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Caractérisation des différents phénotypes du syndrome d'apnée du sommeil et prédiction de la réponse thérapeutique

Characterization of different phenotypes of sleep apnea syndrome and prediction of therapeutic response

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Résumé

Le syndrome d'apnées obstructives du sommeil (SAOS) est une maladie très répandue à l'échelle mondiale qui se caractérise par des arrêts respiratoires répétés au cours du sommeil. Le SAOS est associé à de nombreux symptômes, notamment la somnolence, et à des comorbidités cardio-métaboliques. Le SAOS est majoritairement traité par pression positive continue (PPC), un dispositif médical qui envoie de l'air sous pression dans les voies aériennes supérieures du patient empêchant ainsi le collapsus pharyngé et les arrêts respiratoires nocturnes.

La grande hétérogénéité clinique du SAOS, l'association fréquente à d'autres maladies chroniques et la disponibilité croissante de données longitudinales issues des dossiers médicaux électroniques (DME) et des objets connectés soulèvent la question de la caractérisation fine et dynamique des phénotypes de patients SAOS en conditions de vie réelle. Cette problématique constitue le fil conducteur de ce travail de thèse.

Dans un premier article, nous avons caractérisé avec une approche multidimensionnelle les patients ayant une combinaison SAOS et bronchopneumopathie chronique obstructive, appelée overlap syndrome (Sleep Medicine, 2024, 1ère auteure). L'amélioration de la caractérisation de ces profils obtenue à partir d'un DME et l'utilisation d'objets connectés permet de proposer une meilleure prise en charge de ces patients.

Nous avons ainsi étendu nos travaux à l'analyse de données longitudinales multidimensionnelles issues des DME et d'objets connectés. Ces données complexes nécessitent une approche méthodologique appropriée qui décrit les données, définit spécifiquement la question de recherche et choisit la méthode statistique adaptée. Nous avons proposé une synthèse des principales méthodes appliquées aux données longitudinales dans un deuxième article afin de permettre une meilleure appropriation et compréhension de ces méthodes dans le domaine des troubles du sommeil (Sleep Medicine, 2025, 1ère auteure).

Ces approches longitudinales ont pu être appliquées à des questions de recherche clinique, notamment l'évolution dans le temps de l'utilisation des objets connectés comme les tensiomètres connectés pour mesurer l'évolution de la pression artérielle (PA) des patients à haut risque d'événements cardiovasculaires ou l'utilisation du télémonitoring pour mesurer l'observance de la PPC des patients atteints de SAOS. Comme il est également important de bien prendre en compte les profils de patients à risque d'abandon de mesures dans les analyses de données longitudinales, nous avons étudié l'évolution respective de l'utilisation du tensiomètre connecté et de l'utilisation observante de la PPC (Lettre de recherche soumise au journal Sleep Medicine, avril 2026, 1ère auteure). Il nous a été possible de caractériser en situation de vie réelle grâce à l'utilisation d'un tensiomètre connecté, à domicile, et à l'utilisation du télémonitoring de la PPC, l'évolution de la PA chez les patients souffrant d'un SAOS traités par PPC (Annals of ATS, 2025, 1ère auteure). Plus précisément, du point de vue symptomatique, l'impact de la somnolence dans la réponse de la PPC en termes de PA n'est pas précisément connu. Il existe, dans la littérature, une association entre somnolence et événements cardiovasculaires et entre somnolence, événements cardiovasculaires et PPC. Cependant, la plupart des études sur la PA sont réalisées sur des patients non-somnolents. Nous avons donc, dans une lettre de recherche, analysé l'évolution de la PA chez des patients souffrant de SAOS traités par PPC selon leur statut somnolent ou non somnolent au diagnostic (Annals of ATS, 2026, 1ère auteure).

En synthèse, ce travail de thèse apporte des données originales tant sur le plan méthodologique que clinique, concernant le phénotypage multidimensionnel longitudinal du SAOS.

Mots-clefs : données longitudinales ; pression artérielle diastolique ; pression artérielle systolique ; pression positive continue ; observance ; somnolence ; syndrome d’apnées du sommeil ; télémonitoring ; trajectoires

Abstract

Obstructive sleep apnea syndrome (OSAS) is a widespread global disease characterized by repeated breathing interruptions during sleep. OSA is associated with numerous symptoms, including sleepiness, and cardio-metabolic comorbidities. OSA is mainly treated with continuous positive airway pressure (CPAP), a medical device that sends pressurized air into the patient's upper airway, preventing pharyngeal collapse and nocturnal breathing interruptions.

The wide clinical heterogeneity of OSA, its frequent association with other chronic diseases, and the growing availability of longitudinal data from electronic medical records (EMR) and connected devices raise the question of the detailed and dynamic characterization of OSAS patient phenotypes in real-life conditions. This issue is the central theme of this thesis.

In a first article, we used a multidimensional approach to characterize patients with a combination of OSA and chronic obstructive pulmonary disease, known as overlap syndrome (Sleep Medicine, 2024, first author). Improved characterization of these profiles obtained from EMR and the use of connected devices enable better patient care.

We have therefore extended our work to the analysis of multidimensional longitudinal data from EMRs and connected devices. These complex data require an appropriate methodological approach that describes the data, specifically defines the research question, and selects the appropriate statistical method. We have proposed a summary of the main methods applied to longitudinal data in a second article in order to enable better understanding and appropriation of these methods in the field of sleep disorders (Sleep Medicine, 2025, first author).

These longitudinal approaches have been applied to clinical research questions, including the evolution over time of the use of connected devices such as connected blood pressure (BP) monitors to measure changes in BP in patients at high risk of cardiovascular events, and the use of telemonitoring to measure CPAP adherence in patients with OSA. As it is also important to take into account the profiles of patients at risk of discontinuing treatment in longitudinal data analyses, we studied the respective evolution of connected blood pressure monitor use and CPAP compliance (research letter submitted to the journal Sleep Medicine, April 2026, first author). Using a connected blood pressure monitor at home and CPAP telemonitoring, we were able to characterize the evolution of BP in patients with OSA treated with CPAP in a real-life setting (Annals of ATS, 2025, first author). More specifically, from a symptomatic point of view, the impact of sleepiness on the CPAP response in terms of BP is not precisely known. The literature shows an association between sleepiness and cardiovascular events, and between sleepiness, cardiovascular events, and CPAP. However, most studies on BP are conducted on non-sleepy patients. We therefore analyzed, in a research letter, the evolution of BP in patients with OSA treated with CPAP according to their sleepiness status at diagnosis (Annals of ATS, 2026, first author).

In summary, this thesis provides original data, both methodologically and clinically, on the multidimensional longitudinal phenotyping of OSA.

Keywords: adherence; continuous positive airway pressure; diastolic blood pressure; longitudinal data; sleep apnea syndrome; sleepiness; systolic blood pressure; telemonitoring; trajectories

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Abréviations

ANOVA, analysis of variance

ARIMA, autoregression integrated moving average

BPCO, bronchopneumopathie chronique obstructive

ESS, Epworth sleepiness scale

GBTM, group-based trajectory modelling

GMM, growth mixture modelling

HMM, hidden Markov model

IAH, indice d'apnées-hypopnées

LTA, latent transition analysis

MARS, multimorbidity apnea respiratory failure sleep database

OS, overlap syndrome

PA, pression artérielle

PPC, pression positive continue

PSG, polysomnographie

SAOS, syndrome d'apnées obstructive du sommeil

Publications dans des revues internationales à comité de lecture

Article original n°1 : **Ophélie Coiffier**, Pasquale Tondo, Marie Joyeux-Faure, Renaud Tamisier, Khier Amrani, Jean-Claude Cornu, Robin Terrail, Christian Caussé, Sébastien Bailly, Jean-Louis Pépin, on behalf of e-Meuse investigators. Multidimensional phenotyping to distinguish among distinct obstructive sleep apnea, chronic pulmonary disease, and overlap syndrome phenotypes. Sleep Medicine, 2024, https://doi.org/10.1016/j.sleep.2024.04.038

Article original n°2 : **Ophélie Coiffier**, Ina Jandric, Christian Caussé, Jean-Louis Pépin, Monique Mendelson, Sébastien Bailly. An overview of longitudinal data analyses in sleep research. Sleep Medicine, 2025, https://doi.org/10.1016/j.sleep.2025.106871

Lettre de recherche n°1 : **Ophélie Coiffier**, Sébastien Bailly, Marie Joyeux-Faure, Renaud Tamisier, Khier Amrani, Jean-Claude Cornu, Thibaut Gentina, Robin Terrail, Christian Caussé, Jean-Louis Pépin, on behalf of eMEUSE and SLEEPCONNECT investigators. Respective evolution of the completion rate of home self-measurements of blood pressure and continuous positive airway pressure adherence rate in obstructive sleep apnea. Sleep Medicine, soumis, avril 2026

Article original n°3 : **Ophélie Coiffier**, Sébastien Bailly, Marie Joyeux-Faure, Renaud Tamisier, Khier Amrani, Jean-Claude Cornu, Thibaut Gentina, Robin Terrail, Christian Caussé, Carolina Lombardi, Martino F.Pengo, Gianfranco Parati, Jean-Louis Pépin, on behalf of eMEUSE and SLEEPCONNECT investigators. Home Blood Pressure Trajectories during 6 Months of Continuous Positive Airway Therapy, Results from the eMEUSE-SANTE and SLEEPCONNECT Clinical Trials. Annals of ATS, 2025, DOI: 10.1513/AnnalsATS.202505-504OC

Lettre de recherche n°2 : **Ophélie Coiffier**, Sébastien Bailly, Marie Joyeux-Faure, Renaud Tamisier, Khier Amrani, Jean-Claude Cornu, Thibaut Gentina, Robin Terrail, Christian Caussé, Carolina Lombardi, Martino F. Pengo, Gianfranco Parati, Jean-Louis Pépin, on behalf of e-Meuse and Sleep Connect investigators. Home blood pressure trajectories during 3 months of continuous positive airway pressure therapy in sleepy vs. non-sleepy patients. Annals of ATS, 2026

Participation à des congrès/conférences

Présentation de posters aux congrès/conférences :

- European Respiratory Society 2024, septembre 2024, Vienne, Autriche

- Sleep and Breathing 2025, avril 2025, Anvers, Belgique

- American Thoracic Society 2025, mai 2025, San Francisco, EU, soumission de l'abstract faite par Ophélie Coiffier et présentation réalisée par Pr. Jean-Louis Pépin

- European Respiratory Society 2025, septembre 2025, Amsterdam, Pays-Bas

- Congrès du Sommeil 2025, novembre 2025, Strasbourg, France

I. Introduction générale sur le syndrome d'apnées du sommeil

Le Syndrome d'Apnées du Sommeil - définition

Le syndrome d'apnées du sommeil (SAS) est caractérisé par des arrêts respiratoires réguliers au cours du sommeil (plus de 5 ou plus de 15 par heure de sommeil) et peut être d'origine centrale ou obstructive. Dans le cadre de ce manuscrit, nous nous intéresserons uniquement au syndrome d'apnées obstructives du sommeil (SAOS) qui est caractérisé par des épisodes répétés de collapsus complet ou partiel des voies aériennes supérieures au niveau du pharynx (Figure 1).

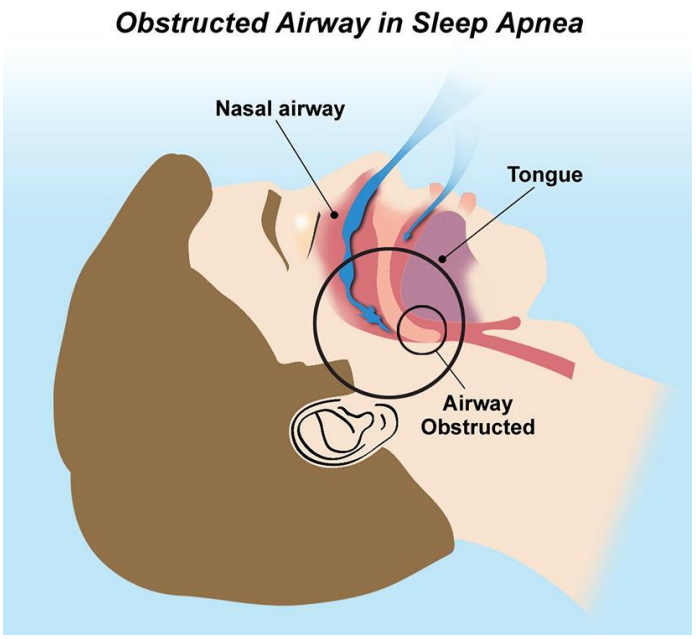


Figure 1. Mécanismes du SAOS
Source : Bailey et al., 2010 [1]

Le SAOS a une prévalence globale importante, estimée à près d'un milliard de personnes affectées[2] dans le monde (5-15% de la population globale[3]) et pouvant atteindre une prévalence de plus de 50% dans certains pays[2]. De surcroît, les projections en 2050 annoncent une augmentation de patients atteints de SAOS, du fait des épidémies d'obésité et de diabète de type 2 et du vieillissement de la population[4]. En France, en 2017, la prévalence des patients non traités pour un SAOS mais présentant une probabilité significative d'avoir ce syndrome (mesuré par le questionnaire de Berlin) était de 18.1% et celle des participants traités était de 3.5%. Ainsi, la prévalence pondérée totale de l'apnée du sommeil traitée ou du risque élevé de SAOS était de 20.9% en France, en 2017[5]. Le SAOS représente par conséquent un problème de santé publique, un fardeau à la fois individuel pour le patient mais également médical, économique et social[4–8].

Le Syndrome d'Apnées du Sommeil – hétérogénéité de la pathologie et des phénotypes

Les multiples phénotypes de présentation du SAOS[9] rendent le diagnostic parfois plus difficile et justifient une caractérisation multidimensionnelle de la maladie[5]. Les comorbidités associées aggravent le SAOS et augmentent les risques de décès[3]. Plusieurs analyses de cluster se sont attachées à caractériser des groupes homogènes de patients en termes de présentation clinique, de comorbidités et de pronostic[10–13]. Plusieurs associations comorbides pertinentes ont aussi été rapportées. C'est le cas des « overlap » syndromes avec le SAOS, c'est-à-dire la coexistence d'un SAOS et d'une seconde maladie comme par exemple la bronchopneumopathie chronique obstructive (BPCO). La BPCO est la maladie respiratoire la plus courante dans le monde, correspondant à une obstruction bronchique chronique, avec une prévalence mondiale de 13.1%[14] et une prévalence française estimée à 7.5%[15]. Les patients souffrant d'un OS ont une présentation clinique qui associe les symptômes et comorbidités du SAOS et ceux de la BPCO, complexifiant le diagnostic du SAOS qui est, par conséquent, sous-estimé chez ces patients[16–18]. Cette comorbidité fréquente du SAOS amène à une prévalence haute de l'OS en population générale[19] (28.3% des patients BPCO parmi les 41 études incluses dans l'étude de Li et al.[20]) et en France (4.3%[21] des patients traités par PPC). D'autres comorbidités ou complications sont également associées au SAOS et à la BPCO comme le diabète[22] ou les accidents de la route[23,24] mais les comorbidités cardiovasculaires (accident vasculaire cérébral, arythmie, coronaropathie, insuffisance cardiaque, infarctus du myocarde, fibrillation auriculaire, etc.) sont plus courantes dans l'overlap syndrome que dans le SAOS ou la BPCO pris isolément[19,22,25]. En particulier, l'hypertension artérielle (une pression artérielle anormalement élevée) est une comorbidité prédominante parmi les patients présentant un SAOS[26]. Hypertension et syndrome d'apnées du sommeil partagent de nombreux facteurs de risque comme l'obésité et un mode de vie sédentaire et les patients hypertendus ont une plus grande prévalence de SAOS qu'en population générale. De plus, d'après les données collectées ces dernières années, entre 80% et 90% des patients ayant une hypertension résistante, souffrent d'un SAOS[25].

Le Syndrome d'Apnées du Sommeil - facteurs de risque

La survenue du SAOS peut être favorisée par différents facteurs de risque[5]. En effet, certains facteurs sont associés à un risque plus élevé de SAOS comme l'obésité[27–29], l'indice de rondeur corporelle[27,30] ou BPI (body roundness index) qui évalue la distribution des graisses corporelles, un large tour de cou[27,29,30], le sexe masculin[29,31–33], un âge avancé[29], de mauvaises règles d'hygiène de vie (tabagisme[29,34], alcoolisme[29,35,36]) ou une hypertrophie des tissus mous pharyngés et/ou un profil maxillo-facial[3,37,38] à risque avec une rétrognathie ou une rétromaxillie. Plus généralement, la prévalence du SAOS augmente en population générale dû notamment aux épidémies d'obésité et de diabète de type 2 et au vieillissement de la population[4,8].

Le Syndrome d'Apnées du Sommeil - symptômes

Une multiplicité de symptômes parfois non spécifiques sont associés à l'hétérogénéité de la maladie[5,9]. En effet, les ronflements[5], les apnées détectées par l'entourage et les éveils nocturnes conduisent à un sommeil fragmenté et non réparateur[3] ; la fatigue[39,40], une concentration réduite[39,41], des changements de personnalité[42], la dépression[43], les déficits cognitifs et de l'attention[44–46] font partie des nombreux symptômes d'un patient souffrant de SAOS[25,47]. Cependant, le symptôme le plus

commun est la somnolence diurne[39,40,48,49] (50% des patients SAOS) qui se définit par une tendance à l'endormissement dans des situations inadaptées au cours de la journée[50,51]. Ce symptôme subjectif peut être mesuré par des tests objectifs comme les tests de maintien de l'éveil[24,52] ou les tests itératifs des latences d'endormissement[52] mais la première évaluation de la somnolence et la plus utilisée car plus facile et rapide qu'un test objectif, est le questionnaire mesurant le score d'Epworth (Epworth Sleepiness Score (ESS))[49,53].

Le Syndrome d'Apnées du Sommeil - diagnostic

Pour diagnostiquer le SAOS, les paramètres de sommeil, cardiovasculaires et respiratoires du patient doivent être enregistrés au cours d'une nuit, en laboratoire du sommeil ou à domicile selon la technique envisagée. Deux techniques sont essentiellement utilisée en pratique quotidienne : la polygraphie ventilatoire surtout réalisée à domicile et sans paramètres de sommeil[3] et la polysomnographie (PSG)[3]. Actuellement, le supposé « gold standard » du diagnostic du SAOS est la PSG qui associe des paramètres ventilatoires, une oxymétrie et une étude de l'activité cérébrale par électroencéphalogramme, une étude de l'activité oculaire par électro-oculogramme et une étude du tonus musculaire du menton par électromyogramme (Figure 2)[3,54,55]. La PSG peut être effectuée en ambulatoire ou au sein d'un laboratoire du sommeil où un technicien entraîné équipe, pour la nuit le patient et supervise son enregistrement.

Ensuite, les données issues de ces enregistrements sont analysées pour déterminer la présence et la sévérité du SAOS. L'indice d'apnées-hypopnées (IAH) est la métrique de référence permettant de détecter un SAOS, et c'est celle utilisée dans nos analyses pour apprécier la sévérité du SAOS ; bien que d'autres mesures soient exploitables comme l'indice de désaturation en oxygène ou l'indice de perturbations respiratoires. L'IAH est défini comme le rapport du nombre total d'événements (apnées, hypopnées) sur le nombre d'heures de sommeil au cours d'une nuit d'étude du sommeil ; une apnée correspondant à une baisse du flux d'air supérieure ou égale à 90% du flux de base avant l'événement, et une durée de réduction du flux supérieure ou égale à 10 secondes[56,57], et une hypopnée correspondant à une réduction du débit d'air d'au moins 30% pendant plus de 10 secondes, accompagnée soit d'une désaturation en oxygène d'au moins 3-4%, soit d'un éveil nocturne mesuré par l'électroencéphalogramme[2,54–58]. L'IAH permet donc de déterminer la sévérité du syndrome[58] : un sujet sain présente un IAH inférieur à 5 événements/h, un SAOS léger équivaut à un IAH compris entre 5 et 15 événements/h, un SAOS modéré équivaut à un IAH entre 15 et 30 événements/h et un SAOS sévère équivaut à un IAH supérieur à 30 événements/h.

Traditionnellement, le diagnostic du SAOS repose sur une polysomnographie nocturne réalisée dans une clinique du sommeil, ce qui nécessite beaucoup de ressources humaines et ne tient pas compte de la variabilité entre les nuits des marqueurs de sévérité du syndrome d'apnées du sommeil, tels que l'indice d'apnée-hypopnée[54,59–62]. Parmi les principales améliorations qui pourraient être apportées à la stratégie de diagnostic du syndrome d'apnées du sommeil sont les innovations technologiques. Une analyse automatique par intelligence artificielle permettant des tests à domicile sur plusieurs nuits sont en cours de développement pour simplifier, améliorer l'accès et réduire les coûts des tests diagnostics tout en évitant les erreurs de classification de la gravité du SAOS[63–70].

