2013; 73 (4): 349-62
3. Young T, Palta M, Dempsey J, et al. The occurrence of Sleep disorders breathing among middle aged adults. N Engl J Med 1993; 328: 1230-1236
4. Durán J, Esnaola S, Ramón R, Iztueta A. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 years. Am J Respir Crit Care Med 2001; 163: 685-689
5. Kim J, In K, Kim J, et al. Prevalence of sleep-disordered breathing in middle-aged Korean men and women. Am J Respir Crit Care Med 2004; 170: 1108-13
6. Ip MS, Lam B, Tang LC, et al. A community study of sleep-disordered breathing in middle-aged Chinese women in Hong Kong: prevalence and gender differences. Chest 2004; 125: 127-34
7. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001; 163: 608-13
8. Leung RST, Bradley TD. Sleep apnea and cardiovascular disease. Am J Respir Crit Care Med 2001; 164: 2147-65
9. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. N Engl J Med 1999; 340: 847-51
10. Ronald J, Delaive K, Roos L, Manfreda JH, Kryger MH. Obstructive sleep apnea patients use more health care resources ten years prior to diagnosis. Sleep Res Online 1998; 1(1): 71-4

11. Smith R, Ronald J, Delaive K, Walld R, Manfreda J, Kryger MH. What are obstructive sleep apnea patients being treated for prior to this diagnosis? Chest 2002 Jan; 121(1): 164-72
12. Durán-Cantolla J, Aizpuru F, Montserrat JM, et al. Spanish Sleep and Breathing Group. Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial. BMJ 2010; (24); 341: c5991
13. Cano-Pumarega I, Durán-Cantolla J, Aizpuru F, et al. Obstructive sleep apnea and systemic hypertension: longitudinal study in the general population: the Vitoria Sleep Cohort. Am J Respir Crit Care Med 2011; 184(11): 1299-304
14. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, et al. Spanish Sleep And Breathing Network. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA 2012; 23; 307(20): 2161-8
15. Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ. Randomized placebocontrolled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. American Journal of Respiratory& Critical Care Medicine 1999; 159: 461-467
16. Barnes M, Houston D, Worsnop CJ, et al. A randomized controlled trial of continuous positive airway pressure in mild obstructive sleep apnea. American Journal of Respiratory& Critical Care Medicine 2002; 165: 773-780
17. Zimmerman ME, Arnedt JT, Stanchina M, Millman RP, Aloia MS. Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. Chest 2006; 130(6): 1772-8.
18. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. American Reviews in Respiratory Diseases 1993; 147: 887-895
19. Weaver TE, Kribbs NB, Pack AI, et al. Night-to-night variability in CPAP use over first three months of treatment. Sleep 1997; 20: 278-283.
20. Kribbs NB, Pack AI, Kline LR, Smith PL, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993; 147: 887-95. [Links]
21. Weaver TE, Kribbs NB, Pack AI, et al. Night-to-night variability in CPAP use over the first three months of treatment. Sleep 1997: 20: 278-83. [Links]
22. Nogueira F, De Luca M, Simonelli G, Vera D, Vera S, Rey R. "¿Qué pasa con los pacientes luego de que se les diagnostica Apneas del Sueño?". Rev Am Med Resp 2007; 2: 41-7. [Links]
23. Nogueira F, De Luca M, Simonelli G, Vera D, Vera S, Rey R. ¿Qué pasa con los pacientes con SAHOS luego de que se les indica tratamiento con CPAP?". Abstract en 36vo Congreso Argentino de Medicina Respiratoria. AAMR. Mar del Plata, octubre de 2008
24. Krieger H, Kurtz D, Petiau C, Sforza E, Trautmann D. Long-term compliance with CPAP therapy in obstructive sleep apnea patients and in snorers. Sleep 1996; 19 supl 9:136-43.
25. McArdle N, Devereux H, Heidarnejad H, Engleman HM, Mackay TW, Douglas NJ. Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999;159:1108-1114
26. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurements of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993;147:887-895.
27. Rauscher H, Popp W, Wanke T, Zwick H. Acceptance of CPAP therapy for sleep apnea. Chest 1991;100:1019-1023.