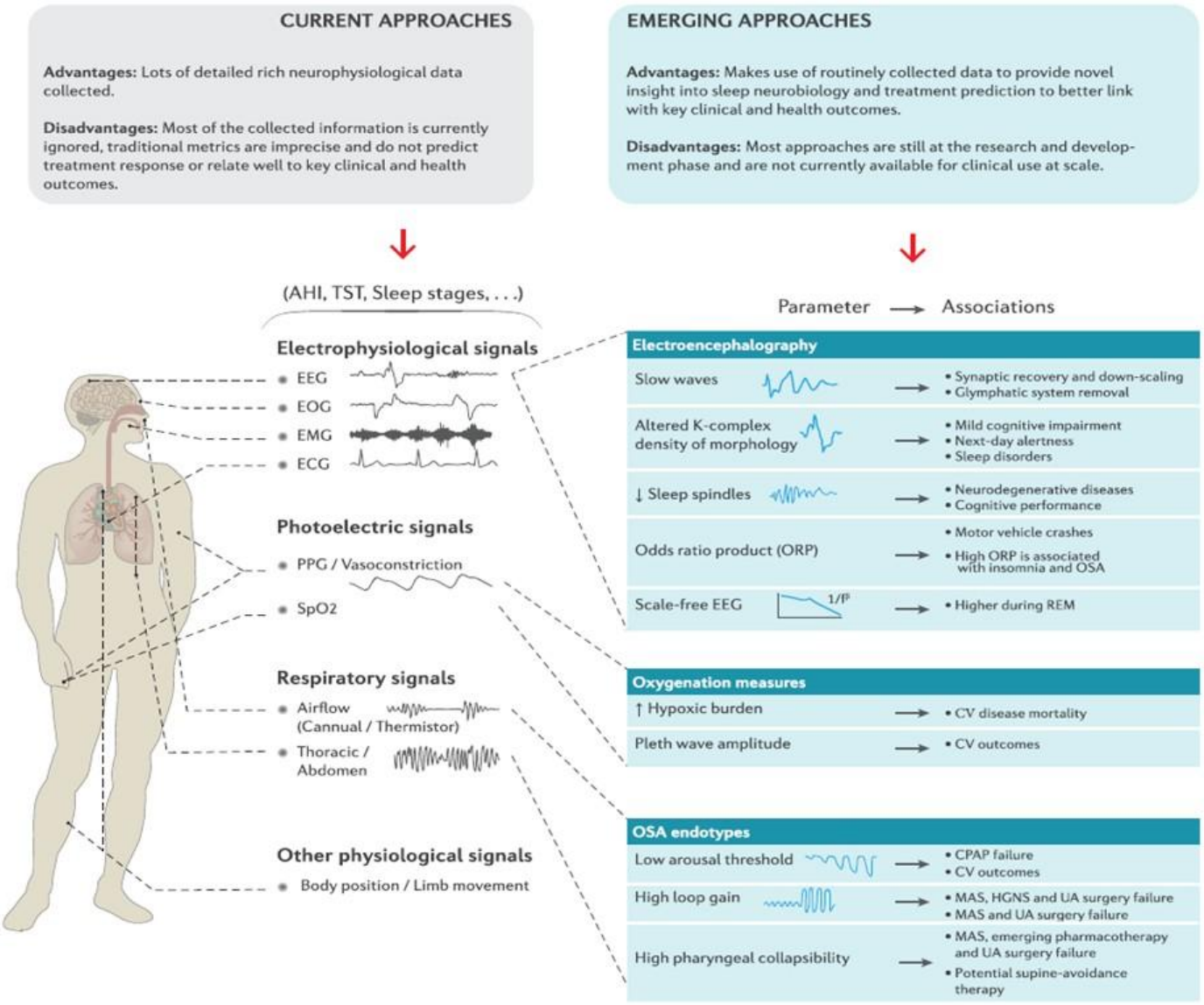


Figure 2. Paramètres évalués par la polysomnographie
Source : Lechat et al., 2020[70].
Abréviations : AHI : indice d'apnées-hypopnées ; CPAP : pression positive continue ; CV : cardiovasculaire ; ECG : électrocardiogramme ; EEG : électroencéphalogramme ; EMG : électromyogramme ; EOG : électro-oculogramme ; HGNS : stimulation nerveuse de l'hypoglosse ; MAS : appareil d'avancée mandibulaire ; PPG : photoplethysmographie ; REM : mouvement rapide des yeux (sommeil paradoxal) ; SAOS : syndrome d'apnées du sommeil ; SpO2 : saturation pulsée en oxygène ; TST : temps total de sommeil ; UA : voies aériennes supérieures

Le Syndrome d'Apnées du Sommeil - traitements

Le syndrome d'apnées obstructives du sommeil est une affection chronique fréquente associée à des complications cardiométaboliques et neurocognitives et qui justifie donc un traitement. Si la ventilation en pression positive continue (PPC) reste le traitement de première intention, son efficacité est limitée par une observance insuffisante, ce qui souligne la nécessité d'évaluer des alternatives telles que les orthèses d'avancée mandibulaire (OAM), la stimulation du nerf hypoglosse (HNS), la chirurgie

ORL et maxillo-faciale, les traitements positionnels, l'activité physique, différentes modalités de gestion de la perte de poids, notamment les agonistes du peptide-1 similaire au glucagon (GLP-1) et les stimulants de la vigilance[71]. Il est également crucial d'évaluer et de mettre en place des traitements combinés (Figure 3).

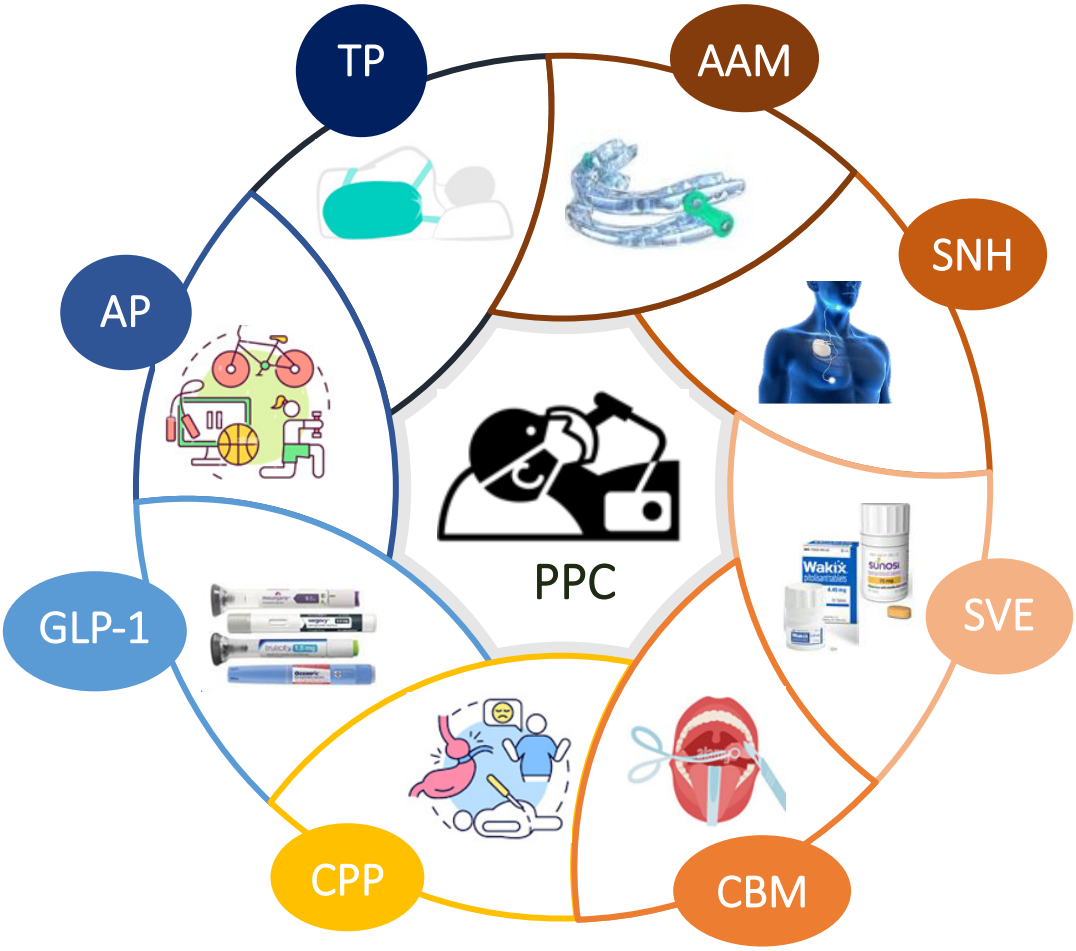


Figure 3. Modalités thérapeutiques du syndrome d'apnées obstructives du sommeil

Abréviations : PPC : pression positive continue ; GLP-1 : agonistes du peptide-1 similaire au glucagon ; SNH : stimulation du nerf hypoglosse ; AAM : appareil d'avancée mandibulaire ; CBM : chirurgie buccale et maxillofaciale ; AP : activité physique ; TP : thérapie positionnelle ; CPP : chirurgie de perte de poids ; SVE : stimulants de la vigilance et de l'éveil

Notre équipe a publié récemment une revue en ombrelle qui synthétise l'efficacité respective de ces modalités thérapeutiques[71]. Cette revue systématique a identifié la PPC comme l'intervention la plus efficace pour réduire l'IAH et la somnolence diurne chez les patients atteints de SAOS, tandis que l'activité physique a permis d'obtenir les meilleures améliorations en termes de qualité de vie (Figure 4). Les réductions pondérales de plus de 15% sont associées aux réductions les plus importantes de la pression artérielle (Figure 5). Ainsi le choix du traitement est une décision partagée avec les patients en fonction des objectifs que l'on souhaite atteindre en priorité.

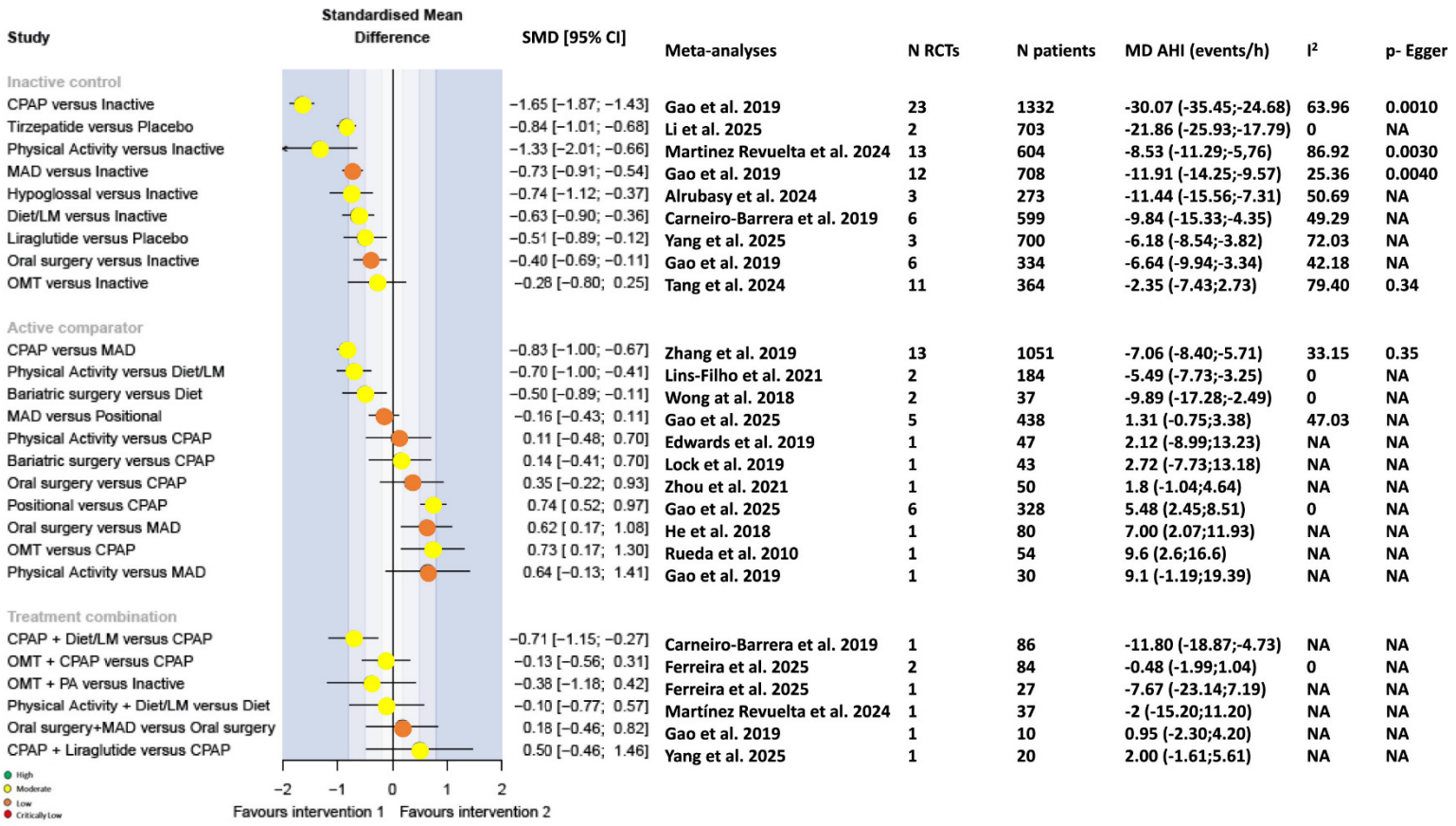


Figure 4. Efficacité des modalités thérapeutiques pour réduire l'IAH

Source : Figard et al., 2025[71]

Les SMD jaunes correspondent à un effet modéré tandis que les SMD orange correspondent à un effet faible.

Abréviations : CI : intervalle de confiance ; CPAP : pression positive continue ; IAH : indice d'apnées-hypopnées ; I^2 : évaluation de l'hétérogénéité ; LM : mesures du mode de vie ; MAD : appareil d'avancée mandibulaire ; MD : différence des moyennes ; OMT : thérapie myofonctionnelle oropharyngée ; PA : activité physique ; SMD : différence des moyennes standardisée

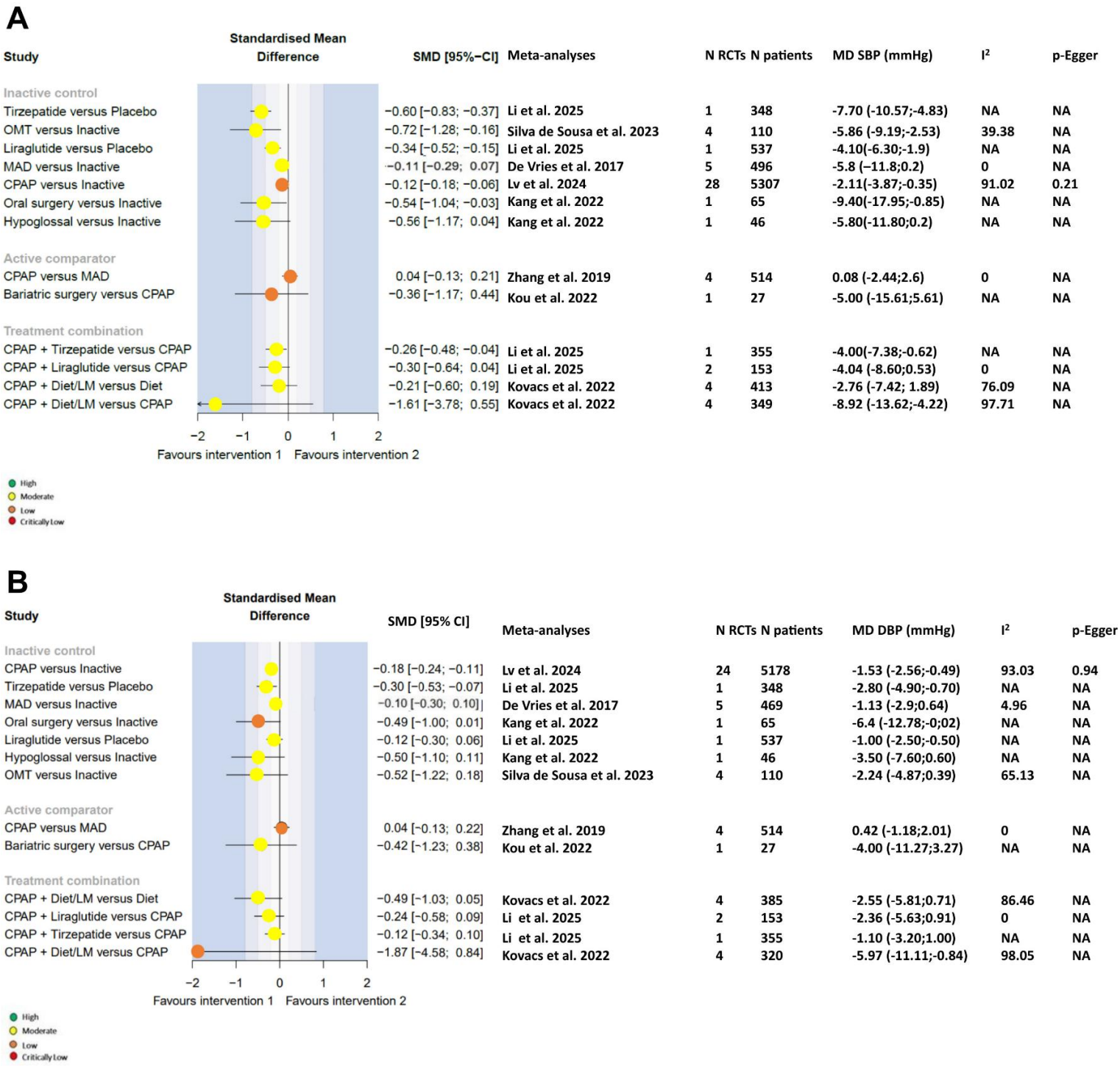


Figure 5. Efficacité des modalités thérapeutiques pour réduire la pression artérielle systolique (A) et diastolique (B)

Source : Figard et al., 2025[71]

Les SMD jaunes correspondent à un effet modéré tandis que les SMD orange correspondent à un effet faible.

Abréviations : CI : intervalle de confiance ; CPAP : pression positive continue ; DBP : pression artérielle diastolique ; I² : évaluation de l'hétérogénéité ; LM : mesures du mode de vie ; MAD : appareil d'avancée mandibulaire ; MD : différence des moyennes ; OMT : thérapie myofonctionnelle oropharyngée ; SBP : pression artérielle systolique ; SMD : différence des moyennes standardisée

Au cours de ce projet de thèse, la PPC a été le seul traitement étudié.

Traitement par pression positive continue - problématiques de son suivi à long terme

Comme énoncé précédemment, le traitement le plus fréquemment utilisé pour le SAOS reste la PPC ; un appareil composé d'une machine reliée à un masque par un tuyau qui stabilise les voies aériennes supérieures en insufflant une pression positive continue[3]. En 2021, 1.2 millions de patients utilisaient ce traitement en France[21] pour 2 millions en 2026.
Les conditions de prescription de la PPC, en France, sont les suivantes[72] :

Avoir un IAH supérieur ou égal à 30 évènements/h ;

Ou avoir un IAH supérieur ou égal à 15 évènements/h et inférieur à 30 évènements/h avec somnolence diurne sévère et/ou risque accidentel pouvant entraîner un dommage corporel direct ou indirect ;

Ou avoir un IAH supérieur ou égal à 15 évènements/h et inférieur à 30 évènements/h avec comorbidité cardiovasculaire ou respiratoire grave associée (hypertension, BPCO sévère, etc.) ;

Ou avoir un IAH supérieur ou égal à 15 évènements/h et inférieur à 30 évènements/h avec au moins trois des symptômes suivants : somnolence diurne, ronflements sévères et quotidiens, sensations d'étouffement ou de suffocation pendant le sommeil, fatigue diurne, nycturie, céphalées matinales.

Bien que très souvent prescrit et performant, il est nécessaire d'être vigilant quant aux problématiques d'observance et de taux d'arrêts élevés que ce traitement soulève[21]. L'observance de la pression positive continue repose sur de nombreux critères. Les principaux sont :

Une bonne prise en charge que ce soit au niveau des prestataires de santé à domicile ou au niveau des professionnels de santé. Cette prise en charge qui comprend le suivi technique de la PPC (observance, efficacité, gestion des alertes), la gestion des comorbidités et la surveillance multimodale utilisant la médecine digitale, doit être partagée efficacement entre tous les intervenants[73,74]. La prise en charge représente de nombreux défis comme par exemple la fragmentation des soins entre différents acteurs, la gestion inadéquate des comorbidités et la mise en œuvre sous-optimale des solutions de médecine numérique[73,74].

Une adaptation réussie du patient. Ce traitement entraine des contraintes personnelles et pour le partenaire ou des effets indésirables comme l'intolérance de la pression, l'inconfort du masque, des dessèchements ou des irritations notamment au niveau des yeux dues aux fuites[75,76]. Des solutions existent comme l'ajout d'un humidificateur à l'appareil, des techniciens sont disponibles afin de prévenir ou remédier aux problèmes techniques des machines, des questionnaires sont envoyés au patient pour déterminer les problèmes rencontrés au niveau physique, psychologique ou matériel mais le port du masque peut être perçu, en premier abord, comme une contrainte et entrainer une non-utilisation ou une utilisation non conforme de la PPC[77–79].

Une bonne observance, c'est-à-dire une utilisation de l'appareil d'au moins 4h/nuit[21,72,80–82]. Si la machine est convenablement utilisée, la qualité de vie en journée est améliorée, l'IAH, la somnolence diurne sont normalisée, la pression artérielle et les événements cardiovasculaires peuvent être réduits[3,82]. C'est l'un des défis le plus important, et qui est également un problème majeur de ce traitement avec des taux d'abandon de 23.1% après un an de traitement en France, 37.1% après 2 ans et 47.7% après 3 ans de traitement[21].

Une autre problématique soulevée par l'utilisation de la PPC et, plus précisément par l'observance du traitement, est la réponse hétérogène et mal comprise du traitement en termes de comorbidités et de

symptômes. Le nombre d'heures optimal d'utilisation de l'appareil pour observer un changement dans le bien être du patient, une améliorations des symptômes, le contrôle des comorbidités et l'impact du traitement par PPC sur les évènements cardiovasculaires incidents et la mortalité, restent débattus[3,79,82–87].

Pour optimiser l'observance de la PPC, un programme de télémonitoring de la PPC a été mis en place en France et concerne plus de 90% des patients SAOS. Ce programme est associé à un paiement « à la performance » avec des niveaux de remboursement différents pour les prestataires de soins à domicile selon l'observance nocturne. Ce schéma de remboursement a facilité une approche plus personnalisée de la prise en charge thérapeutique, en concentrant les ressources sur les patients présentant une observance faible à moyenne[81,88].

De plus, le suivi au long cours de la PPC nécessite une approche multidisciplinaire pour réduire les symptômes et améliorer l'observance, une évaluation longitudinale des résultats rapportés par les patients et une attention particulière portée aux risques cardiovasculaires à long terme avec des interventions combinées nutritionnelles et des programmes d'activité physique.

L'utilisation des objets connectés dans le domaine du sommeil

L'emploi d'objets connectés pourrait donc être une aide au suivi des patients notamment concernant leur utilisation de la PPC et l'évaluation et le contrôle de leurs comorbidités. En effet, l'utilisation des objets connectés dans la vie de tous les jours et notamment dans le domaine du sommeil est de plus en plus présente[89]. De nombreuses informations sont maintenant disponibles et partagées via des cloud internet, permettant l'implication des patients dans la création de cohortes, permettant l'étude de données en condition de vie réelle et permettant l'analyse de différents paramètres (activité physique, sommeil, données de santé, activités/loisirs via les réseaux sociaux par exemple, données atmosphériques comme les polluants atmosphériques, la pollution de l'air ou la météo, données sociaux-économiques, etc.) (Figure 6)[90].

En particulier dans le domaine du sommeil, le télémonitoring, c'est-à-dire le suivi des données à distance, est employé lors de l'utilisation de la PPC[79,81,89,91–96]. Le prestataire de soins à domicile et le médecin peuvent détecter les problèmes des machines mais également les problèmes d'observance des patients et vérifier les données de sommeil transmises par la PPC. Si un problème apparaît, le médecin en est informé ce qui permet un suivi régulier et précis du traitement de ses patients et une prise en charge personnalisée[89,91,93]. Les mesures de symptômes et leurs évolutions sont également possibles grâce à l'utilisation des objets connectés[81,89,92] comme les montres et balances connectées mais également les tensiomètres connectés.

L'exploitation de ces données multidimensionnelles et longitudinales est un des sujets centraux de cette thèse et représente un fort potentiel pour améliorer les stratégies personnalisées de prévention et de traitement des conséquences cardio-métaboliques du SAOS[97].

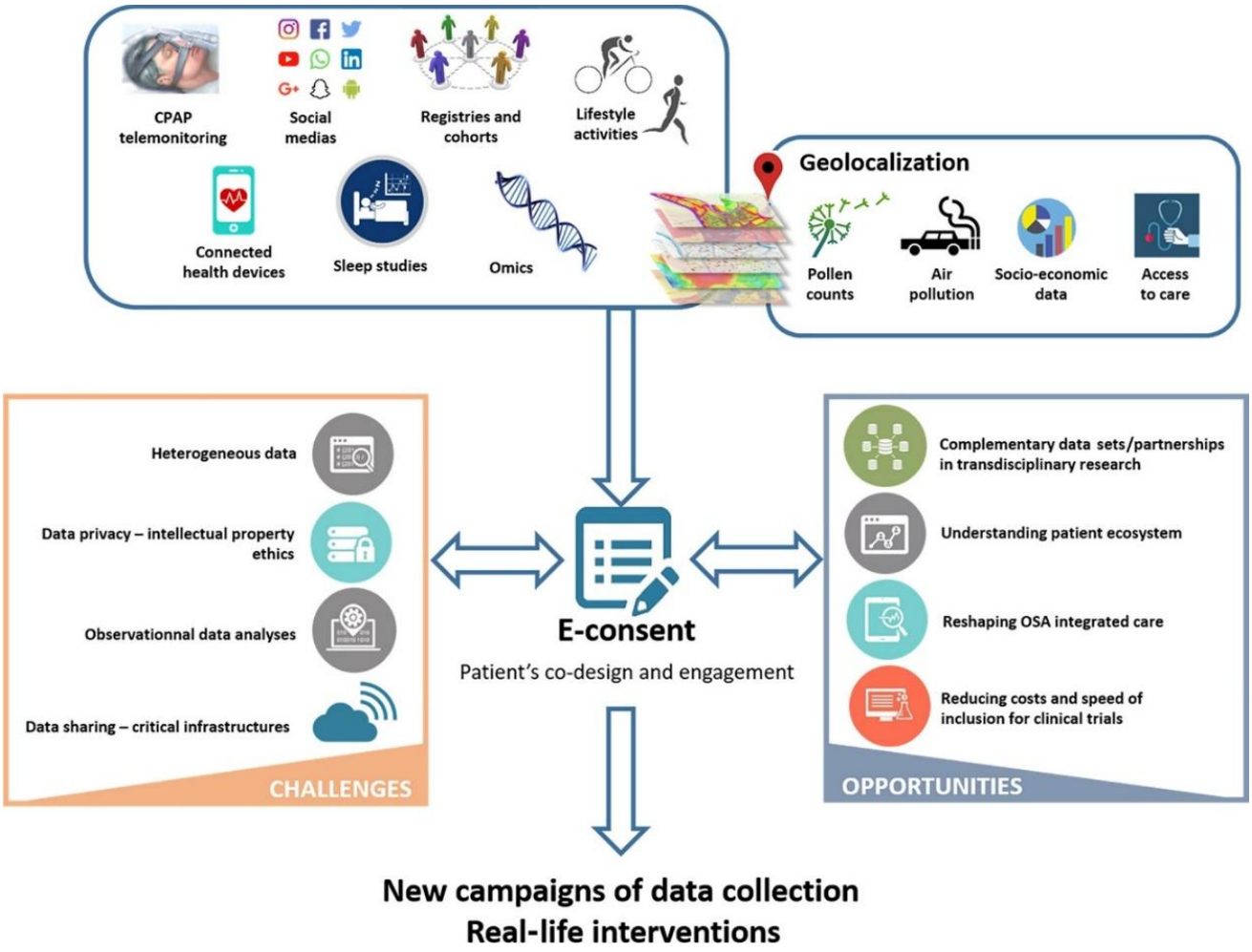


Figure 6: Utilisation des objets connectés dans le domaine du sommeil, avantages et problématiques
Source : Pépin et al., 2020[90].

Le télémonitoring ou le suivi régulier à domicile sur plusieurs mois ou années avec des objets connectés fournissent une quantité de données importantes. Les données issues de ces techniques de suivi des patients sont des données transmises régulièrement au cours du temps et sont appelées données longitudinales[98]. Leur analyse doit être adaptée[89,99–101] : ces données multidimensionnelles nécessitent un plan d'analyse précis et une méthodologie spécifique d'analyses des données longitudinales. Par exemple, les problèmes d'abandons de mesures ou de données manquantes restent une problématique à ne pas négliger et impactent directement les analyses statistiques et résultats obtenus[98,101].

Problématiques abordées pour la démarche scientifique de la thèse

Comme énoncé précédemment, le sujet conducteur de ce travail de thèse porte donc sur la caractérisation fine et dynamique des phénotypes des patients SAOS en condition de vie réelle, questionnée par l'hétérogénéité clinique du SAOS, l'association fréquente avec d'autres maladies chroniques et la disponibilité croissante des données longitudinales issues des objets connectés et des dossiers médicaux électroniques.

Premièrement, par une approche multidimensionnelle, nous avons caractérisé les patients ayant un overlap syndrome SAOS et BPCO (Sleep Medicine, 2024, 1ère auteure). Une meilleure prise en charge des patients pouvant ainsi être proposée grâce à l'amélioration de la caractérisation de ces profils obtenue à partir des dossiers médicaux électroniques et l'utilisation des objets connectés. Cette approche sera étudiée dans la première partie du manuscrit, à travers le premier article original.

Nous avons ensuite étendu nos travaux à l'analyse de données longitudinales multidimensionnelles issues des objets connectés et dossiers médicaux électroniques. Une approche méthodologique appropriée est toutefois nécessaire pour étudier ces données complexes. Il faut successivement, décrire les données, définir spécifiquement la question de recherche et choisir la méthode statistique adaptée. Nous avons synthétisé les principales méthodes statistiques applicables lors de l'analyse de données longitudinales afin de permettre une meilleure appropriation et compréhension de ces méthodes dans le domaine du sommeil (Sleep Medicine, 2025, 1ère auteure). Ces méthodes seront décrites dans la seconde partie du manuscrit, à travers l'article de revue.

Troisièmement, nous avons pu appliquer ces différentes étapes d'analyse des données longitudinales à nos questions de recherche clinique portant sur l'évolution, dans le temps, de l'utilisation des objets connectés comme les tensiomètres connectés pour mesurer l'évolution de la pression artérielle (PA) des patients à haut risque d'événements cardiovasculaires ou l'utilisation du télémonitoring pour mesurer l'observance de la PPC des patients atteints de SAOS. D'après les recommandations énoncées pour l'analyse de ces données, la prise en compte des profils de patients à haut risque d'abandon de mesures est importante. Nous avons donc étudié l'évolution respective de l'utilisation du tensiomètre connecté et de l'utilisation observante de la PPC dans la seconde partie du manuscrit, à travers la première lettre de recherche (soumise au journal Sleep Medicine, avril 2026, 1ère auteure). De plus, par l'utilisation du tensiomètre connecté, à domicile, et par l'utilisation du télémonitoring de la PPC, nous avons pu caractériser l'évolution de la PA chez les patients souffrant d'un SAOS traités par PPC, en situation de vie réelle (Annals of ATS, 2025, 1ère auteure). Cette analyse sera étudiée dans la troisième partie du manuscrit, à travers le second article original. Enfin, l'impact de la somnolence pour la réponse à la PPC en termes de PA a été abordé (Annals of ATS, 2026, 1ère auteure). Dans la littérature, il est démontré qu'il existe une association entre somnolence et événements cardiovasculaires et entre somnolence, événements cardiovasculaires et PPC[102–104]. Cependant, la plupart des études randomisées sur la PA sont réalisées sur des patients non-somnolents[86]. Nous avons par conséquent analysé l'évolution de la PA chez des patients souffrant de SAOS traités par PPC selon leur statut somnolent ou non somnolent au diagnostic. Cette problématique sera abordée dans la troisième partie du manuscrit, à travers la seconde lettre de recherche.

II. Bases de données utilisées au cours de la thèse pour la valorisation scientifique

Deux études observationnelles et une base de données digitale prospective ont été utilisées pour aborder ce sujet de thèse (Figure 7) : E-Meuse (NCT04963192), Sleep Connect (NCT04054180) et Multimorbidity Apnea Respiratory failure Sleep (MARS, MR003 N°1996650v0) database. Pour chaque étude, les comités d'éthiques ont validé les protocoles d'étude et tous les patients ont signé un document de consentement éclairé avant leur inclusion.

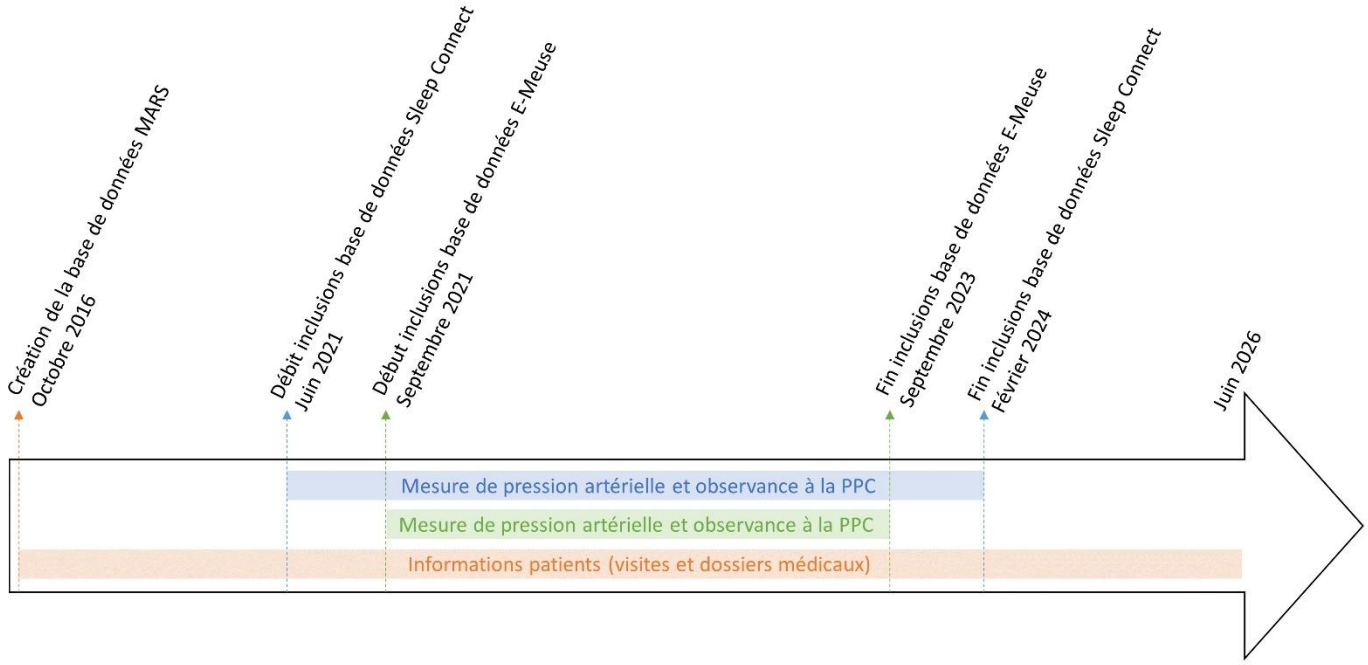


Figure 7. Chronologie des bases de données

Abréviations : MARS : multimorbidity apnea respiratory failure sleep; PPC : pression positive continue

La base de données MARS

La base de données MARS, créée en octobre 2016, est une base de données multicentrique, qui constitue dorénavant un entrepôt de données de santé, crée par le CHU de Grenoble qui contient les données collectées prospectivement de plus de 10 000 patients telles que leurs traitements, antécédents médicaux, caractéristiques physiques et données cliniques (âge, sexe, poids, Indice de Masse Corporelle (IMC), pression artérielle, etc.), comorbidités, mais aussi les résultats des questionnaires sur les symptômes comme la somnolence (ESS), le syndrome des jambes sans repos, l'insomnie (ISI), la dépression, et les paramètres mesurés par PSG ou polygraphie, comme l'IAH, l'indice de désaturation en oxygène (ODI), les stades de sommeil, les micro-éveils, etc. Les données sont validées par un médecin lors de la visite initiale et les visites de suivi après que le patient ait complété à domicile un questionnaire électronique (durée 30 à 40 minutes). Des visites régulières de suivi sont organisées avec les médecins, permettant l'acquisition de données longitudinales. Toutes les données sont désidentifiées lors de leurs analyses.

Ainsi, la base de données MARS est une base multidimensionnelle longitudinale qui regroupe des données issues de plusieurs villes françaises.

Les études e-Meuse et Sleep Connect

Les études e-Meuse et Sleep Connect ont des objectifs particulièrement intéressants pour ce sujet de thèse portant sur le phénotypage multidimensionnel du SAOS (SAOS, BPCO et OS) et la prédiction de ses réponses thérapeutiques, en particulier l'évolution de la pression artérielle sous PPC des patients atteints d'un SAOS.

En effet, l'étude e-Meuse avait pour objectifs [eMEUSE-SANTE NCT04963192[105]] :

1. D'objectiver l'effet des traitements comme la PPC chez des patients atteints de SAOS ou la ventilation non-invasive et/ou l'oxygénothérapie chez les patients atteints de BPCO, non seulement sur la prévention de la décompensation respiratoire mais aussi sur les facteurs de risques cardiovasculaires et métaboliques qui sont des éléments majeurs du pronostic ;
2. De démontrer la faisabilité et de déployer un parcours de soins multi-acteurs dans un territoire rural (La Meuse) avec un accès aux soins limité ;
3. D'étudier l'évolution de paramètres comme l'observance au traitement, l'activité physique, le poids, la pression artérielle, la somnolence diurne, la fatigue, etc., avant et après 6 mois de traitement ;
4. D'analyser des trajectoires de mesures collectées au cours du traitement afin d'identifier des profils spécifiques ;
5. D'analyser les données journalières des différents objets connectés et traitements selon les profils des patients (selon l'âge, le sexe, les comorbidités, etc.).

L'étude Sleep Connect a pour objectifs [SLEEPCONNECT NCT04054180[106–110]] :

1. D'évaluer l'impact de la télésurveillance multimodale via des objets connectés et une application de smartphone, sur la pression artérielle après 3 mois de PPC ;
2. D'évaluer l'impact de cette prise en charge intégrée sur l'activité physique et la perte de poids.

L'étude e-Meuse était localisée à Verdun (Meuse, France) tandis que l'étude Sleep Connect est localisée à Lille (Nord, France) et Grenoble (Isère, France). Ces études permettent l'analyse de données longitudinales de pression artérielle et d'observance à la PPC, au cours d'une première semaine avant traitement et de 6 mois de mesures sous traitement par PPC (Figure 8).

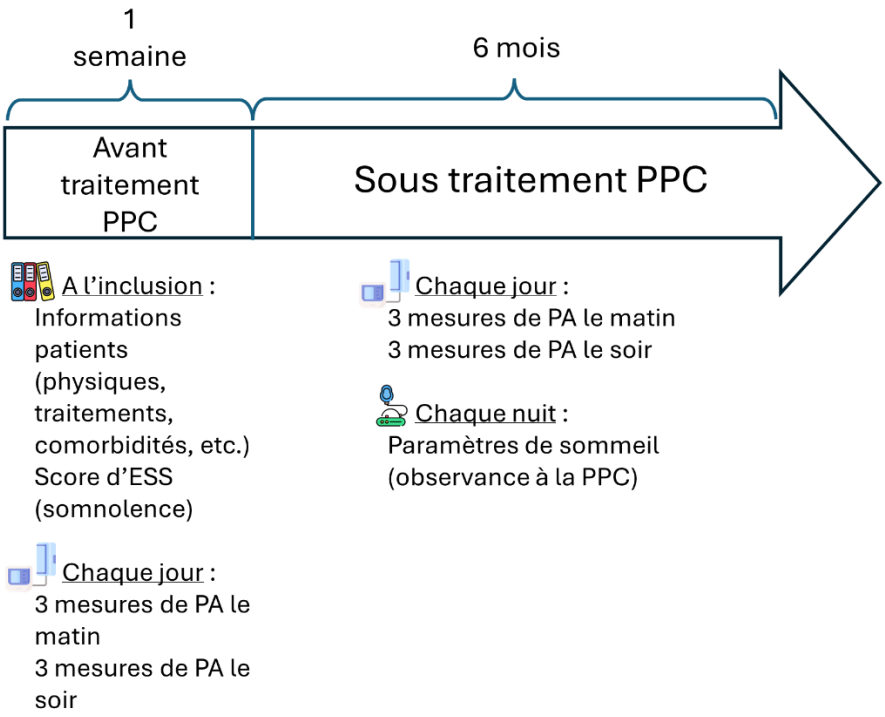


Figure 8. Schéma des études e-Meuse et Sleep Connect
Abréviations : ESS : Epworth Sleepiness Scale ; PA : pression artérielle ; PPC : pression positive continue

Les inclusions ont eu lieu entre septembre 2021 et septembre 2023 pour la cohorte E-Meuse et entre juin 2021 et février 2024 pour la cohorte Sleep Connect (Figure 7). Les critères d'inclusion de la cohorte e-Meuse étaient :

- Être un homme ou une femme entre 18 et 75 ans ;
- Avoir une pathologie respiratoire chronique (SAOS nouvellement diagnostiqué et avec une indication pour un traitement par PPC et/ou une BPCO avec ou sans indication de traitement) ;
- Être en mesure d'utiliser une application mobile sur smartphone ou tablette ;
- Accepté le télémonitoring des données d'observance de la PPC ;
- Être affilié à la sécurité sociale.