28. Rolfe I, Olson LG, Saunders NA. Long-term acceptance of continuous positive airway pressure in obstructive sleep apnea. Am Rev Respir Dis 1991;144:1130-1133.
29. Sin DD, Mayers I, Man GC, Pawluk L. Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study. Chest 2002;121:430-5.
30. Massie C, McArdle N, Hart R, et al. Comparison between automatic and fixed positive airway pressure therapy in the home. Am J Respiratory& Critical Care Medicine 2003; 167: 20-23
31. Hukins C. Comparative study of autotitrating and fixed-pressure CPAP in the home: A randomized, single-blind crossover trial. Sleep 2004; 27: 1512-1517
32. Mador MJ, Krauza M, Pervez A, Pierce D, Braun M. Effect of heated humidification on compliance and quality of life in patients with sleep apnea using nasal continuous positive airway pressure. Chest 2005; 128: 2151-2158
33. Wiese HJ, Boethel C, Phillips B, Wilson JF, Peters J, Viggiano T. CPAP compliance: Video education may help! Sleep Medicine 2005; 6: 171-174
34. Golay A, Girard A, Grandin S, et al. A new educational program for patients suffering from sleep apnea syndrome. Patient Educ Couns 2006; 60: 220-227.
35. McArdle N, Devereux H, Heidarnejad H, Engleman HM, Mackay TW, Douglas NJ. Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999;159:1108-1114
36. 26. Likar LL, Panciera TM, Erickson AD, Rounts S. Group education sessions and compliance with nasal CPAP therapy. Chest 1997; 111(5): 1273-1277.
37. Antic N, Buchan C, Esterman A, Hensley M, Naugton MT, Rowland S, Williamson B, Windler S,Eckermann S, McEvoy RD. A Randomised controlled trial of nurse led care for symptomatic moderate-severe obstructive sleep apnea. Am J Respir Crit Care Med 2009;179:501-8.
38. Smith I, Nadig V, Lasserson TJ. Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines for adults with obstructive sleep apnoea. Cochrane Database Syst Rev 2009;(2):CD007736.
39. Fletcher EC, Luckett RA. The effect of positive reinforcement on hourly compliance in nasal continuous positive airway pressure users with obstructive sleep apnea. Am Rev Respir Dis 1991;143:936-941.
40. Likar LL, Panciera TM, Erickson AD, Rounds S. Group education sessions and compliance with nasal CPAP therapy. Chest 1997;111:1273-1277.
41. Chervin RD, Theut S, Bassetti C, Aldrich MS. Compliance with nasal CPAP can be improved by simple interventions. Sleep 1997;20:284-289.
42. Hoy CJ, Vennelle M, Kingshott RN, Engleman HM, Douglas NJ. Can intensive support improve continuous positive airway pressure use in patients with the sleep apnea/hypopnea syndrome? Am J Respir Crit Care Med 1999;159:1096-100.
43. Hui DS, Chan JK, Choy DK, Ko FW, Li TS, Leung RC, Lai CK. Effects of augmented continuous positive airway pressure education and support on compliance and outcome in a chinese population. Chest 2000;117:1410-15.
44. Aloia MS, Di Dio L, Ilniczky N, Perlis ML, Greenblatt DW, Giles DE. Improving compliance with nasal CPAP and vigilance in older adults with OAHS. Sleep Breath 2001;5:13-21.
45. DeMolles DA, Sparrow D, Gottlieb DJ, Friedman R. A pilot trial of a telecommunications system in sleep apnea management. . Med Care 2004;42:764- 769.
46. Wiese HJ, Boethel C, Phillips B, Wilson JF,Peters J, Viggiano T. CPAP compliance: video education may help! Sleep Med 2005;6:171-174.
47. Taylor Y, Eliasson A, Andreada T, Kristo D, Howard R. The role of telemedicine in CPAP compliance for patients with obstrucive lseep apnea syndrome. Sleep Breath 2006 ;10:132-8.