Les critères d'inclusion de la cohorte Sleep Connect étaient :

- Avoir un SAOS non traité par PPC, défini par un IAH ≥ 15 événements/h et avec plus de 80% d'événements obstructifs déterminés par PSG ou polygraphie dans les 6 derniers mois ;
- Être traité pour une hypertension ou être récemment diagnostiqué hypertendu, défini par une PA systolique entre 140 mmHg et 180 mmHg et une PA diastolique entre 90 mmHg et 110 mmHg ;
- Avoir un IMC > 28 kg/m² ;
- Avoir un smartphone ;
- Être capable d'utiliser une application mobile sur son smartphone ;
- Avoir un certificat médical pour la pratique d'activité physique/exercice ;
- Être affilié à la sécurité sociale.

Une fois inclus dans les cohortes, les patients atteints d'un SAOS, diagnostiqués par PSG ou polygraphie respiratoire, et traités par PPC doivent mesurer leur pression artérielle 3 fois le matin et 3 fois le soir pendant toute la durée de l'étude à l'aide d'un tensiomètre oscillométrique automatique (Andon ihealth-feel BP5[111], Figure 8). Une à deux minutes de pause sont préconisées entre les mesures. Une fois les valeurs obtenues, le tensiomètre connecté les envoie, via Bluetooth, à l'application mobile associée, puis celles-ci sont transmises de façon sécurisée et anonymisée à la base de données MARS. Concernant les données issues de la PPC, le télémonitoring est utilisé. Chaque nuit, les valeurs d'observance sont envoyées au prestataire de santé à domicile puis transmises à une plateforme sécurisée liée à la base de données MARS pour que nous puissions y avoir accès (Figure 8). De plus, des prestataires de soin à domicile vérifient le bon fonctionnement, la tolérance de l'appareil par le patient au cours de trois visites pour les quatre premiers mois d'utilisation de la PPC puis une fois par an. Des centres d'appel sont également disponibles toute la journée, toute la semaine en cas de problème et le fournisseur vérifie la bonne observance des patients à la PPC, informant le médecin du patient si ce n'est pas le cas.

De par son design, il est nécessaire que les patients aient une bonne connexion internet et la capacité d'utiliser un smartphone ou une tablette étant donné que des objets connectés et une application mobile sont nécessaires.

Ces études étaient innovantes notamment via l'utilisation d'objets connectés pour le suivi des patients. Ces études avaient également un objectif peu abordé dans la littérature : démontrer la faisabilité et le déploiement d'un parcours de soin multidisciplinaire et une prise en charge intégrée à domicile.

Populations d'étude

Au cours de nos analyses, les deux populations ont été regroupées et une sélection plus fine de la population totale a été réalisée. Sur les 181 patients inclus atteints d'un SAOS et traités par PPC, 102 patients ont mesuré leur PA au moins une fois au cours des 6 mois d'étude et 132 patients ont des données d'observance de leur PPC. Finalement, 98 patients ont été sélectionnés ayant à la fois au moins une mesure de PA et une mesure d'observance à la PPC au cours des 6 mois de mesures (Figure 9).

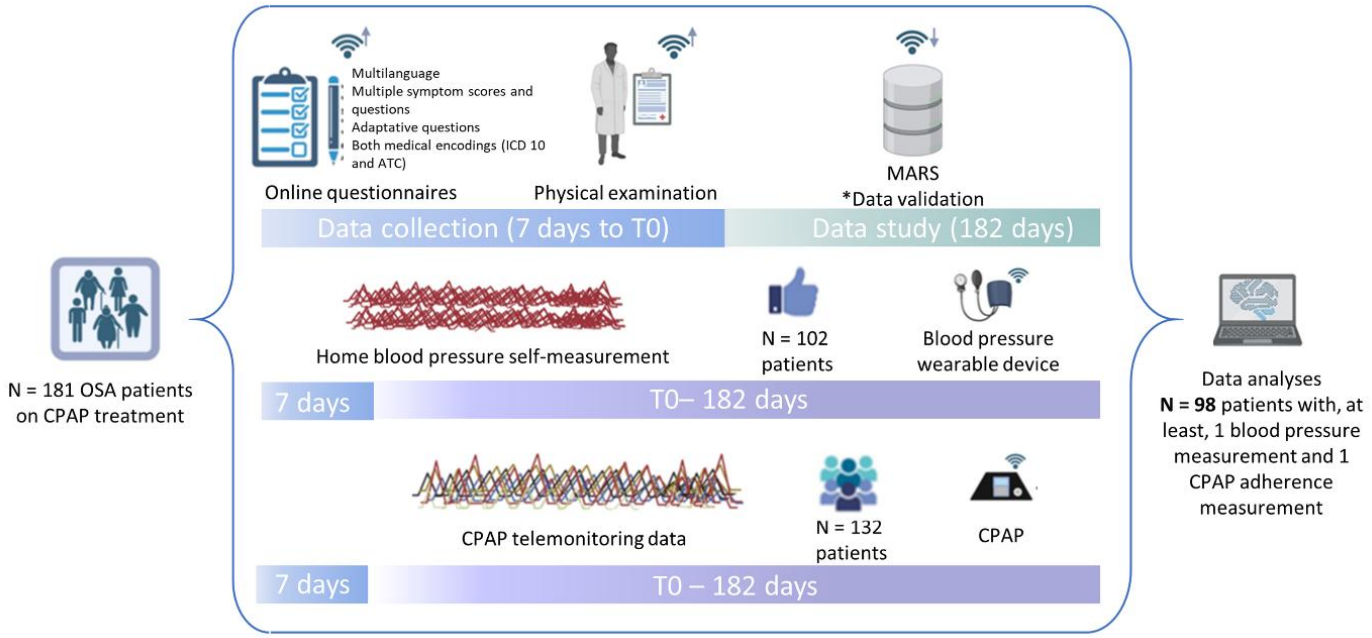
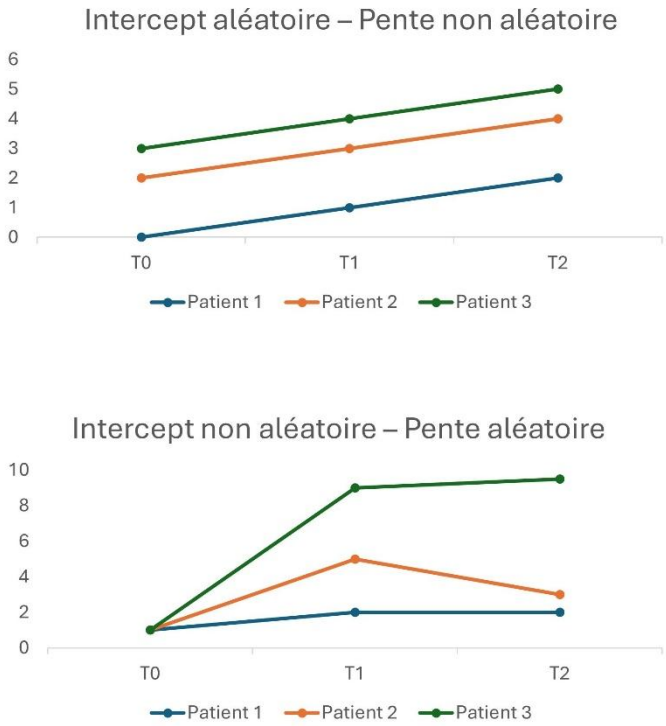


Figure 9. Populations d'études e-Meuse et Sleep Connect
Abréviations : ATC : anatomique thérapeutique chimique, CPAP : pression positive continue, ICD-10 : classification internationale des maladies - 10ème révision, MARS : multimorbidity apnea respiratory failure sleep, OSA : syndrome d'apnées obstructives du sommeil

Analyser ces données

Les différentes méthodes d'analyse des données longitudinales représentent une partie à part entière de ce manuscrit (partie IV) et font l'objet d'un article de revue, c'est pourquoi nous ne décrirons ici que succinctement la méthode statistique utilisée tout au long de cette thèse : le modèle mixte.

Le modèle mixte permet d'étudier l'évolution d'un facteur en fonction du temps. Il s'applique lorsque les individus ont des mesures répétées (données longitudinales)[112–115]. Les régressions linéaires mixtes sont dites mixtes car elles possèdent à la fois des effets fixes et des effets aléatoires. Les effets fixes concernent les effets associés aux variables explicatives d'intérêt qui peuvent être constants ou variables dans le temps tels que l'âge, le sexe ou les comorbidités. Les effets aléatoires visent à capturer la part d'information qui varie entre les individus (ou selon le niveau hiérarchique considéré dans le modèle). Par exemple, pour la pression artérielle, les patients ont des mesures répétées au cours du temps. Le niveau initial (intercept) et l'évolution au cours du temps (pente) peuvent varier d'un individu à un autre (variabilité inter-individuelle), et les mesures d'un même patient varient également d'un point de temps à un autre (variabilité intra-individuelle). Les modèles à effets mixtes permettent de capturer simultanément ces deux sources de variabilité (Figure 10).



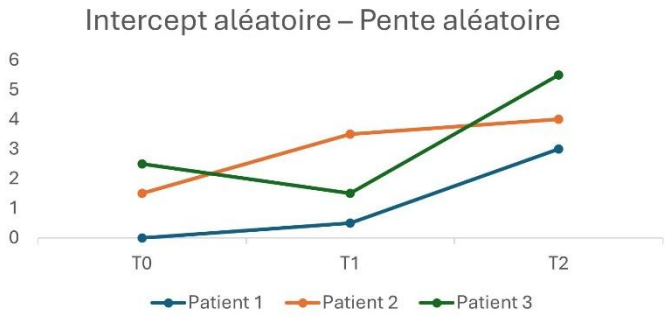


Figure 10. Effets aléatoires sur la pente et/ou l'intercept

Quelques contraintes sont à respecter pour obtenir un modèle satisfaisant comme l'utilisation de variables catégorielles et non continues pour les effets aléatoires, avoir un minimum de 50 individus, avoir des données manquantes « missing at random » c'est-à-dire que les données manquantes dépendent des réponses observées mais ne sont pas liées aux valeurs manquantes, et avoir un minimum de 4 points de temps pour des régressions non linéaires (2 suffisent dans le cas contraire)[98].

III. Recueil multidimensionnel des symptômes pour une adaptation aux différents contextes de survenue et de diagnostic des patients atteints du Syndrome d'Apnées Obstructives du Sommeil – Article original publié n°1[116]

Introduction

Le diagnostic des patients atteints d'un SAOS est parfois difficile notamment du fait des nombreux contextes de survenue du syndrome et par l'aspect hétérogène de sa présentation clinique[5]. Une constellation de symptômes, de comorbidités, de caractéristiques physiques peuvent amener à un diagnostic d'apnées du sommeil. Un patient BPCO peut, par exemple, être atteint du SAOS (il est alors atteint d'un Overlap Syndrome (OS)) et cumuler des symptômes, comorbidités qui rendent l'évocation d'un SAOS plus compliquée[16–18]. La littérature actuelle évalue parfois des symptômes non adaptés à cette association comorbide[117], ne renseigne pas clairement les comorbidités ou traitements[118–120] et analyse majoritairement des données rétrospectives[117]. Il est pourtant important de bien décrire les différents phénotypes des patients atteints de SAOS, BCPO ou OS qui constituent des maladies chroniques fréquentes[2,3,121] et sont un réel fardeau que ce soit pour les patients, pour les systèmes de santé ou pour la société[6,122]. Une mauvaise caractérisation diagnostic est un facteur d'augmentation de risque d'évènements cardiovasculaires incidents et plus généralement de décès de la personne[80,123].

Objectifs

Cet article original vise à décrire précisément les 3 différents phénotypes des patients atteints d'un SAOS, d'une BPCO et d'un OS grâce à des données multidimensionnelles pertinentes. Plus précisément, il vise à détailler le profil symptomatique, les profils de comorbidités, de traitements, de caractéristiques physiques afin de faciliter le diagnostic des médecins.

Méthodes

Les données utilisées dans cette étude sont issues de la cohorte observationnelle prospective E-Meuse (Verdun, France) et de la base de données « Multimorbidity Apnea Respiratory failure Sleep (MARS) » (France). Les patients étaient inclus dans l'étude s'ils étaient diagnostiqués souffrant d'un SAOS avec une indication pour un traitement par PPC ou s'ils étaient diagnostiqués souffrant de BPCO avec ou sans indication pour un traitement par ventilation non invasive/oxygénothérapie. Les patients devaient également être capable d'utiliser un smartphone, de télécharger des applications et d'être affiliés au régime français d'assurance maladie.

L'utilisation de mesures physiques, questionnaires multidimensionnels sur le sommeil, la fatigue, la dépression, les symptômes respiratoires fournis par les patients ; les comorbidités et traitements fournis par les médecins et les automesures de la pression artérielle des patients ont permis de décrire les populations souffrant de SAOS, BPCO et OS. Les 3 profils symptomatiques distincts ont pu être identifiés par des tests de comparaison statistique comme les tests de Wilcoxon ou Kruskal-Wallis pour les variables continues et le test du χ^2 de Pearson ou le test de Fisher pour les variables catégorielles.

Résultats

308 patients ont été inclus dans cette étude et ont été répartis en trois phénotypes distincts : les patients atteints d'un SAOS, ceux atteints d'une BPCO et ceux ayant un OS. En effet, les patients souffrant d'un SAOS ont une corpulence ronde mais un ratio taille-hanche équilibré avec des apnées fréquemment détectées par l'entourage, des nycturies, une somnolence diurne, de la dépression et une pression artérielle diastolique élevée. Les patients atteints de BPCO ont, quant à eux, une corpulence fine avec un ratio taille-hanche équilibré, de nombreuses plaintes de fatigue et une fréquence cardiaque au repos élevée. Enfin, les patients atteints d'OS ont également une corpulence ronde mais un ratio taille-hanche plus élevé et rapportent une légère somnolence et dépression avec un sommeil de mauvaise qualité et le plus haut taux de comorbidités cardio-métaboliques. De plus, les patients atteints de SAOS et d'OS ont une somnolence au volant plus marquée. Une analyse de la pression artérielle de ces patients montre que 80% des patients considérés comme non hypertendus ont en fait une hypertension non diagnostiquée et chez les patients connus pour être hypertendus, 80% ont une hypertension artérielle non contrôlée par leur traitement médicamenteux.

Cette étude a été publiée sous forme d'article original dans Sleep Medicine en juillet 2024 et a été présentée sous forme d'un poster au congrès de l'ERS en 2024.

Perspectives

L'association comorbide BPCO et SAOS est très sous-estimée en pratique clinique courante, en particulier lors du phénotypage de la BPCO ou l'évaluation du sommeil est quasiment systématiquement oubliée. Il serait nécessaire de disposer d'outils de dépistage (questionnaires spécifiques à cette situation plutôt que génériques) permettant d'améliorer la détection du SAOS chez les BPCO. Notre étude a rapporté un taux étonnamment élevé d'hypertension non diagnostiquée ou non contrôlée chez les participants déjà sous traitement antihypertenseur. On sait que la tension artérielle mesurée à domicile est un meilleur indicateur que les mesures effectuées en cabinet pour prédire les événements cardiovasculaires[89,124,125]. Nos données soulignent l'intérêt de mettre en œuvre systématiquement des programmes de télésuivi de la pression artérielle mesurée à domicile pour apprécier la réponse à la PPC. Ces résultats constituent le rationnel de l'article original n°2[126]. Mais la mise en place d'un télésuivi soulève également quelques problématiques notamment le choix de la méthode statistique pour étudier ces données et le taux d'abandons de mesures.

Article

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Multidimensional phenotyping to distinguish among distinct obstructive sleep apnea, chronic obstructive pulmonary disease, and overlap syndrome phenotypes

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ABSTRACT

Objective/background: Chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA) and their comorbid association called Overlap Syndrome (OS) are frequent chronic diseases with high individual and societal burdens. Precise descriptions of the respective symptoms, comorbidities, and medications associated with these three conditions are lacking. We used a multidimensional phenotyping approach to identify relevant phenotypes characterizing these 3 disorders.

Patients/methods: 308 patients with OSA, COPD and OS were prospectively assessed using a combination of body shape measurements and multidimensional questionnaires evaluating sleep, fatigue, depression and respiratory symptoms. Comorbidities and medications were confirmed by physicians. Patients made home blood pressure self-measurements using a connected wearable device to identify undiagnosed or uncontrolled hypertension.

Results: Three distinct relevant phenotypes were identified. OSA patients were round in shape with a balanced waist-to-hip ratio, frequent witnessed apneas, nocturia, daytime sleepiness, depression, and high diastolic blood pressure. COPD patients had a thinner body shape with a high waist-to-hip ratio, complained mainly of fatigue, and exhibited a higher resting heart rate. OS patients were round in shape with a balanced waist-to-hip ratio, reported little sleepiness and depression, but had impaired sleep and the highest rate of cardio-metabolic comorbidities. Diminished fitness-to-drive was most apparent in patients with OSA and OS. Home blood pressure measurements identified undiagnosed hypertension in 80 % of patients and in nearly 80 % of those with hypertension it was uncontrolled by their current medications.

Conclusions: Our systematic multidimensional phenotyping approach identified distinct body shapes, symptoms, and comorbidity profiles among patients with OSA, COPD, and OS.

Abbreviations: BDI, Beck Depression Index; BQ, Berlin Questionnaire; CAT, COPD Assessment Test; COPD, Chronic Obstructive Pulmonary Disease; ESS, Epworth Sleepiness Scale; ISI, Insomnia Severity Index; MARS, Multimorbidity Apnea Respiratory failure Sleep; OS, Overlap Syndrome; OSA, Obstructive Sleep Apnea; SGRQ, St George's Respiratory Questionnaire.

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1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnea (OSA) are among the most frequent and disabling chronic diseases [1–3]. These conditions pose high burdens on patients, health systems and society [4,5]. COPD is the third leading cause of death worldwide [5]. Untreated OSA is an independent risk factor for incident cardiovascular disease and all-cause mortality [6,7]. The combination of these two diseases, called "Overlap Syndrome"(OS) [8–11], is often underrecognized and underdiagnosed because it is at the frontiers of two respiratory fields [8–10]. Overlap syndrome is suspected as having a specific clinical presentation and a higher burden of comorbidities compared to each disease alone [9,12,13].

Studies consistently show that anthropometrics, symptoms and comorbidities may vary when comparing OSA and OS patients [4,12, 14]. However, the validity of these findings are questionable as the data are frequently retrospective, with inadequate assessment of multidimensional symptoms (sleepiness, fatigue, dyspnea, insomnia, depression etc.) [15] and incomplete documentation of comorbidities and medications [16–18].

Our hypothesis was that patients with OS and OSA differ in many aspects, including symptoms, body shape, cardiovascular risk, comorbidities, and medications. To date, all these dimensions and factors have not been extensively prospectively investigated together in a single study. We propose a prospective multidimensional-phenotyping approach for identifying the most relevant distinct phenotypes to differentiate among obstructive sleep apnea, chronic obstructive pulmonary disease, and overlap syndrome. To this end we prospectively assessed multidomain symptoms, measured body shape, gathered related risk factors, objectively monitored home blood pressure through connected wearables and collected data on comorbidities and medications (with strict validation by physicians) [Fig. 1] at baseline of patients included in the French "e-Meuse" study.

2. Material & methods

2.1. Study design

This multidimensional phenotyping of patients with newly diagnosed obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD) or overlap syndrome (OS) (the combination of OSA and COPD) is the first stage of the Integrated Management of Chronic Respiratory Diseases (e-Meuse) study ('registered on ClinicalTrials: NCT04963192). The main objective of the e-Meuse study is to evaluate home-based multidisciplinary integrated management of patients with OSA, COPD and OS, living in rural areas, with limited access to conventional care. Management includes the use of connected wearables to collect home self-measurements of blood pressure and weight. The goal of the current analysis was to apply a multidimensional phenotyping approach to compare the baseline data of the three distinct populations of patients (OSA, COPD and OS) included in the e-Meuse study.

2.2. E-meuse inclusion criteria

Participation in the study was proposed to residents of rural areas of the Meuse county of north-eastern France attending a pneumology consultation at the Verdun Hospital between 09/2021 and 09/2023, newly diagnosed with OSA with an indication for Continuous Positive Airway Pressure (CPAP) treatment, or with COPD with or without an indication for noninvasive ventilation (NIV)/oxygen therapy. Participants needed to be able to use a smartphone and download apps, and to be affiliated to the French national social security health insurance scheme.

2.3. Ethics

All procedures were performed and data was collected in compliance with relevant laws and institutional guidelines. The e-Meuse study protocol was approved by the ethics committee CPP Sud Est III on June 1, 2021 (n° 2021-043B). All patients signed written informed consent to participate before inclusion in the study.

2.4. Multidimensional phenotyping at study inclusion (Fig. 1)

Multidimensional data were prospectively collected via a highly secured research database "Multimorbidity Apnea Respiratory failure Sleep (MARS)" with personal access codes. All data were de-identified. At inclusion in the study patients completed electronic questionnaires (at home) allowing multidimensional assessment of symptoms: Epworth Sleepiness Scale (ESS) [19], Pichot fatigue scale [20], Pichot depression scale [20], Beck Depression Index (BDI) [21], COPD Assessment test (CAT) [22], Insomnia Severity Index (ISI) [19], St George Respiratory Questionnaire (SGRQ) [22], Nasal Obstruction Symptom Evaluation (NOSE) [23], and the Berlin Questionnaire (BQ) [24]. As well as these scores and validated questionnaires, participants were also asked to answer some additional questions and self-assess using visual analog

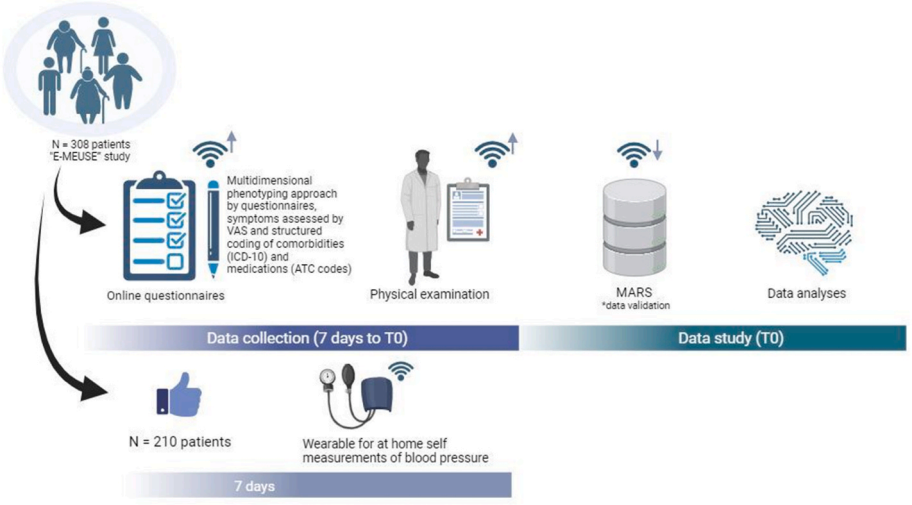

Fig. 1. Data collection process
Abbreviations: MARS: Multimorbidity Apnea Respiratory failure Sleep database.

scales (VAS) evaluating symptoms. These data were checked during a face-to-face clinical consultation at the hospital with a study investigator during which anthropometric and body shape data (body mass index (BMI), neck, abdominal, calf and thigh circumferences, and waist-to-hip ratio) were collected. An objective assessment of comorbidities was validated by the clinical investigator and coded using ICD-10 codes for diseases and ATC codes for medications. Medications in the ATC classes C02, C03, C07 and C09 were considered to be antihypertensives [25].

Respiratory polygraphy or polysomnography data were available for the OSA and overlap syndrome populations (collected at diagnosis). Pulmonary function tests and blood gases were mandatory for participants with COPD and were measured at the clinical investigator's discretion in the OSA population.

2.5. Connected wearables for home measurements of blood pressure and heart rate

A subgroup of patients who consented to home-based blood pressure and heart rate monitoring was formed. They used the iHealth feel BP5/BP5s wearable device (SEFAM, Nancy, France) for one week. This device transmits systolic and diastolic blood pressure and heart rate measurements to a secure platform linked to the research database and readily consultable by clinicians, via an application programming interface (API). Patients were classified as hypertensive when they reported a history of hypertension or had medications with ATC codes related to hypertension. This data was verified during the face-to-face clinical consultation.

The one-week BP measurements, made it possible to identify patients with undiagnosed hypertension and those with uncontrolled hypertension (inadequate treatment). The thresholds for systolic blood pressure was a mean value $\geq$ 135 mmHg and for diastolic blood pressure $\geq$85 mmHg for at least one measurement per day over one week [26].

2.6. Study population

Three hundred eight patients were prospectively included, with approximately similar numbers of patients with OSA, COPD and QS.

2.7. Statistical analysis

Data analyses were conducted with R-4.3.0. Categorical variables are expressed as number of values and percentage, while continuous variables are reported as median and interquartile range (IQR). The population was divided into three groups according to diagnosis: OSA, COPD and OS. Anthropometrics, demographics, body shape measurements, clinical characteristics and questionnaire scores were compared using the Wilcoxon rank sum test and Kruskal-Wallis test for continuous variables, while Pearson's Chi-squared test and Fisher's exact test were used to analyze categorical variables. A p-value less than 0.05 was considered statistically significant.

Statistically significant differences among the three groups regarding symptoms and comorbidities are shown using radar charts for a better visualization of clinically relevant phenotypes [27]. In detail, radar charts displaying subjective variables and scores were plotted using the percentage of patients with values above the median for the total population, while the radar chart displaying comorbidities was constructed using the percentage of patients with the prevalent comorbidity. To summarize the data, a heatmap was plotted to show the main characteristics (symptoms, comorbidities and blood pressure measurements) that differed significantly among the three groups (OSA, COPD and OS). For each group, the mean scores and the percentage of patients with one or more comorbidities were calculated. For systolic and diastolic blood pressure assessed using the wearable device, the percentage of patients diagnosed with hypertension [26] is shown.

3. Results

Complete baseline data were available for 308 participants included in the e-Meuse study. Table 1 shows the anthropometrics, body dimensions and comorbidities in the three diagnosis groups: OSA (108 patients), COPD (105 patients) and OS (95 patients).

Table 1
Anthropometrics, external body dimensions and comorbidities across the three groups: OSA, COPD and OS.

	N	OSA N = 108[a]	COPD N = 105[a]	OS N = 95[a]	p-value[b]
Anthropometrics, external body dimensions and smoking status					
Sex	308				0.4
Female		47 (44 %)	44 (42 %)	33 (35 %)	
Male		61 (56 %)	61 (58 %)	62 (65 %)	
Age (years)	308	54 (47, 64)	65 (58, 69)	65 (59, 69)	**<0.001**[d]
BMI (kg/m^2)	308	30 (27, 36)	24 (20, 28)	31 (27, 36)	**<0.001** [e]
Neck circumference (cm)	308	41.0 (38.0, 44.0)	38.0 (35.0, 42.0)	44.0 (40.0, 46.5)	**<0.001**[d,e]
Waist circumference [c] **(cm)**	307	110 (100, 117)	96 (84, 107)	115 (105, 125)	**<0.001**[d,e]
Calf circumference [c] **(cm)**	307	40.0 (36.8, 43.0)	35.0 (32.0, 38.0)	38.0 (36.0, 40.0)	**<0.001**[d,e]
Thigh circumference [c] **(cm)**	307	52 (47, 58)	45 (41, 50)	50 (46, 53)	**<0.001**[d,e]
Waist to hip ratio [c]	307	0.98 (0.91, 1.04)	0.98 (0.91, 1.03)	1.06 (0.97, 1.13)	**<0.001** [d,e]
Smoking status	308				**<0.001**[d]
Current smoker		17 (16 %)	43 (41 %)	34 (36 %)	
Former smoker		47 (44 %)	60 (57 %)	53 (56 %)	
Non smoker		44 (41 %)	2 (1.9 %)	8 (8.4 %)	
Comorbidities					
Cardiovascular disease	308	54 (50 %)	52 (50 %)	69 (73 %)	**<0.001** [d,e]
Hypertension	308	44 (41 %)	32 (30 %)	51 (54 %)	**0.004** [d,e]
Arrythmias	308	8 (7.4 %)	16 (15 %)	17 (18 %)	0.070 [d]
Diabetes	308	13 (12 %)	10 (9.5 %)	21 (22 %)	**0.028** [d,e]
Neoplasms	308	6 (5.6 %)	19 (18 %)	6 (6.3 %)	**0.003** [e]
Abnormal lipid profile	308	29 (27 %)	25 (24 %)	48 (51 %)	**<0.001** [d,e]
Cerebrovascular - disease, stroke	308	9 (8.3 %)	5 (4.8 %)	8 (8.4 %)	0.5
Coronary heart disease	308	13 (12 %)	15 (14 %)	26 (27 %)	**0.009** [d,e]

Abbreviations: COPD: chronic obstructive pulmonary disease, IQR: Interquartile range, OS: overlap syndrome, OSA: obstructive sleep apnea.

[a] n (%); Median (IQR).

[b] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test.

[c] One missing value for the OS group.

[d] P value of the comparison between the OSA and OS groups is statistically significant, i.e. when the symbol is bold $p \leq 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

[e] P value of the comparison between the COPD and OS groups is statistically significant, i.e. when the symbol is bold $p \leq 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

3.1. Anthropometrics and body shape

Patients with COPD or OS were significantly older than those with OSA only (Table 1). The BMI was significantly higher in the OSA and OS groups compared with COPD patients (Table 1). The external body circumferences were highly specific to the three subgroups of patients, as shown in Fig. 2. The dimensions of OSA patients revealed a round shape (high waist, calf, thigh and neck circumferences) with a balanced waist-to-hip ratio compared to COPD patients who were generally thinner (small neck, calf, thigh and waist circumference) but with a balanced waist-to-hip ratio. OS patients also presented with body dimensions that reflected roundness (high neck and waist circumferences, but reduced calf and thigh circumferences compared to OSA patients) with a high waist-to-hip ratio.

3.2. Multidimensional assessment of symptoms

The details of symptoms, profiles and questionnaire scores are presented in Table S1. Figs. 3–5 show radar charts and a heatmap summarizing the results of the multidimensional phenotyping. Patients with OSA more frequently reported witnessed apnea, nocturia, snoring, daytime sleepiness or somnolence when driving, morning discomfort (asthenia, headaches), nocturnal sweating and had higher scores in the BQ, ESS, Pichot fatigue, and ISI questionnaires than patients with COPD or OS. The ESS score was significantly higher in OSA and OS groups with positive responses to subjective questions related to daytime sleepiness. Fatigue scores reflected greater severity in OSA and OS subgroups. Accordingly, fitness to drive was diminished in these two groups. Patients with OS presented libido and memory disorders and had higher Pichot depression, BDI, CAT and SGRQ scores. As expected, the SGRQ, NYHA (New York Heart Association) and CAT scores related to dyspnea were higher in patients with COPD and OS.

3.3. Home self-measurement of blood pressure and heart rate

Among the 210 participants who consented to using the connected wearable BP monitoring device, 63 patients had COPD, 75 had OSA and 72 had OS. OSA patients exhibited higher mean diastolic blood pressure (83 [77–92] mmHg) compared to OS patients (Table 2). COPD patients had faster heart rates compared to OS patients (Table 2).

In the 108 patients previously diagnosed as having hypertension (based on medical history and antihypertensive medication), the hypertension was uncontrolled by their current medication in 85 (78.7 %). While in the 102 who had not reported hypertension, we found undiagnosed hypertension in 79/102 (77.5 %) using home blood pressure monitoring.

Regarding the three groups, the OSA group included more patients with high diastolic blood pressure than the COPD or OS group (50 patients vs. 36 and 33 with diastolic blood pressure above the normal range, respectively), while the OS and OSA groups included more patients with above normal systolic blood pressure than the COPD group (Fig. 5).

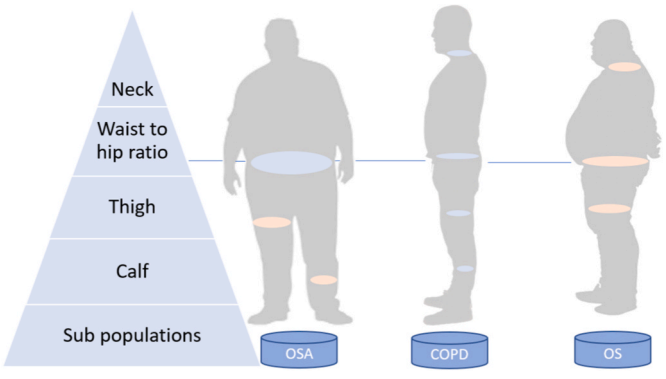

Fig. 2. Body shape in the three chronic respiratory sub-groups
OSA and OS patients presented with a round body shape (high waist and neck circumference, but high calf and thigh circumferences for OSA patients only). However, OSA patients were thinner (small neck, calf, thigh circumferences, moderate increase in waist circumference) and a balanced waist-to-hip ratio.
Abbreviations: COPD: chronic obstructive pulmonary disease, OS: overlap syndrome, OSA: obstructive sleep apnea.

3.4. Burden of comorbidities

OS patients presented with a higher prevalence of diabetes, lipid disorders and cardiovascular diseases such as hypertension and coronary heart disease compared to those with COPD or OSA alone (Figs. 4 and 5, Table 1). The prevalence of these comorbidities was similar in the COPD and OSA groups.

3.5. Medications (ATC codes)

In line with the burden of comorbidities, patients with OS, took a wider range of medications from different pharmacological classes. In particular they were more frequently prescribed medications for the management of metabolic disorders and cardiovascular diseases (Table S2). Patients with COPD (i.e. COPD and OS groups) were very often receiving bronchodilators and corticosteroids for respiratory system disorders, unlike patients with OSA alone (Table S2).

3.6. Sleep studies

While in-depth sleep studies were performed for nearly all the patients with OSA (107; 99 %), less than a third (26; 27 %) of patients with OS and even fewer with COPD alone (9; 8.6 %) benefited from a sleep study. Total sleep time (TST) did not appear to differ among the three groups. The OS group exhibited lower percentages of light sleep (stage N2) in favor of longer slow-wave sleep (N3) and rapid eye movement (REM) stages compared to patients with OSA alone (Table 3). By definition, OSA and OS groups had a higher apnea hypopnea index (AHI). Mean nocturnal SaO_2 appeared to be lower in the OS group in comparison with patients with OSA alone. In addition, mean nocturnal SaO_2 was significantly higher ($p < 0.001$) in non-smokers than in current or former smokers (94 % (93, 95) vs. 93 % (90, 94) and 92 % (91, 94) respectively).

3.7. Pulmonary function tests and blood gazes

Pulmonary function data was available for about two-thirds of the OSA group (Table S3). Patients with COPD had a lower forced expiratory volume in the 1st second (FEV_1) of 54 [39–68] % of predicted values compared to the OS group (61 [45–73] % of predicted), while the OSA group exhibited the highest FEV_1 values (95 [87–107] % of predicted) (Table S3). Residual volume was increased in COPD patients. Daytime gas exchanges were also more impaired in the OS group than in patients with OSA alone.

4. Discussion

Our multidimensional phenotyping identified distinct and clinically relevant profiles among patients with OSA, COPD, and OS included in the e-Meuse study. Patients with OSA are more frequently obese with a round body shape and a balanced waist-to-hip ratio. They report a higher burden of symptoms including daytime sleepiness, snoring, nocturia, witnessed apneas, morning discomfort, night sweats, libido and memory disturbances, and have high scores in the Berlin, Epworth, Pichot fatigue, and ISI scales. They also have the highest self-measured diastolic blood pressure among the three groups. OS patients are obese with a round body shape and a high waist-to-hip ratio. They experience



Fig. 3. Radar charts displaying multidimensional phenotyping based on symptoms, by sub-group.
The radar charts show the percentage of patients with values above the median number for the total population. Purple lines represent COPD patients, black lines OS patients and orange lines OSA patients.
Chart A shows scores and symptoms and Chart B shows subjective symptoms.
Abbreviations: BDI: Beck depression index, BQ: Berlin questionnaire, CAT: COPD assessment test, COPD: chronic obstructive pulmonary disease, ESS: Epworth sleep scale, ISI: insomnia severity index, OS: overlap syndrome, OSA: obstructive sleep apnea, SGRQ: St George's respiratory questionnaire. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

libido and memory disturbances, daytime and morning fatigue and are classified as more severe in the NYHA classification. They have high Pichot depression scores, Beck scores, and CAT and SGRQ questionnaire scores. Patients with OS have a higher prevalence of cardio-metabolic comorbidities than patients with OSA or COPD alone, and in consequence receive a greater number of different medications.

Strengths of the present study are the prospective collection of a combination of body shape measurements, all stages of sleep, depression, fatigue and respiratory failure related symptoms, comorbidities, medications and the determination of undiagnosed or uncontrolled hypertension in OSA, COPD and overlap syndrome.

Our results regarding body shape are in line with the majority of previous studies [16,28–31] showing that OS essentially occurs in people with an obese cardiometabolic COPD phenotype [32,33]. This is of particular clinical relevance as this population with obesity, COPD and OSA responds well to positive airway pressure (PAP) therapies [34–36]. We recently demonstrated that PAP usage by patients with OS was associated with fewer all-cause hospitalizations, emergency room visits, severe acute exacerbations, and reduced healthcare costs [37].

Regarding symptom profiles, data from the literature are somewhat contradictory. This certainly reflects selection biases and the retrospective nature of the majority of available studies. In some studies, daytime sleepiness is reported to be high in both the OSA and OS groups [8,13,16,29,38], while other studies report no significant sleepiness in the OS group [12,17,31]. Our results confirm that daytime sleepiness is more pronounced in the OSA group compared to both OS and COPD. Conversely, fatigue is more common in the COPD and OS groups, as previously suggested by studies linking deterioration in pulmonary function with increased fatigue and dyspnea [39]. This combination of disabling symptoms probably explains the high prevalence of depression in the OS population. Poorer quality of life in the different patient groups can be largely explained by the disabilities induced by the underlying primary disease (i.e. daytime sleepiness and sleep disruption in patients with OSA versus fatigue and dyspnea in those with COPD or OS) [40]. This diversity and complexity in symptom profiles translate into poor performances in the conventional questionnaires used for OSA screening in COPD and OS populations [41]. New diagnostic strategies need to be validated in these populations to accurately detect associated OSA and potentially improve outcomes [37,42].

The e-Meuse study baseline data highlight the high burden of multimorbidity in patients with OS [43], with a high prevalence of metabolic disorders and cardiovascular disease in this group. Both COPD and OSA generate local and systemic inflammation, with oxidative stress that can lead to cardiovascular morbidity. Consequently, it is not surprising that OS is associated with an increased likelihood of cardiovascular disease and mortality compared with either disorder alone. Indeed, the co-occurrence of nocturnal hypoxemia and COPD has been associated with an increased hazard of cardiovascular events and mortality [44] which seems to be mitigated by PAP therapies [45].

A feature of the e-Meuse study is home self-measured BP during one week at baseline (as well as at regular intervals during long-term follow-up) using a connected wearable device. This has revealed an unexpectedly high rate of undiagnosed or uncontrolled hypertension even in participants already being treated by anti-hypertensive drugs. Home blood pressure monitoring is known to be superior to office blood pressure measurements in predicting cardiovascular events [46]. Thus, in this population at high cardiovascular risk our data underline the interest of systematically implementing self-measured blood pressure (SMBP) telemonitoring programs [47].

Our analysis of the e-Meuse study baseline data has many strengths, but also some limitations. The main limitation is the relatively small sample size and the lack of systematic sleep studies in patients with COPD alone and pulmonary function tests in those with OSA without COPD.