48. Smith CE, Dauz ER, Clements F, Puno FN, Cook D, Doolittle G, Leeds W. Telehealth services to improve nonadherence: a placebo controlled study. Telemed J E Health 2006 ;12:289-96.
49. Lewis KE, Bartle IE, Watkins AJ, Seale L, Ebden P. Simple Interventions improve re-attendance when treating the sleep apnoea syndrome. Sleep Medicine 2006;7:241- 247.
50. Tomlinson M, Gibson.Obstructive sleep apnoea syndrome: a nurse-led domiciliary service. J Adv Nurs 2006;55:391-397.
51. Stepnowsky CJ, Palau JJ, Marler MR, Gifford AL. Pilot Randomized Trial of the Effect of Wireless Telemonitoring on Compliance and Treatment Efficacy in Obstructive Sleep Apnea. J Med Internet Res. 2007;9:e14.
52. Richards D, Bartlett DJ, Wong K, Malouff J. Increased adherence to CPAP with a group cognitive behavioral treatment intervention: A randomized trial. Sleep 2007;30:635-40.
53. Meurice JC, Ingrand P, Portier F, Arnulf I, Rakotonanahari D, Fournier E, Philip-Joet F, Veale D; ANTADIR Working Group "PPC", CMTS ANTADIR. A multicentre trial of education strategies at CPAP induction in the treatment of severe sleep apnoea-hypopnoea syndrome. Sleep Med 2007;8:37-42.
54. Damjanovic D, Fluck A, Bremer H, Müller-Quernheim J, Idzko M, han Sorichter S. Compliance in Sleep Apnea Therapy: influence of home care support and pressure mode. Eur Respir J 2009;33:804-11
55. Smith CE, Dauz ER, Clements F, Werkowitch M, Whitman R. Patient education combined in a music and habit-forming intervention for adherence to continuous positive airway (CPAP) prescribed for sleep apnea. Patient Educ Couns 2009;74:184- 90.
56. Sparrow D, Aloia M, DeMolles DA, Gottlieb D. A telemedicine intervention to improve adherence to continuous positive airway pressure: a randomised controlled trial. Thorax 2010;65:1061-66.
57. Parikh R, Touvelle MN, Wang H, Zallek SN. Sleep telemedicine: patient satisfaction and treatment adherence. Telemed J E Health 2011;17:609-14.
58. Olsen S, Smith SS, Oei TP, Douglas J. Motivational interviewing (MINT) improves continuous positive airway pressure (CPAP) acceptance and adherence: a randomized controlled trial. J Consult Clin Psychol 2012;80:151-163.
59. Wang W, He G, Wang M, Liu L, Tang H. Effects of patient education and progressive muscle relaxation alone or combined on adherence to continuous positive airway pressure treatment in obstructive sleep apnea patients. Sleep Breath 2012;16:1049-57
60. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis 1993; 147: 887-95.
61. Hair, J.F, Anderson, R.E., Tathan, R.L. y Black, W.C. (1999). Análisis multivariante. (5ª Ed.). Madrid: Prentice Hall Iberia. Edelman, S., Bell, D. y Kidman, A. (1999). A group cognitive behavior therapy programme with metastatic breast cancer patients. Psychooncology, 8, 295-305.
62. Edelman, S., Lemon, J., Bell y Kidman A. (1999). Effects of group CBT on the survival time of patients with metastatic breast cancer. Psychooncology, 8, 474-481.
63. Goodwin, P., Leszcz, M., Ennis, M., Koopmans, J., Vincent, L., Guther, H.,Hunter, J. (2001). The effect of group psychosocial support on survival in metastatic breast cancer. New England Journal of Medicine, 345, 1719-1726.

HYPOTHESIS

The stratification / segmentation of the patient allows the elaboration of an individualized plan to improve adherence to treatment with CPAP, using telemonitoring for a specific profile; this stratification improves adherence to CPAP treatment of sleep apnea.

OBJECTIVES

Main goal:

● Improve adherence to CPAP treatment. To measure this variable, the definition of adherence / compliance with SEPAR is taken as a criterion: 3.5 hours per night.

Secondary objective:
● Identify the characteristics of patients that influence the development of their CPAP treatment plan.
● Develop an individualized plan to improve adherence based on the patient's profile and personal characteristics.
● Use telemonitoring for patients at risk of low adherence to improve compliance.

EXPECTED RESULTS

• Adherence is multidimensional and this implies the development of an individualized plan. (Rotenberg, Murariu, Pang, 2016; Sawyer, Gooneratne, Marcus, Ofer, Richards, Weaver, 2013; Ibarra, Morillo, Rudi, Ventura, Navarro, 2013).
• Adherence improves when patient characteristics, disease characteristics, technological factors, clinical factors such as side effects, psychological factors, and social factors are taken into account. (Rotenberg, Murariu, Pang, 2016)
• Influence on adherence to mood, perception of self-efficacy and expectations. (Orruño, Asua, 2016).
• The actions carried out at the beginning of treatment are key to improving adherence. (Orruño, Asua, 2016; Rotenberg, Murariu, Pang, 2016).
• Educational actions improve adherence results, without negative effects. (Rizk AK, Wardini R, Chan-Thim E, Bacon SL, Lavoie KL, Pepin. 2015)
• Support and follow-up measures such as protocolized telephone follow-up and telemonitoring improve adherence. (Ruiz-López, 2009; Rotenberg, Murariu, Pang, 2016)
• The Adhesion Improvement Plan based on a cost-effectiveness balance achieves better adherence results. (Ibarra, Morillo, Rudi, Ventura, Navarro, 2013).

METHODOLOGICAL SECTION

1. Design. Experimental, prospective and controlled study. All participants will sign informed consent after knowing in depth the objectives, methods and risks of the study. The CONSORT Criteria for non-pharmacological trials will be followed (Boutron, Moher, Altman, Schulz & Ravaud, 2008).
2. Sample size: The sample size is defined by the research design, in which the subjects are randomly distributed to the two experimental conditions, that is, the Control Group and the PIMA Group. It is thus necessary to determine at the beginning the minimum size of the groups based on the following factors. Taking into account that the intervention process is based on the motivational interview, in the first place, we establish a type I error of 0.05, and a type II error of 0.20 (power = .8), as is usually assumed in research in the framework of the study of the therapeutic efficacy of motivational / psychological interventions (Hair, Anderson, Tathan & Black, 1999). On the other hand, reviews of previous research on the efficacy of motivational / psychological interventions on the outcome variables to be considered (behavioral change / adherence, quality of life), revealed that there are hardly any studies of this nature, without detail data on standardized effect size that serve as a starting point in defining, among other aspects, the ideal sample size for our research. Due to the characteristics of the existing studies (Edelman, Bell and Kidman, 1999; Edelman, Lemon, Bell and Kidman, 1999; Goodwin et al. 2001), we observed effect size values around 0.50. In addition, for a study such as the one proposed in this study, a sufficient number of subjects is required to allow observing and assuming the normality of the scores in the variables considered, as well as performing multivariate analyzes, with a sufficient number of observations to carry them out.