5. Conclusion and perspectives

The multidimensional phenotyping approach adopted in the current study accurately identified body shape, symptom and comorbidity profiles corresponding to distinct clinically relevant phenotypes of patients with OSA, COPD, and OS. The association between COPD and OSA often goes unrecognized in routine clinical practice especially in COPD phenotyping. Screening tools that improve the detection of OSA in patients with COPD are required so as to provide a suitable diagnostic pathway that facilitates optimal management. Large scale prospective and randomized controlled interventional studies to determine the course, clinical consequences and prognosis of overlap syndrome versus OSA alone are needed.

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Table 2
Home self-measurement of blood pressure and heart rate.

Characteristic	N missing[c]	OSA[a]	COPD[a]	OS[a]	p-value[b]
Heart rate (bpm)	6	N = 73	N = 61	N = 70	
Mean		72 (66, 81)	76 (70, 86)	73 (64, 81)	**0.026** [e]
Median		72 (65, 80)	76 (68, 87)	73 (64, 80)	**0.046** [e]
Min		62 (56, 70)	68 (61, 74)	64 (56, 71)	**0.021** [e]
Max		85 (73, 92)	91 (77, 101)	83 (73, 96)	0.087 [e]
Systolic BP (mmHg)	6	N = 73	N = 61	N = 70	
Mean		131 (124, 144)	134 (126, 144)	139 (129, 147)	0.12 [d]
Median		133 (122, 142)	135 (125, 143)	139 (128, 147)	0.13 [d]
Min		114 (102, 125)	117 (102, 127)	118 (104, 128)	0.5
Max		150 (141, 163)	153 (139, 163)	162 (147, 174)	0.051 [d, e]
Diastolic BP (mmHg)	6	N = 73	N = 61	N = 70	
Mean		83 (77, 92)	80 (73, 87)	80 (75, 84)	**0.050** [d]
Median		82 (77, 90)	80 (73, 86)	80 (74, 85)	0.069 [d]
Min		71 (62, 76)	66 (54, 75)	66 (55, 73)	0.058 [d]
Max		97 (92, 109)	93 (87, 102)	96 (85, 110)	0.10

Abbreviations: BP: blood pressure, bpm: beats per minute, COPD: chronic obstructive pulmonary disease, IQR: interquartile range, mmHg: millimeter of mercury, OS: overlap syndrome, OSA: obstructive sleep apnea.

[a] Median (IQR).

[b] Wilcoxon rank sum exact test; Wilcoxon rank sum test; Kruskal-Wallis rank sum test.

[c] False values were removed (e.g. weight <40 kg) and were counted among missing values. The mean number of values per patient, during the week of measurement, was 25.3 for heart rate, 25.6 for systolic arterial pressure and 25.4 for diastolic arterial pressure.

[d] P value of the comparison between the OSA and OS groups shows statistical significance, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

[e] P value of the comparison between the COPD and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

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CRediT authorship contribution statement

Ophélie Coiffier: Writing – original draft, Validation, Methodology, Formal analysis, Conceptualization. **Pasquale Tondo:** Writing – original draft, Investigation, Conceptualization. **Marie Joyeux-Faure:** Writing – review & editing, Supervision, Investigation. **Renaud Tamisier:** Conceptualization, Data curation, Investigation, Writing – review & editing. **Khier Amrani:** Investigation, Writing – review & editing. **Jean-Claude Cornu:** Investigation, Writing – review & editing. **Robin Terrail:** Writing – review & editing, Investigation, Data curation. **Christian Caussé:** Writing – review & editing, Resources, Investigation, Funding acquisition, Conceptualization. **Sebastien Bailly:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Jean-Louis Pépin:** Writing – original draft, Supervision, Funding acquisition,

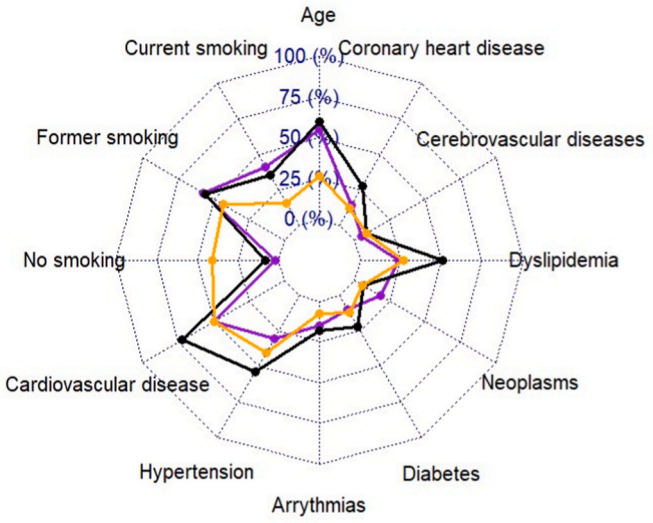

Fig. 4. Radar chart displaying burden of comorbidities by sub-group
The radar chart shows the percentage of patients having each comorbidity and the percentage of patients over 64 years of age (median age of the study population). Purple lines represent COPD patients, black lines OS patients and orange lines OSA patients.
Abbreviations: COPD: chronic obstructive pulmonary disease, OS: overlap syndrome, OSA: obstructive sleep apnea. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

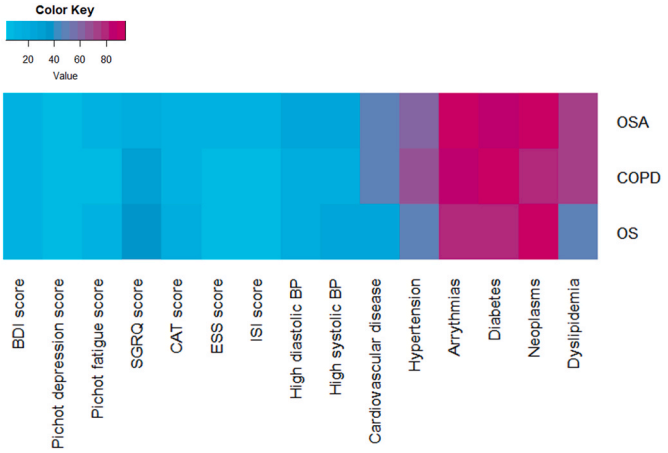

Fig. 5. Heatmap displaying the main characteristics that differ according to the disease
The heatmap shows, for each sub-group, the mean for the scores and the percentage of patients with the comorbidity for each comorbidity variable. The two variables of diastolic and systolic blood pressure show, by group, the percentage of patients for whom hypertension was detected using a connected blood pressure measuring device.
The graduation of colors corresponds to scores in the questionnaires and to the percentage of comorbidities and blood pressure measurements (light blue < dark blue < purple < pink).
Abbreviations: BDI: Beck depression index, CAT: COPD assessment test, COPD: chronic obstructive pulmonary disease, ESS: Epworth sleepiness scale, ISI: insomnia severity index, OS: overlap syndrome, OSA: obstructive sleep apnea, SGRQ: St George's respiratory questionnaire. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Sleep studies; comparison between OSA, COPD and OS.

	N	OSA N = 108[a]	COPD N = 105[a]	OS N = 95[a]	p-value[b]
Multidimensional symptom assessment					
Sleep study data available	308	107 (99 %)	9 (8.6 %)	26 (27 %)	[d]
TST (min)	142	399 (339, 455)	456 (368, 469)	428 (325, 479)	0.5
Missing		1	96	69	
WASO (%TST)	87	16 (9, 38)	13 (7, 27)	11 (7, 45)	
Stage N1 (%TST)	87	5.5 (3.7, 8.0)	6.6 (5.4, 8.1)	5.3 (3.8, 11.6)	
Stage N2 (%TST)	87	79 (74, 82)	75 (63, 79)	62 (36, 75)	[c]
SWS (%TST)	87	2 (0, 6)	8 (2, 18)	22 (7, 28)	[c]
REM sleep (%TST)	85	11.8 (8.9, 15.8)	2.9 (2.9, 12.0)	19.0 (14.3, 21.6)	[c]
Respiratory micro-arousal index	88	9 (6, 13)	2 (1, 3)	6 (4, 7)	**0.003** [c,d]
AHI	142	34 (25, 47)	9 (7, 11)	30 (24, 36)	**<0.001** [c,d]
Missing		1	96	69	
ODI	142	19 (11, 36)	8 (5, 10)	12 (4, 20)	**<0.001** [c]
Obstructive apnea index	142	7 (4, 15)	1 (0, 3)	4 (1, 10)	**<0.001** [c,d]
Missing		1	96	69	
Obstructive hypopnea index	142	23 (18, 32)	7 (6, 9)	22 (13, 30)	**<0.001** [d]
Missing		1	96	69	
T90 (min)	137	24 (4, 67)	31 (16, 135)	75 (1, 200)	0.3
Missing		4	97	70	
Mean SaO_2 (%)	138	93 (92, 94)	93 (88, 93)	92 (89, 94)	**0.011** [c]
Missing		3	96	71	

When the number of patients in a category was less than 5, the test iwas not performed.
Abbreviations: AHI: Apnea hypopnea index, COPD: chronic obstructive pulmonary disease, NOSE: Nasal obstruction symptom evaluation, ODI: Oxygen Desaturation index, OS: overlap syndrome, RDI: Respiratory disturbance index, SaO_2: Arterial oxygen saturation, OSA: obstructive sleep apnea, REM: Rapid Eye Movement, SWS: Slow wave sleep, TST: Total sleep time, T90: Cumulative time spent below 90 % of SaO_2, WASO: Wake after sleep onset.

[a] n (%); Median (IQR).

[b] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test.

[c] P value of the comparison between the OSA and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

[d] P value of the comparison between the COPD and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test.

Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Christian Causse reports a relationship with Bioprojet Pharma, Paris, France that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

None of the other authors (OC, PT, MJF, RTa, KA,JCC, RTe, SB and JLP) has a competing interest or personal relationship to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2024.04.038.

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Supplementary Material

E-Meuse investigators

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Table S1: Multidimensional symptom assessment; comparison between OSA, COPD and OS

	N	OSA, N = 108[1]	COPD, N = 105[1]	OS, N = 95[1]	p-value[2]
Multidimensional symptom assessment					
Subjective sleep duration (hours)	304	8.5 (7.5, 9)	8 (7, 9)	8 (7.1, 9)	0.3
Missing		0	3	1	
Witnessed apneas	284	42 (44%)	5 (5.2%)	7 (7.6%)	**<0.001** [α]
Missing		13	8	3	
Nocturia	308	67 (62%)	57 (54%)	43 (45%)	0.057 [α]
Snoring	308	85 (79%)	34 (32%)	28 (29%)	**<0.001** [α]
Snoring intensity (VAS)	303	6 (3, 8)	0 (0, 3)	0 (0, 2)	**<0.001** [α]
Missing		1	2	2	
Reported daytime sleepiness [3,4]	304	3 (0, 5)	0 (0, 3)	1 (0, 3)	**<0.001** [α]
Morning fatigue [3,4]	304	5 (1.5, 7)	0 (0, 5)	0 (0, 5)	**<0.001** [α]
Frequency of morning headaches (VAS) [3]	304	1 (0, 4.5)	0 (0, 0)	0 (0, 0)	**<0.001** [α]
Libido disorders	308	32 (30%)	16 (15%)	25 (26%)	**0.037** [β]
Memory disorders	308	65 (60%)	38 (36%)	48 (51%)	**0.002** [β]
Night sweating (VAS) [3]	304	2 (0, 5)	0 (0, 3.3)	0 (0, 3)	**0.002** [α]
NYHA [3]	304				**<0.001** [α]
1		71 (66%)	43 (41%)	32 (34%)	
2		19 (18%)	17 (16%)	14 (15%)	
3		11 (10%)	16 (15%)	16 (17%)	
4		6 (5.6%)	28 (27%)	31 (33%)	
Berlin score ≥ 2	308	71 (66%)	13 (12%)	31 (33%)	**<0.001**[α, β]
Driving License	308	96 (89%)	79 (75%)	77 (81%)	**0.035**
Number of km per year	252	15,000 (6,750, 25,000)	10,000 (5,000, 20,000)	10,000 (5,000, 15,000)	**0.011** [α]
Missing		12	26	18	
Sleepiness-related accident	307	5 (4.7%)	3 (2.9%)	4 (4.2%)	
Missing		1	0	0	
Near miss accident	308	11 (10%)	3 (2.9%)	6 (6.3%)	
Frequency of sleepiness at the wheel	252				
At least once a week		9 (9.4%)	2 (2.5%)	3 (3.9%)	
Less than once a week		87 (90.6%)	77 (96.5%)	74 (96.1%)	
Missing		12	26	18	
Epworth score	308	10 (5, 13)	6 (3, 9)	6 (3, 9)	**<0.001** [α]
Pichot fatigue score	308	9 (3, 16)	5 (2, 11)	8 (4, 14)	**0.005** [β]
Pichot Depression score	197	2 (0, 6)	1 (0, 5)	4 (0.3, 9)	0.054 [α, β]
Missing		31	47	33	
Beck depression score	188	8 (4, 15)	6 (2, 16)	10 (5, 19)	0.089 [β]
Missing		31	50	39	
CAT score	197	11 (6, 16)	13 (8, 19)	15 (10, 22)	**0.005** [α]
Missing		31	47	33	
ISI score	193	12 (8, 17)	4 (2, 9)	8 (4, 13)	**<0.001** [α, β]
Missing		32	48	35	
SGRQ score	185	16 (10, 28)	32 (21, 43)	37 (24, 47)	**<0.001** [α]
Missing		38	51	34	
RLS severity	30	13 (8, 21)	19 (18, 21)	23 (18, 27)	[α]
Missing		88	102	88	
NOSE score (calculated)	205	4 (0, 8)	2 (0, 5)	4 (0, 10)	0.055 [β]
Missing		25	44	34	

[1] n (%); Median (IQR)

[2] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test

[3] One missing value for OSA and COPD groups and 2 for OS groups

[4] Scale: 1 = almost every day, 2 = 3 to 4 times per week, 3 = 1 to 2 times per week, 4 = 1 to 2 times per month, 5 = never or almost never

[α] P value of the comparison between the OSA and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

[β] P value of the comparison between the COPD and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

When the number of patients in a category is less than 5, the test was not performed

Abbreviations: CAT: COPD assessment test, COPD: chronic obstructive pulmonary disease, ISI: insomnia severity index, NOSE: nasal obstruction symptom evaluation, OS: overlap syndrome, OSA: obstructive sleep apnea, SGRQ: St George's respiratory questionnaire, RLS: restless legs syndrome, VAS: visual analogue scale (0-10)

Table S2: Medications: comparison between OSA, COPD and OS

Characteristic	N	OSA, N = 108[1]	COPD, N = 105[1]	OS, N = 95[1]	p-value[2]
Medications					
Alimentary tract and metabolism	308	46 (43%)	45 (43%)	56 (59%)	**0.031** [α, β]
For acid related disorders	308	33 (31%)	23 (22%)	37 (39%)	**0.032** [β]
Used in diabetes	308	11 (10%)	10 (9.5%)	19 (20%)	**0.050** [α, β]
Antithrombotic agents	308	23 (21%)	38 (36%)	50 (53%)	**<0.001** [α, β]
For cardiovascular disorders	308	52 (48%)	52 (50%)	72 (76%)	**<0.001** [α, β]
Diuretics	308	10 (9.3%)	11 (10%)	25 (26%)	**<0.001** [α, β]
Beta blocking agents	308	18 (17%)	16 (15%)	28 (29%)	**0.023** [α, β]
Agents acting on the renin-angiotensin system	308	33 (31%)	28 (27%)	41 (43%)	**0.037** [α, β]
Corticosteroids for systemic use	308	7 (6.5%)	20 (19%)	17 (18%)	**0.016** [α]
For respiratory system	308	19 (18%)	93 (89%)	88 (93%)	**<0.001** [α]
For obstructive airway conditions	308	18 (17%)	92 (88%)	88 (93%)	**<0.001** [α]

[1] n (%); Median (IQR)

[2] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test

[α] P value of the comparison between the OSA and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

[β] P value of the comparison between the COPD and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

Abbreviations: COPD: chronic obstructive pulmonary disease, OS: overlap syndrome, OSA: obstructive sleep apnea

Table S3: Pulmonary function tests and blood gases: comparison between OSA, COPD and OS

Parameter	N	OSA N = 108[1]	COPD N = 105[1]	OS N = 95[1]	p-value[2]
Pulmonary function parameters					
Pulmonary function test performed	308	81 (75%)	104 (99%)	93 (98%)	<0.001 α
FVC (L)	270	3.68 (2.92, 4.30)	2.63 (2.17, 3.28)	2.77 (2.05, 3.71)	<0.001 α
Missing		30	4	4	
FVC (% of pred.)	270	100 (89, 107)	78 (65, 94)	80 (68, 93)	<0.001 α
Missing		30	4	4	
FEV1 (L)	270	2.91 (2.35, 3.30)	1.46 (1.06, 1.85)	1.62 (1.19, 2.23)	<0.001 α, β
Missing		30	4	4	
FEV1 (% of pred.)	270	95 (87, 107)	54 (39, 68)	61 (45, 73)	<0.001 α, β
Missing		30	4	4	
RV (L)	268	2.28 (1.80, 2.61)	3.98 (3.12, 4.96)	3.72 (3.01, 4.44)	<0.001 α
Missing		29	5	6	
RV (% of pred.)	268	111 (92, 125)	181 (148, 223)	165 (137, 191)	<0.001 α, β
Missing		29	5	6	
TLC (L)	268	5.63 (5.06, 6.57)	6.88 (5.77, 7.86)	6.89 (5.63, 7.92)	<0.001 α
Missing		29	5	6	
TLC (% of pred.)	268	97 (86, 105)	115 (103, 127)	109 (100, 121)	<0.001 α, β
Missing		29	5	6	
DLCO (L)	182	6.50 (5.52, 7.78)	4.09 (3.26, 4.59)	4.79 (3.54, 5.96)	<0.001 α, β
Missing		43	43	40	
DLCO (% of pred.)	141	25 (22, 27)	17 (12, 18)	18 (14, 22)	<0.001 α, β
Missing		51	65	51	
Alveolar volume (L)	182	5.00 (4.19, 5.93)	4.66 (4.06, 5.40)	4.56 (3.95, 5.74)	0.3
Missing		43	43	40	
Alveolar volume (% of pred.)	141	82 (76, 90)	80 (70, 86)	77 (68, 85)	0.047 α
Missing		51	65	51	
Hb (g/L)	168	150 (142, 159)	144 (132, 151)	152 (146, 159)	<0.001 β
Missing		41	57	42	
Diffusion coefficient of CO (L)	182	1.33 (1.18, 1.50)	0.87 (0.70, 1.00)	0.99 (0.80, 1.17)	<0.001 α, β
Missing		43	43	40	
Diffusion coefficient of CO (% of pred.)	141	27 (3, 31)	12 (2, 21)	20 (8, 25)	<0.001 α, β
Missing		51	65	51	
Vital capacity (% of pred.)	271	98 (87, 107)	79 (64, 95)	79 (69, 93)	<0.001 α
Missing		29	4	4	
Expiratory reserve vol (% of pred.)	266	75 (48, 108)	86 (49, 117)	55 (36, 83)	0.002 α, β
Missing		29	5	8	
Inspiratory capacity (% of predicted.)	268	101 (83, 118)	75 (57, 93)	85 (68, 104)	<0.001 α, β
Missing		29	5	6	
FRC (L)	268	3.08 (2.53, 3.67)	4.93 (4.09, 5.75)	4.34 (3.74, 5.34)	<0.001 α, β
Missing		29	5	6	
Thoracic gas volume corrected by FRC (% of predicted.)	268	96 (82, 115)	156 (127, 176)	134 (115, 155)	<0.001 α, β
Missing		29	5	6	
Blood gases					
Blood gases test performed	308	66 (63%)	63 (66%)	69 (64%)	0.9
PaO_2 (kPa)	198	11.25 (10.26, 12.35)	9.89 (8.91, 10.85)	9.78 (9.00, 10.53)	<0.001 α
Missing		39	39	32	
$PaCO_2$ (kPa)	198	5.22 (4.89, 5.61)	5.36 (5.07, 5.69)	5.59 (5.17, 5.94)	0.006 α, β
Missing		39	39	32	
pH	198	7.42 (7.41, 7.44)	7.43 (7.40, 7.44)	7.42 (7.40, 7.44)	0.6
Missing		39	39	32	
HCO_3 (mmol/L)	197	25.60 (24.70, 26.80)	26.10 (24.73, 27.70)	26.40 (24.85, 27.88)	0.12 α
Missing		39	39	33	
SaO_2 (%)	198	97.30 (96.40, 97.90)	95.65 (94.00, 96.90)	95.20 (94.15, 96.25)	<0.001 α
Missing		39	39	32	
Lactate (mmol/L)	182	1.10 (0.80, 1.65)	1.10 (0.70, 1.68)	1.20 (0.80, 1.70)	0.7
Missing		41	47	38	

[1] n (%); Median (IQR)

[2] Pearson's Chi-squared test; Kruskal-Wallis rank sum test; Fisher's exact test

[α] P value of the comparison between the OSA and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

[β] P value of the comparison between the COPD and OS groups is significative, i.e. when the symbol is bold $p < 0.05$ otherwise $0.05 \leq p \leq 0.1$. Pearson's Chi-squared test; Wilcoxon rank sum test were performed

Abbreviations: CO: carbon monoxide, COPD: chronic obstructive pulmonary disease, DLCO: diffusing capacity for carbon monoxide, FEV1: forced expiratory volume in 1 sec, FRC: functional respiratory capacity, FVC: forced vital capacity, HCO_3: bicarbonate, Hb: hemoglobin, OS: overlap syndrome, OSA: obstructive sleep apnea, $PaCO_2$: arterial blood CO_2 pressure, PaO^2: partial pressure of oxygen, RV: residual volume, TLC: total lung capacity

IV. Problèmes méthodologiques de préparation et d'analyses dans le suivi du traitement de données longitudinales multidimensionnelles multiples - Article de revue publié n°1[127]

Introduction

Analyser des données collectées au cours du temps pour décrire et prédire les trajectoires de patients[81], est aujourd'hui largement facilité par le développement du télémonitoring et du self-monitoring via des objets connectés[89] comme les montres, les balances, les capteurs sous les matelas, etc. Ces dispositifs génèrent des données longitudinales, caractérisées par des mesures répétées, acquises à différents points de temps de suivi. Elles permettent d'étudier à la fois les différences inter-individuelles et intra-individuelles au cours du temps, ainsi que leurs associations avec des facteurs évolutifs tels que les facteurs de risques. Cependant, l'analyse de ces données nécessite un choix méthodologique rigoureux pour éviter les biais dans l'estimation des paramètres ou dans les performances prédictives, susceptibles de conduire à des conclusions erronées et, par conséquent, à des répercussions inappropriées en recherche, en santé publique ou en pratique clinique. De nombreuses publications ont détaillé ces techniques spécifiques dans un domaine d'analyse précis (pour décrire[99,128–130], modéliser[99,100,130–133] ou regrouper[131,133,134] les données longitudinales) mais à notre connaissance, aucune revue n'a synthétisé plusieurs méthodes issues de différents champs analytiques dans le contexte des études du sommeil.