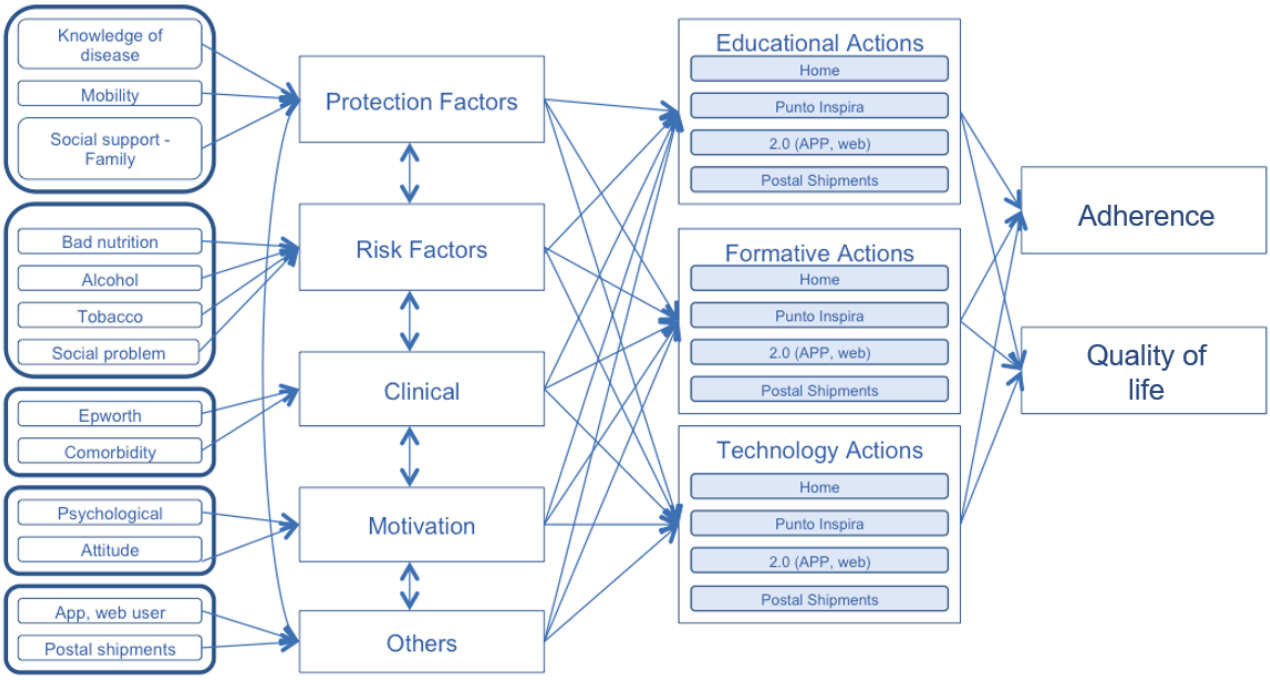
finished. For all the above considerations, we conclude that around 33 subjects per group would be the size of the sample necessary to assess the therapeutic efficacy of the interventions developed. On the other hand, we take into account the type of patient we are dealing with, who may be abandoned, for which a number of 35 subjects per group is established (anticipating a certain experimental mortality). The design effect size as defined is d = 0.60, which is a moderate effect size.

3. Stages of the study:

3.1. Referral / recruitment phase and randomization. In patients diagnosed with OSA, 2 groups of at least 35 patients will be constituted. Following the CONSORT Criteria (Boutron, Moher, Altman, Schulz & Ravaud, 2008) for non-pharmacological trials, the randomization method has been selected through a simple method: each time the prescribers evaluate the sleep test, they include in one of the two groups according to the following randomization algorithm: each patient is assigned to a group alternatively, that is, one patient is assigned to the Control group and the next to the PIMA group; This sequence is followed in 6 pairs, being that the following 6 pairs were assigned starting with one patient to the PIMA group and another to the Control group later. This allocation mechanism is also the one used to compensate for experimental mortality in both groups. In this way 2 groups will be configured:

- 1) Control Group or PIMA 0, which will start treatment with regular CPAP WITHOUT stratification;
- 2) PIMA 1 Group, which will start treatment according to stratification; This will be the result of a comprehensive initial evaluation and the result of stratification.

3.2. Stratification process: To achieve stratification, two types of variables are taken into account that the bibliography indicates influence the treatment of CPAP: personal variables and modulating variables. Personal variables are those that refer to patient characteristics. These are grouped into 4 categories: protective factors, risk factors, clinical factors and motivation (in the case of OSA). The following figure shows the set of variables used for patient stratification, and their relationship with individualized protocols.



Regarding the modulating variables, these refer to the characteristics of both the patient's environment (distance between the patient's home and the hospital) or relative to options and

preferences of the service (use of app, email; preference for home visit or in consultation, etc.)

The modulating variables that are taken into account for stratification are:

Profile	Age	Socio-Cultural Level	Accessibility	Technologies 2.0	2.0 Mobility
a	≤50 years	High	Isocrhone ≤20 min	Use app, email, internet	Registration: Punto Inspira, accepts postal shipments
b	>51 years	Medium	Isocrhone >20<40 min	Use internet, with or without email	Media: Punto Inspira, can accept postal shipments
c	>70 years	Low	Isocrhone ≥40 min	Not use of app, internet, email	Low: No Punto Inspira or accept postal shipments

For personal variables, the Perceived Competence Evaluation Questionnaire is used, and the Epworth Scale Test and the Motivation Initial Assessment Questionnaire. This questionnaire has "predictive" capacity. Through this questionnaire, we know if the patient has assimilated the necessary knowledge to start therapy, information and knowledge of the disease, information and knowledge about the treatment, perception of the benefits of the therapy team, clinical stability, compliance with other treatments, social support, bad eating habits, bad exercise habits, sedentary lifestyle, tobacco and / or alcohol consumption and social problems.

With the information from the initial questionnaire and the identified profile, the healthcare provider calculates the stratification label that will determine the best treatment plan for each patient. The clinical situation of the patient is taken into account at all times. The components that determine the patient segmentation label and that will involve the development of a treatment plan or another are: type of diagnosis of OSA (mild, moderate, severe), AHI of the sleep test, patient profile, level of patient motivation, scores obtained in the questionnaire in general and the score obtained in the Epworth test. The results can be:

- High adherence
- Moderate Adhesion
- Low Adherence

Regarding telemonitoring, it is used in patients who in stratification have obtained a label of low adherence:

- The patient who is telemonitored must sign their consent for said procedure to be carried out.
- The monitoring parameters are:Horas cumplimiento
    - IAH
    - Leakage (loss of air from the sides of the mask)

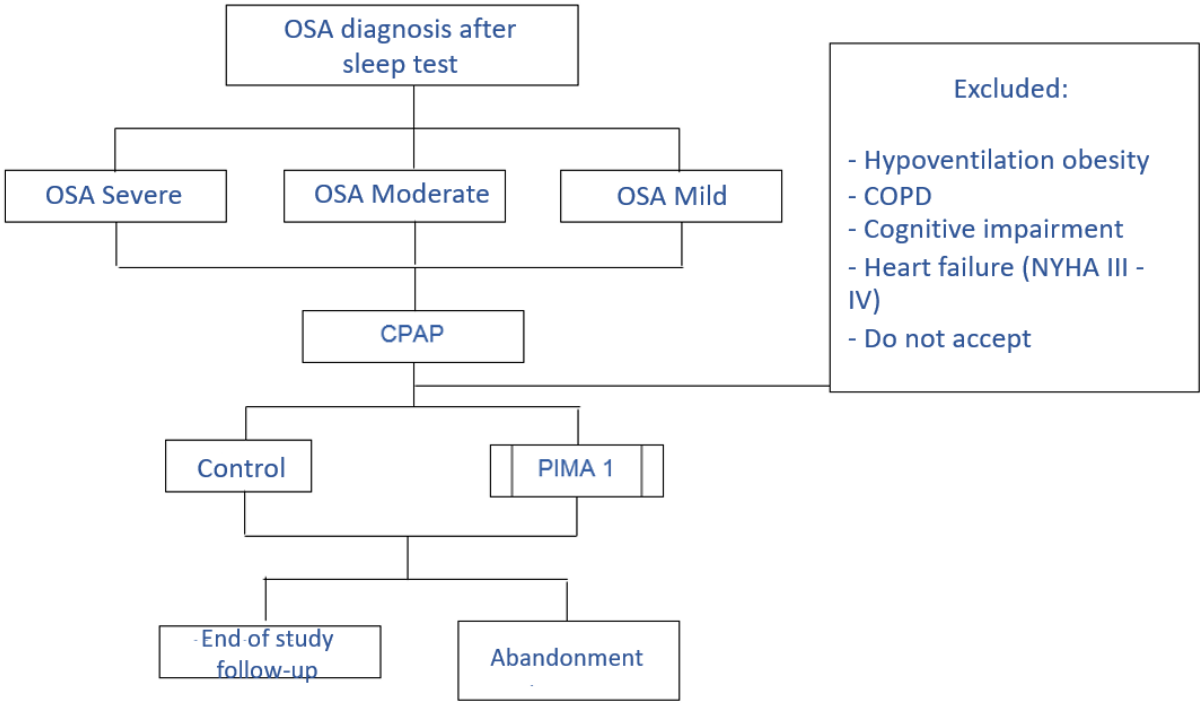
To know these parameters, the CPAP provider's platform will be accessed, which includes telemonitoring. In this case it is PHILIPS, and the platform is EncoreAnywhere.