Objectifs

Cet article vise à présenter et illustrer dix méthodes statistiques couramment utilisées dans le domaine du sommeil. Plus précisément, il a pour objectif de décrire les principes de chaque méthode et de fournir aux cliniciens et chercheurs une vision structurée et globale des stratégies d'analyse des données longitudinales.

Méthodes

Dans un objectif pédagogique, un jeu de données simulé incluant l'observance à la PPC et le score de somnolence d'Epworth (ESS) sur un échantillon de 300 patients et 90 points de temps a été construit. A partir de cet exemple, un guide a été proposé, étape par étape, pour l'analyse des données longitudinales : décrire et visualiser les données, formuler une question de recherche pertinente puis sélectionner la méthode statistique adaptée. Enfin, chaque méthode est présentée de façon détaillée et illustrée par une application concrète, afin de faciliter sa compréhension et son appropriation par un large public intéressé par l'analyse de ce type de données.

Résultats

Aucune méthode unique ne permet de répondre à l'ensemble des questions posées par les données longitudinales et le choix analytique doit être guidée par l'objectif scientifique, la structure et le type

de données disponibles. Dans ce cadre, les méthodes présentées s'organisent de manière complémentaire en trois grands ensembles : des approches de comparaison (ANalysis Of Variance pour mesures répétées ou χ^2 selon que les données sont quantitatives ou qualitatives) permettant d'évaluer des variations au cours du temps, des méthodes de clustering et de phénotypage (K-means, Latent Transition Analysis, Growth Mixture Modelling, Group-Based Trajectory Modelling) visant à identifier des profils ou trajectoires homogènes de patients, et des méthodes de modélisation (modèles mixtes, AutoRegression Integrated Moving Average et cross-corrélation, modèles de survie, modèles de Markov cachés) permettant d'analyser les relations dynamiques et de prédire l'évolution des variables. Cette organisation met en évidence une progression analytique, allant d'approches descriptives vers des modèles plus complexes.

Cette étude a été publiée sous forme d'article de revue dans Sleep Medicine en octobre 2025.

Perspectives

Cet article apporte un cadre structuré et pédagogique pour l'analyse des données longitudinales, en mettant en évidence la complémentarité des méthodes selon les questions de recherche et la structure des données. Il souligne la nécessité d'un choix méthodologique rigoureux, notamment face à la complexité de ces données (corrélations intra-individuelles, données manquantes), afin de limiter les biais d'estimation et d'interprétation. Dans un contexte de disponibilité croissante de données longitudinales en médecine du sommeil, ce travail constitue ainsi une base pour guider l'utilisation et le développement futur d'approches analytiques adaptées. Ainsi, les travaux suivant de la thèse étant basés sur des analyses de données longitudinales, cet article est une synthèse des questions que nous nous sommes posées et des recherches que nous avons menées de façon à identifier les méthodes adaptées aux problématiques soulevées. C'est notamment le cas de la problématique portant sur les abandons de mesures, très courants dans l'analyse de données longitudinales provenant d'objets connectés notamment la PPC[21].

Article

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An overview of longitudinal data analyses in sleep research

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ABSTRACT

Background: Repeated measures or longitudinal data, are commonly used in sleep apnea research to assess changes in weight, symptoms or continuous positive airway pressure (CPAP) treatment adherence over time. Such data allow the examination of both between-person differences and within-person changes in outcomes. However, analyzing longitudinal data can be challenging, particularly in selecting the appropriate statistical method, as an inadequate choice may introduce bias into parameter estimates and outcome predictions.
Objective: This paper aims to provide a structured and accessible overview of longitudinal data analysis in sleep research by describing the most commonly used statistical methods and illustrating their applications through a simulated example.
Dataset: A simulated dataset of 300 patients with 90 repeated measurements over time was created illustrating changes in CPAP adherence and Epworth Sleepiness Scale score over time considered as binary, categorical and continuous outcomes.
Analytical framework: A stepwise analytical framework encompassing the main stages of longitudinal data analysis—data description, visualization, formulation of the research question, and selection of the statistical method. Within this framework, ten commonly used analytical approaches are presented, covering descriptive (ANOVA, χ^2), clustering (K-means, LTA, GMM, GBTM), and modeling methods (mixed models, ARIMA, survival analysis, HMM), with emphasis on their assumptions, scope, and interpretation.
Conclusion: This structured overview proposes a coherent analytical pathway for longitudinal data, supported by implementation examples, to help researchers and clinicians navigate complex longitudinal-measure analyses in sleep research and related fields.

1. Introduction

Recent technological advances have resulted in the widespread use of connected devices [1], such as smart watches, fitness or sleep trackers, that enable collection of large-scale data, used for faster diagnosis and personalized treatment in sleep research. In particular, the rising interest of using telemonitoring data in sleep studies has led to innovative solutions for patient profiling or adherence prediction [2]. One of the main characteristics of the data generated by these technologies is their longitudinal nature.

Longitudinal or repeated measurement data are observations that have been collected from the same individuals at multiple time points, typically spaced at regular intervals. These data allow for tracking individual and group-level changes over time, offering valuable insights into health trajectories – that is, the sequence and progression of health-related events or conditions over time. This includes, for example, identifying the underlying state of treatment efficacy and enabling early detection of deterioration [3]. By capturing both between-person differences and within-person changes, longitudinal data enable the identification of patterns and risk factors over time, which is not possible

Abbreviations: ANOVA, analysis of variance; ARIMA, autoregression integrated moving average; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness scale; GBTM, group-based trajectory modelling; GMM, growth mixture modelling; HMM, hidden Markov model; LTA, latent transition analysis.

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with ad hoc or baseline measures. For example, longitudinal studies have examined out to assess how changes in weight over time influence the risk of obstructive sleep apnea (OSA) [4], how ethnic disparities are associated with insomnia symptoms [5] and how daytime sleepiness evolves after ischemic stroke with transient ischemic attack [6].

Three terms are often used to refer to this type of data: 1) longitudinal data are repeated observations collected from the same individuals over time, often with irregular intervals and multiple types of measures (e.g., tracking patients' blood pressure over several years) [7], 2) time series data are sequential observations of the same variable measured at regular intervals, typically at the population or system level (e.g., continuous tracking of a patient's heart rate) [8] and 3) trajectories are statistical patterns or latent classes derived from longitudinal data that describe typical evolution profiles in subgroups of individuals [9].

Analyzing longitudinal data involves specific methodological considerations that differ from those used in cross-sectional studies. The repeated nature of observations generates within-subject correlations and complex data structures that require dedicated analytical approaches. Moreover, numerous statistical methods exist — from simple descriptive analyses to advanced modeling techniques — which can make it difficult for researchers to select the most suitable approach for their research questions. These aspects highlight the need for a clear overview of analytical strategies for longitudinal data, particularly in sleep studies, where such data are becoming increasingly available.

This overview of longitudinal data analysis aims to provide a structured and accessible introduction to the overall analytical process, from initial data description and visualization to formulation of the research question and selection of appropriate statistical methods. Previous publications have described specific statistical techniques within isolated analytical domains (to describe [10–13], model [12–17], or cluster [14,16,18] longitudinal data), but to our knowledge, no review has described several different methods within a single analytical framework.

Based on a simulated dataset used for illustrative and pedagogical purposes, this paper explores this analytical framework by highlighting ten commonly used statistical methods for longitudinal data analysis, providing detailed explanations and key references for further exploration.

2. An overview of the applied example

To illustrate the longitudinal data analysis methods, the context of CPAP adherence will be considered as it offers a large panel of situations for such data with many challenges already reported [19]. Obstructive sleep apnea is a chronic disease with multi factor and heterogeneous presentation [20,21]. CPAP is the first line treatment for moderate to severe obstructive sleep apnea patients [22]. The adherence, measured in hours of treatment device use per night, is daily collected by CPAP which is a connected machine. CPAP adherence is a continuous value which can also be considered as a binary variable, according to the admitted threshold of 4 h per night which is the minimum usage required for clinical benefit [22,23]. Alternatively, it can be used as a categorical variable considering non-adherent patients ([0h; 2h[usage per night), moderate adherent ([2h; 4h[usage per night) and adherent patients ($\geq$4 h per night). Additionally, we use the daytime sleepiness, which is a major symptom of OSA patients and is assessed by the Epworth sleepiness scale (ESS). The ESS ranges from 0 to 24 and patients with a score of 10 or more are considered having an excessive daytime sleepiness (EDS).

Taking this into consideration, an educational dataset was simulated using R version 4.3.0, consisting of 300 patients with 90 time points, representing CPAP adherence and 2 ESS score assessments. Given that some methods require two different parameters and the question of how EDS changes with CPAP adherence is often raised in the context of sleep medicine, the ESS score is added to the CPAP adherence variable. For educational purposes, we simulated 3 groups of patients following different trajectories of CPAP adherence [24]. At first, three CPAP adherence profiles were created using three distinct parameters (respectively, $\mu = 2.2$, $\sigma = 1$; $\mu = 4.8$, $\sigma = 0.6$; $\mu = 6.3$, $\sigma = 0.7$), all followed a normal distribution in positive space and representing non-adherent, adherent and highly adherent patients. Next, patients were pooled to follow the same trajectory over the 90 time points using different CPAP adherence profiles every 30 time points. In this way, the first group represented patients who were non-adherent during the first 30 time points, then became highly adherent during the second 30 time points, finally stabilizing in the adherent group during the last 30 time points. The second group represents patients who were adherent during the first 30 time points, then became non-adherent during the second 30 time points, finally becoming highly adherent during the last time points. The third group represents highly adherent patients who decreased their adherence to become non-adherent over the last 30 time points. It is worth mentioning that, for simplicity, we did not simulate treatment discontinuations, assuming all patients remained under treatment for 3 months. Most dropouts occurred within the first 3 months, and between 20 % and 35 % of patients discontinued treatment in the long term [24]. The simulated dataset does not contain any missing values either, leading to possible biases (Supplementary Material, Appendix B) but this represents a simulated, educational database that is close to reality. The ESS score was created as a discrete variable ranging from 0 to 24 following a beta binomial distribution ($\alpha = 9$, $\beta = 15$). These parameters were chosen based on the high ESS score of OSA patients (mean = 12 and standard deviation = 3); thus, $\alpha = 12\text{-}3$ and $\beta = 12 + 3$.

3. Step 1 – data description

Longitudinal data can be either numerical (e.g. continuous measurements) or categorical (e.g. presence or absence of a condition over time), and the nature of the data directly influences the choice of the adequate statistical methods. Longitudinal studies can address a variety of research questions - some focus on detecting temporal trends, while others examine individual trajectories or the impact of event frequency. When dealing with continuous variables, changes can be captured across the full range of measurement values, whereas categorical data restrict observations to predefined categories. For example, CPAP adherence is a continuous variable which varies over time: patients can be adherent at time point 1 ($\geq$4h), become non-adherent at time point 2 (<4h), then increase their adherence again at time point 3 (Fig. 1). This example illustrates the type of variations that can occur in longitudinal data and raises a broader question: what do we need to understand about longitudinal data before choosing an appropriate analytical method? This involves identifying the nature of the variables, the timing and frequency of measurements, the presence of missing data, and the type of variation we aim to capture. These elements are essential to guide the choice or adaptation of statistical approaches.

A common approach to summarizing longitudinal data at the group-level is to report aggregated statistics, such as mean and standard deviation or median and interquartile range for continuous variables, and number of patients and category frequencies for categorical ones. However, these aggregate statistics fail to capture the individual-level dynamics and temporal patterns that are central to longitudinal data. Going further, we can assess the data structure by verifying the analyzed period duration and the number of measurements per patient, as well as check if all time points are evenly spaced. If the data contain missing values, is it important to evaluate if they follow a pattern or if they are missing at random. If dealing with time series, seasonality or temporal trends in the data should be verified. Finally, evaluating the correlation pattern of repeated measures within individuals can help in selecting the appropriate statistical method.

To have a better understanding of the data, it is advisable to compute some indicators, depending on the research scope and the data structure. For example, in the case of simulated data of CPAP adherence, the

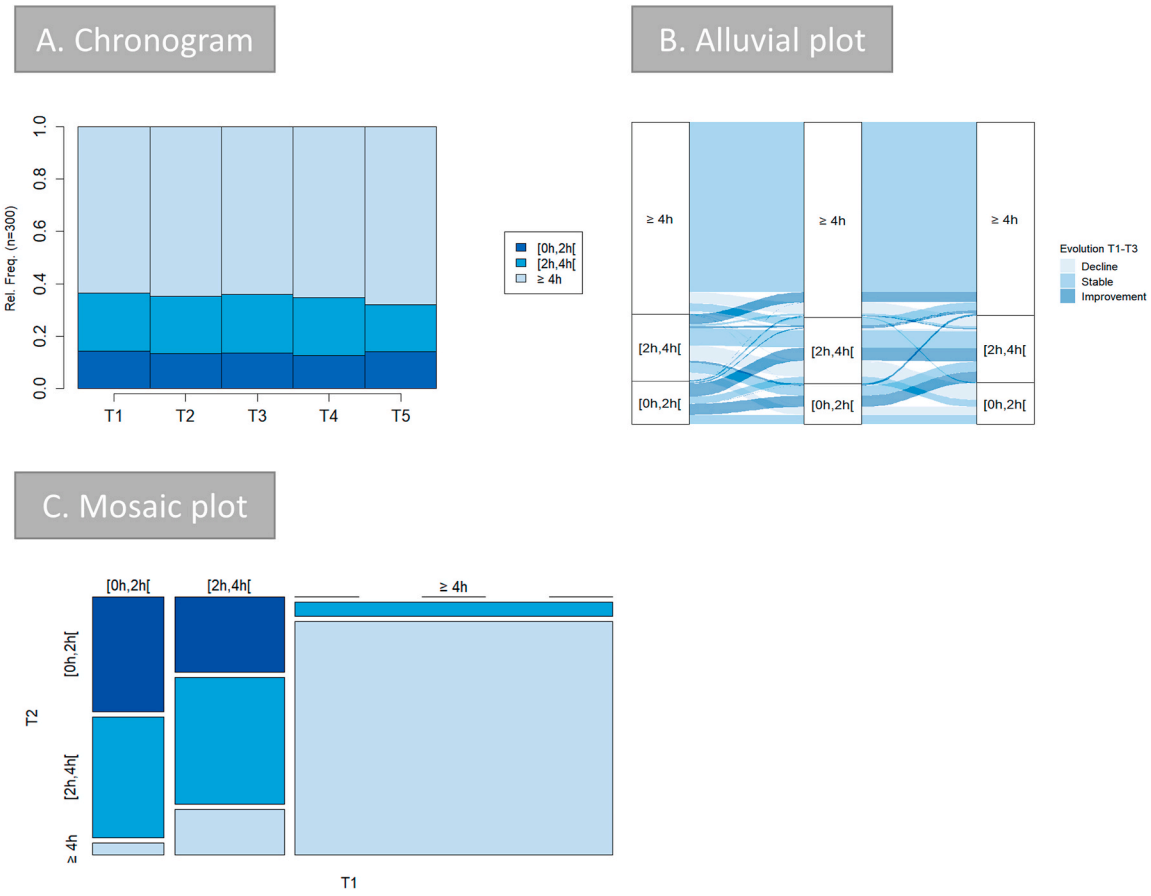

Fig. 1. Different types of categorical trajectories and their visualization, example with CPAP adherence. *Attribute values are characteristics or categories, not numbers. Values changes are instantaneous and each value is valid for an interval of time. Collected by medical records, case report form, questionnaires, interview. Abbreviation: CPAP, continuous positive airway pressure.*

indicators of interest would be the number of time points, number of values equal to 0h, number of adherent patients (≥4h) versus non-adherent (<4h) and the variation coefficient. The summary statistics of the simulated data is available Table 1. However, this list is not exhaustive, as the objective of this step is to explore the dataset studied; other indicators may also be useful.

4. Step 2 – data visualization

In addition to describing longitudinal data, data visualization, depending on the type of data observed, can help identify global and individual trends prior to statistical analyses. It also enables the visual detection of patient clusters defined by intra-class homogeneity (patients with the same characteristics) and inter-class heterogeneity (different groups of patients with different characteristics).

The visualization of categorical CPAP adherence from the simulated data plot can be done using different and non-exhaustive representations: 1) a chronogram (Fig. 1A) – a barplot type that represents the states of variables over time – reveals that all adherence categories are evenly distributed across the analyzed time points, 2) an alluvial plot or Sankey diagram (Fig. 1B) – a plot which shows how categorical data change over time using flows to represent transitions between groups – we can visualize the adherence trajectories of the 3 identified patient groups and their changes over time, 3) a mosaic plot (Fig. 1C) – a graphical representation of contingency tables that displays the relationships between categorical variables using tiled rectangles – provides insights into patients transitions at selected time points. For instance, most patients who were adherent (≥4h) or moderately adherent ([2h,4h[) at T1 remained in the same category at T2, while many initially non-adherent patients ([0h,2h[) improved by the second time point.

The visualization of quantitative trajectories can be based on different graphs such as 1) a spaghetti plot (Fig. 2A) that illustrates individual adherence variability, indicating irregular patterns among patients, 2) a spline plot (Fig. 2A), a type of line graph that uses smoothed curved lines to connect data points, revealing a smooth trend in CPAP adherence over time, 3) a boxplot (Fig. 2B) can provide an overview of adherence distribution among selected patients over time, describing the data distribution at different time points, showing relatively stable median adherence but variation between individuals and a 4) survival plot (Fig. 2C), that shows a decline in CPAP use, where adherence is treated as a binary outcome (null values vs. no null values), with patients switching from users (no null CPAP adherence) to non-users (null CPAP adherence) status over time. No sleepiness-based differences were observed.