The monitoring and visualization of the alerts will be carried out with a determined periodicity: Day 10, Day 20, Day 30 of the period after low adherence detection.
The alerts (situations that imply poor evolution and need to notify the prescriber) are the following:

- - Hours <4
- AHI> X + Hours <4
- IAH> X + Hours> 4
- Leaks> Y

Prescribing physician information report: a report is extracted in PDF format that is reported to the prescribing physician.

3.1. Monitoring and control of adherence. All measurements will be performed in 4 times: Day 1 - Day 30 - Day 60 - Day 90 – Day 180. In the Control Group, the usual methodology of treatment with CPAP will be used. In PIMA 1 Group, the methodology will be used according to the Individualized Adherence Improvement Plan arising from stratification.



3.2. Analysis of results.

Descriptive variables (characterize the sample used and make the study replicable and transparent, thus contributing to generalization). Study of initial homogeneity: categorical variables ($\chi 2$) + associated effect size. Quantitative variables: Student's t test for independent samples, correction (Levene's test).

- Hypothesis:
  - T-tests of means of related samples (to know if through the different interventions there are improvements in adherence and quality of life, they report the effects on the outcome variables)
  - Model of structural equations (to know the relationships between protection and risk factors and educational, training and technological actions)

- Independent samples t-test (know the significance associated with the differences between the two interventions)
- Analysis of variance (ANOVA) (differences were due to the type of intervention in combination with some other categorical variable)
- Linear correlations (know the interrelation between the so-called gains or aspects of change of the 2 interventions)
- Effect size:
    - or (Cohen's d = t / rN) (value exceeds 0.30, which is equivalent to a moderate-high effect size, greater in any case than 0.60)

3.1. Subjects of study.

Inclusion criteria: Being over 18 years of age, OSA diagnosis for whom CPAP treatment has been prescribed)

Exclusion criteria:

- Hypoventilation obesity
    - severe COPD
        - (FEV1 (%) = <50%)
        - mMRC> 2
    - Cognitive disorders
    - ICC (NYHA: Grade III and IV)
    - or reject

4. Variables

- **Sociodemographic variables:** age, gender, marital status, educational level, ...
- **Clinical variables:** No. hours of CPAP use, IAH (TM), Leakage (TM), side effects.
- **Independent variables:** Stratification / Segmentation vs “SEPAR” Model**.**
- **Dependent variables:** adherence, quality of life.
- **Modulating variables:** PROFILE, protective factors, risk factors, motivation

ETHICAL ASPECTS AND MEASURES TO MAINTAIN THE CONFIDENTIALITY OF THE DATA

The prescribers and healthcare personnel participating in this Study undertake not to disclose in any way to third parties or to use Confidential Information of patients outside the study. Confidential Information shall be understood to be information that, regardless of its physical or digital medium or otherwise, is confidential (whether or not it is indicated therein or is derived from its nature) to the extent that:

1. is secret in the sense that it is not, as a body or in the precise configuration and assembly of its components, generally known or easily accessible to persons introduced into the circles in which the type of information in question is normally used;
2. has a commercial value because it is secret; and
3. has been subject to reasonable measures, under the circumstances, to keep it secret, taken by the person who legitimately controls it

The execution and development of the Study will give rise to access by healthcare personnel and prescribers to personal data of natural persons, especially patients, responsibility of the Hospital. That is why all of them expressly undertake to treat such data in compliance with the provisions of Organic Law 15/1999, of December 13, on Data Protection and other regulations that modify or develop this matter, and as of December 25 May 2018, in Regulation (EU) No. 2016/679, of April 27, 2016, guaranteeing the security, confidentiality and integrity of personal data that may be accessed or subjected to treatment within the framework of This studio.

The registration of the information will be carried out following the procedure of the Hospital Universitario de La Princesa, that is, all indications derived from internal regulations will be respected. The participants of this Study undertake to keep the strictest reserve and confidentiality regarding the Personal Data accessed during the execution of the Project work.
The main researchers undertake to implement the appropriate technical and organizational measures, in accordance with article 32 of the RGPD, to guarantee the security of Personal Data.

The principal investigators of this Study guarantee that all the participants have assumed generic confidentiality obligations regarding the information they access in the performance of their duties.

SCHEDULE

Activity / Task
Recruitment, constitution of study subgroups, obtaining clinical and functional information, clinical review of participants.

J	F	M	A	M	J	J	A	S	O	N	D
				X	X	X	X				

Activity / Task
Comprehensive evaluation of patients. Educational process. PIMA identification.

J	F	M	A	M	J	J	A	S	O	N	D
				X	X	X	X	X			

Activity / Task
Cross-sectional analysis of results

J	F	M	A	M	J	J	A	S	O	N	D
								X	X		

Activity / Task
Longitudinal analysis of results

J	F	M	A	M	J	J	A	S	O	N	D
									X	X	X

EXPERIENCE OF THE RESEARCH TEAM ON THE TOPIC

The clinical team of Hospital Universitario La Princesa maintains a specific and continuous care activity, being a reference in the area for the treatment of sleep.
VitalAire, Air Liquide Healthcare's therapy activity, has been in home respiratory therapy treatments for more than 30 years.

DIFFUSION PLAN
1) Clinical impact, assistance and / or technological development. This project has a great impact and clinical and technological significance. From a clinical point of view, the aim is to identify the patient in order to better serve him and ensure adherence to one of the treatments where it is more complex to achieve patient compliance.
2) Bibliometric impact. This project is expected to lead to world-class, high-impact publications.
3) Technological development. This project includes the development of computer applications that allow optimization of resources and better assistance.

RESOURCES AVAILABLE TO CARRY OUT THE PROJECT

Consult “Punto Inspira” located in the Hermanos García Noblejas Specialty Center, belonging to the La Princesa University Hospital area.

Resources of VitalAire, concessionary company of home respiratory therapies of the Hospital Universitario de La Princesa: healthcare personnel, computer, telephone, data line, specific applications, transport vehicles, educational material ...

ANEX

Informed consent sheet for the patient complying with the regulations in this regard.

INFORMED CONSENT

Study on the individualization of a plan to improve adherence in patients with sleep apnea receiving CPAP treatment

We offer you the opportunity to participate in this study, which aims to deepen our understanding of the treatment of sleep apnea with CPAP. Thus, its results will contribute to improving the care and treatment of sleep apnea.

Once you have expressed your desire to participate in this study, the PROCEDURE will be as follows: you will be educated and trained in CPAP treatment. After this, you will be asked a series of questions related to sleep apnea, treatment, expected benefits, etc. We ask that you answer as honestly as possible. We will carry out a monthly monitoring of the evolution of compliance with the treatment. In this follow-up we will pass you questionnaires about the treatment. It will also be necessary to work with the data that the CPAP team reports, and which will be recorded by the healthcare personnel of the company responsible for the team. It is possible that at a certain time you continue treatment with a CPAP that includes telemonitoring (knowing data remotely or telematically); in this case you will be informed in detail.

YOUR RIGHT as a participant is to be informed of any aspect related to the study. If you have any questions regarding this research, your rights as a participant, or about any other aspect, you can communicate it to the person conducting the interview, or also to those responsible for this research that appear at the end of this consent. Since your participation is completely voluntary, you can withdraw at any time. This withdrawal will not affect any aspect of your present or future treatment.

Regarding the CONFIDENTIALITY OF THE DATA, the researchers of this study inform you that the data collected in this study have an exclusively clinical and scientific purpose. Your personal data will be used exclusively by the members of the research team. In accordance with the legislation on data protection currently in force in Europe (Regulation 679/2006 on the Protection of Personal Data), your clinical information will be registered in a way that does not include your personal data, which will be duly pseudonymised to guarantee its confidentiality .

Informed consent:

I, _____, I have been informed by _____ about this study, and I give my consent to the researchers to use my data exclusively for the conduct of this study. No personal information will be used for other purposes or given to any other third party. I have been informed of the possibility of leaving the study at any time for any reason.

In _____, at ____ of _____ de 201__

Responsible researchers:

Dr. Enrique Zamora	Dr. Pedro Landete	Dr. David Rudilla	Cristina Santos
Assistant Physician	Assistant Physician	Psychologist	Healthcare manager
Pneumology	Pneumology	VitalAire	VitalAire