Table 1
Summary statistics of the simulated data at baseline. *The variables CPAP adherence and ESS score are summarized using median [interquartile range].*

	All patients N = 300	Group 1 (0–2h) n = 43 (14 %)	Group 2 (2–4h) n = 66 (22 %)	Group 2 (≥4h) n = 191 (64 %)
CPAP adherence (hour)	4.82 [2.8; 6.1]	1.4 [0.7; 1.8]	2.8 [2.3; 3.5]	5.8 [4.9; 6.5]
ESS score	9 [7; 11]	7 [5; 9.5]	9 [7; 12]	9 [7; 11]
Proportion of patients with ESS ≥ 10 (%)	41.7	25.6	45.5	44

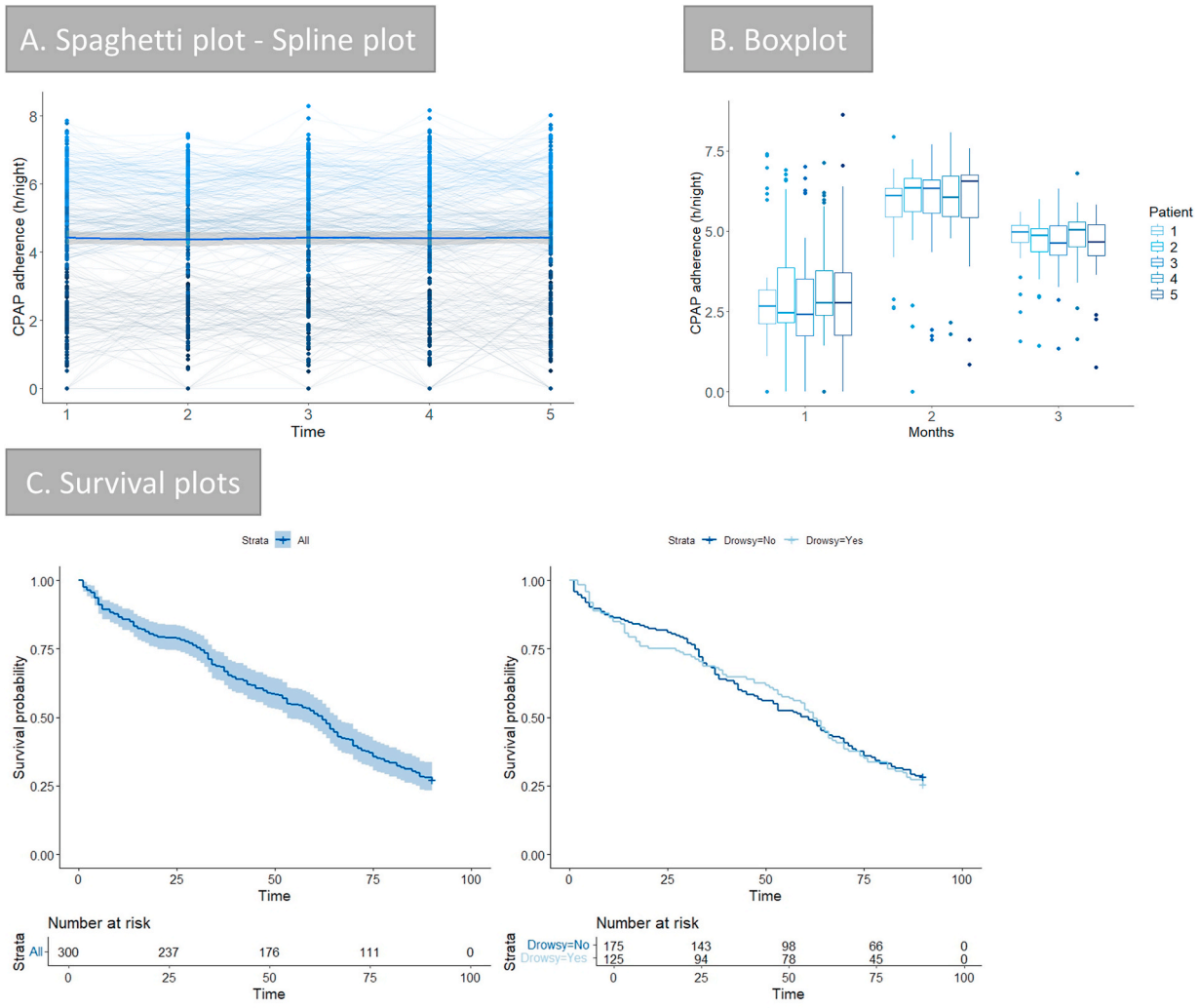

Fig. 2. Different types of numerical trajectories and their visualization, example with CPAP adherence. *2A. Spaghetti plots illustrate individual variability (transparent blue lines) while spline plots use smoothed curved lines to connect data points (full blue line with gray confidence interval). 2B. Boxplots illustrate the median, 1st and 3rd quantile with extreme CPAP adherence values for each individual over the 1st, 2nd and 3rd month of the study. 2C. Survival plots illustrate the survival probability to use the CPAP device (no null adherence values, left figure), according to sleepiness baseline status (right figure). Discrete variables: attribute values exist only at certain points in time; Continuous variables: attribute values change continuously. Collected by medical records, case report form, questionnaires, connected devices, interview. Abbreviation: CPAP, continuous positive airway pressure. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)*

Once data are described and the longitudinal pattern is well understood, we can go further with the longitudinal data analysis, by considering both the research question and the adequate analytical method.

5. Step 3 - defining the research questions

The nature of available data, its structure over time, and the observed patterns can help refine, confirm, or even challenge the initial research questions, which are often formulated prior to any data exploration. Depending on the research question, the statistical methods may differ and vary in complexity ranging from relatively simple descriptive analyses to more advanced modeling and forecasting approaches (Fig. 3). When examining the probability of transitioning from one group to another between two consecutive time points, comparison methods can be applied. This type of question and the results are fairly easy to interpret. When seeking to identify individuals sharing common characteristics or trajectories described in longitudinal data, the use of clustering methods is advised. The application of these methods is more complex, as well as the interpretation of the results. Furthermore, if we aim to evaluate the relationship between variables, whether observable or not, or predict the evolution of these variables, we can use modeling/forecasting methods. These questions are inherently more complex and require advanced statistical approaches.

6. Step 4 - choosing and applying the appropriate statistical method

Based on the data description, visualization and the identified research question, selecting the adequate methodology for longitudinal data analysis requires careful consideration of each method's advantages and limitations. This ensures a proper understanding of the framework within which the results can be generalized. This overview is not an exhaustive description of existing longitudinal data analysis methods, but rather offers an introductory perspective that aligns with the complexity of the data and the research objectives.

To better illustrate and summarize the methods, an example was conducted for each with a simulated longitudinal sleep dataset. The algorithms are available in the Github project (https://github.com/HP2-data/methodo_longitudinal_data). The details of all models, such as model parameters and selection criteria for choosing the optimal model is detailed in Supplementary Material.

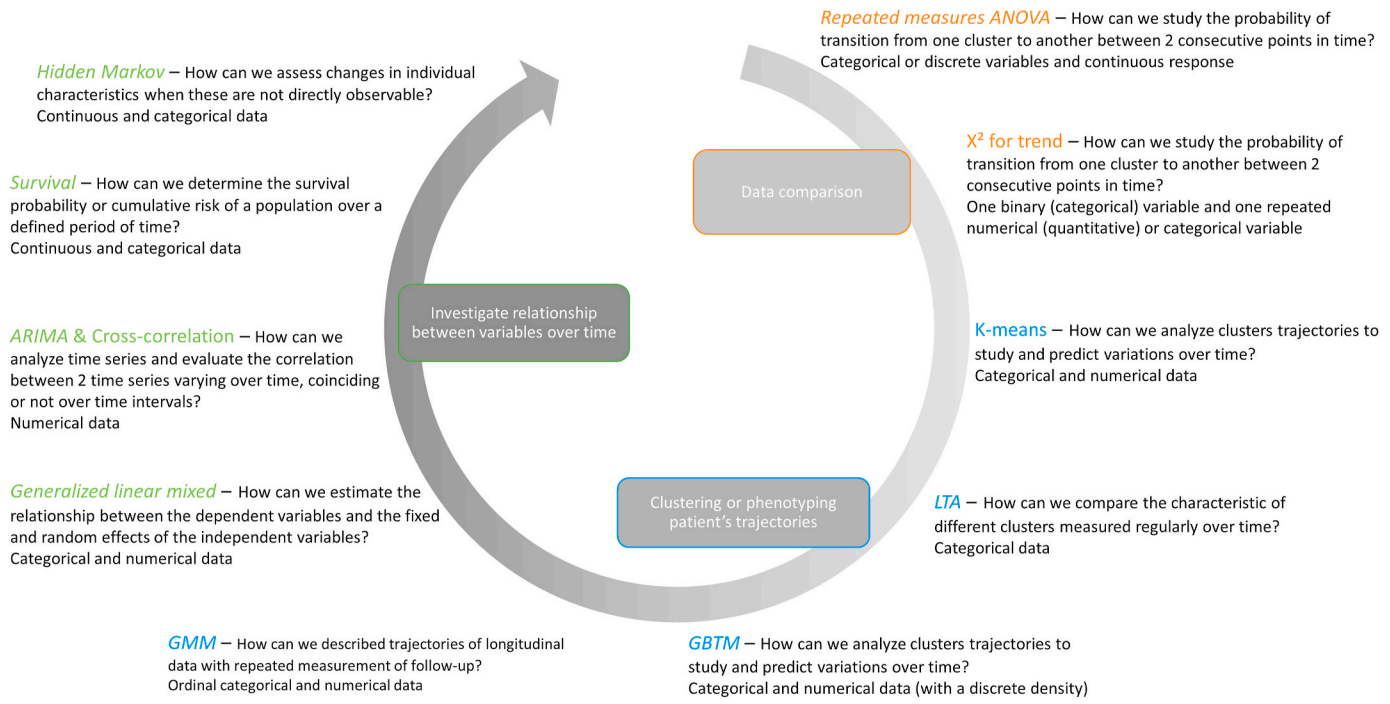

Fig. 3. Statistical methods classified according to research questions and objectives. *ANOVA, analysis of variance; ARIMA, autoregression integrated moving average; GBTM, group-based trajectory modelling; GMM, growth mixture modelling; LTA, latent transition analysis.*

6.1. Data comparison

(A) Repeated measures ANalysis Of VAriance (ANOVA) for quantitative values

Repeated measures ANOVA (Table 2) enables the assessment of whether there is a statistically significant interaction between 2 or 3 within-subjects factors in explaining a continuous outcome [25,26]. In the context of our analysis, we want to test if CPAP adherence significantly changes over time within individuals across the observed time points.

Example – After assessing the normality assumption using QQ plot, the ANOVA resulted in a p-value of 0.96, indicating no significant difference in CPAP adherence over time in our simulated dataset. The mean adherence remained stable at around 4.5h per night, consistent with the trend observed in the spline plot (Fig. 2A).

(B) χ^2 Mantel-Haenszel test for time trend in qualitative variables

The χ^2 test (Table 2) assesses whether the relationship between the variables remains stable across multiple strata (e.g., time points) by analyzing a series of contingency tables.

Example - The aim of this analysis was to assess whether the relationship between CPAP adherence and ESS score remained consistent across two time points. Both variables were categorized, and contingency tables were created for the first two time points. The χ^2 Mantel-Haenszel method was applied, assuming that the two nominal variables are conditionally independent within each stratum (i.e., time point) and that there is no three-way interaction. The resulting p-value of 0.001 indicates a statistically significant difference in the association between the variables over time, suggesting that the relationship between CPAP adherence and daytime sleepiness evolved between the two time points.

6.2. Clustering or phenotyping patient's trajectories

Unsupervised clustering methods aim to identify latent patterns within a population by identifying subgroups of individuals who exhibit comparable characteristics. These techniques do not rely on predefined labels or outcomes, but instead group individuals based on similarity measures. Two broad classes of approaches can be distinguished: distance-based and model-based methods. The first one includes distance-based methods, which form clusters by minimizing the differences within each group while maximizing the differences between groups [27–30]. These approaches rely on specific distance metrics such as Euclidean [31], Manhattan [31], Cosine [31], Correlation-based [31] or dynamic time warping [24,32,33] distances. The second approach

Table 2
Summary of statistical methods for describing longitudinal data.

	Objectives	Minimal sample size	Advantages	Limitations
Repeated measures ANalysis Of VAriance	Statistically significant interaction effect between 2 or 3 within-subjects' factors	To satisfy the normality hypothesis, at least 30 observations are required	Comparison between more than 2 groups	No specification of which groups differs in multi-groups comparison; Normal distribution, metric scale, equal variance across groups; Outliers influence
χ^2 tendency	Independence and differences between variables across a series of contingency tables; Proportions of the binary variable varying over time	All theoretical numbers must be > 5	Different models available; Simple and computationally efficient	No dropouts; Random sample; No covariate

relies on probabilistic models, where each individual is assigned a probability of belonging to each subgroup, allowing for a more flexible representation of overlapping or uncertain classifications [34–37].

(C) Unsupervised clustering: K-means

K-means clustering (Table 3) allows to identify distinct patient subgroups based on similar behavior patterns [18,38–40].

Example - The aim of this analysis was to group patients based on similarities in their CPAP adherence trajectories over time. Numerical CPAP adherence data from all patients and all time points were included. Based on a chosen statistical criterion, the model with 3 clusters provided the best fit (detailed in Supplementary Material, Appendix C). Moreover, the model resulted in a fairly balanced distribution of patients across clusters (in Supplementary Material, Appendix C). These results are consistent with the simulated dataset structure, which includes: one cluster with a steady decline in adherence across all time points; a second cluster, with decreasing adherence from time point 31 to 60, followed by an improvement over the final 30 time points; and a third cluster showing increasing adherence from time point 1 to 60, followed by a decline during the last 30 time points. These findings highlight the presence of distinct adherence trajectories among the studied patients.

(D) Latent Transition Analysis (LTA)

LTA method (Table 3) is used to study the probability of transitioning from one cluster at a given point to another at the next [38,41,42]. The aim of such an analysis was not only to classify patients based on their adherence patterns, but also to assess how likely they are to change adherence behavior over time and to what extent individuals transition between different adherence profiles.

Example – The categorical CPAP adherence data were used and all patients were included, along with all the time points. The optimal model identified 3 latent clusters. The conditional response probabilities (i.e., the likelihood of a specific CPAP adherence level given cluster membership) revealed that transition probabilities between clusters over time showed high stability, with most patients remaining in their cluster (e.g., 97 % stayed in Cluster 1), as well as a very limited movement between clusters (e.g., 3 % transitioned from Cluster 1 to Cluster 2, and only 2 % from Cluster 2 to Cluster 3). These results (detailed in Supplementary Material, Appendix D) suggest that adherence behavior tends to be stable over time.

(E) Group-Based Trajectory Modeling (GBTM)

GBTM method (Table 3) allows for identification of distinct subgroups of individuals who follow similar trajectories, as well as forecasting variations over time [18,41,43–45].

Example - For this analysis, the continuous CPAP adherence was used including 5 time points (for computational efficiency) and all patients. We first applied the GBTM method using a normal distribution, consistent with the characteristics of the simulated data. The method was then tested with various trajectory shapes and different numbers of clusters to

Table 3
Summary of statistical methods for clustering longitudinal data.

	Objectives	Minimal sample size	Advantages	Limitations
K-means	Group patients' trajectories into clusters based on their similarities	N ≈ 100 for reaching stable clusters; Depends on the number of time points and cluster separation	No a priori assumptions; Ability to handle large datasets; Ability to handle trajectory without polynomial degree	Complete data or imputed data; Correlation between individuals not taken into account; A priori initial parameters and number of clusters; Global or local maxima not determine; Trajectory of a single variable; Agglomerate trajectories with similar overall shape; No test for algorithm goodness of fit
Latent Transition Analysis	Probability of transitioning from one cluster at a given point to another at the next	A large sample technique - at minimum, N must be larger than the number of parameters to be estimated at least a few hundred subjects are suggested	Model changes over time and identifies predictors of that change; Comparison of the different clusters	Large dataset requires because of numerous parameters to estimate; Larger number of time points (>6) increases the model complexity; Determine the optimal number of latent clusters and label them; No covariate
Group-Based Trajectory Modeling	Study and forecast variations of cluster trajectories over time	N ≥ 200–300 patients and ≈20–30 individuals per group, with at least 3 time points	Few parameters to estimate; Fast with low error rates; Handle missing values and correlated residuals; Easy to interpret; Single model with ≥2 dependent variables	Missing Completely At Random; Clusters qualitatively different from the dependent variable; Not direct relationship between dependent and independent variables; Strong assumptions on trajectory distributions; Overestimation of the number of clusters and trajectories; No intra-class variation
Growth Mixture Modeling	Identify trajectory patterns and describe longitudinal changes for each unobserved group identified	A large sample technique - at minimum, N must be larger than the number of parameters to be estimated at least a few hundred subjects are suggested	Ability to handle missing data and correlated residuals; Identifies differences between and within individuals over time; Qualitative change of the trajectory over time across different groups	Random effects controlled by the analyst for the interpretation of coefficients; Ability to estimate non-different trajectories in term of clinical relevance; Missing At Random unobserved variables

identify the best-fitting model (detailed in Supplementary Material, Appendix E). According to some criteria for goodness-of-fit (BIC, log-likelihood, Average Posterior Probability and Proportion of assignment parameters), the model with a quadratic curve and 3 clusters provided the best fit. The distribution was relatively balanced, with 33 % in each group, the identified clusters remained stable from the first five time points throughout the study period and reflected expected profiles based on the simulated data: non-adherent patients in the first group, adherent in the second group and highly adherent for the third group.

(F) Growth Mixture Modeling (GMM)

GMM method was used to identify trajectory patterns and describe longitudinal changes for each unobserved group identified [18,41,46–50] (Table 3).

Example – The aim of the analysis was to determine clusters of the population based on their CPAP adherence trajectories over time. According to statistical criteria, the model with four clusters was the best model (detailed in Supplementary Material, Appendix E). Moreover, the distribution of patients across the clusters was relatively balanced (detailed in Supplementary Material, Appendix F). The longitudinal model estimated fixed effects, representing constant levels over time, to assess the relationship between CPAP adherence and time based on patients' adherence. The first cluster, including 99 patients, showed no significant change in CPAP adherence across the five time points. The second cluster, including 44 patients, demonstrated a continuous increase in CPAP adherence across all time points (T2: β [95 %CI] = 0.45 [0.03; 0.88]; T3: β [95 %CI] = 0.50 [0.05; 0.95]; T4: β [95 %CI] = 1.11 [0.55; 1.67]; T5: β [95 %CI] = 1.11 [0.62; 1.60]) compared to the first time point. The third cluster, including 101 patients, showed a decrease at the second time point (β [95 %CI] = −0.27 [−0.45; −0.10]) compared to the first. The fourth cluster, including 56 patients, exhibited a significant decrease in CPAP adherence at the fourth (β [95 %CI] = −0.66 [−1.03; −0.28]) and fifth (β [95 %CI] = −0.79 [−1.16; −0.42]) time points compared to the first time point (see in the Supplementary Material, Appendix E).

6.3. To investigate relationship between variables over time

(G) Generalized linear mixed model

A generalized linear mixed model was used to estimate the relationship between the dependent variables and both the fixed and random effects of the independent variables [43,51,52] (Table 4). Fixed effects indicated factors that did not change over time, whereas random effects capture individual-specific variability.

Example – The aim of the analysis was to evaluate the association between CPAP adherence and time of the study (considering all time points and patients), while adjusting for baseline sleepiness status, which could influence adherence patterns. The model accounted for individual differences in patients' adherence over time by including random intercept and slopes at the patient level. Although the association was not linear, the results were nonetheless presented for educational purposes. Model validation and detailed results are provided in Supplementary Materials (Appendix G). According to the results, CPAP adherence was not significantly associated with either time or sleepiness status (p-value >0.05).

Table 4
Summary of statistical methods for modeling/forecasting longitudinal data.

	Objectives	Minimal sample size	Advantages	Limitations
Generalized linear mixed	Relationship between the dependent variables and the fixed and random effects of the independent variables	Minimum group size = 50 subjects with at least 50 groups	Analysis of simultaneous ≥2 dependent variables; Missing values accepted; Estimation of the odd and rate ratios; Different possible distribution	Random effects controlled by the analyst for the interpretation of coefficients; Ability to estimate non-different trajectories in term of clinical relevance; Missing At Random unobserved variables
AutoRegression Integrated Moving Average & Cross-correlation	Analyze time series and evaluate correlation between 2 time series varying over time	At least 100 observations	Local stationarity only; Robust results; Identify correlations when multiple signals are linked and when the system is complex	Linear relationships between multiple signals
Time to event and survival	Determine the survival probability or cumulative risk of a population over a defined period of time	Large sample size with only 10–20 % of patients who did not experience the event; Small sample size with fewer than 10 patients who did not experience the event.	There are various risk functions to counter the presence of competitive risks; Censored patients have no negative connotation and can be handled by the model; Missing data can be handled using the intention-to-treat strategy, or tracking the number of patients in each arm who withdraw and the reasons for withdrawal to include this information in research reports; Patients may enter the study at different times, and are analyzed as if they all started the study at the same time.	In the presence of competitive risks, the simple one-cause Cox model is inadequate; When estimating the crude incidence of outcome, the Kaplan Meier model is not appropriate, as an overestimation of the incidence of outcome is possible in the presence of competitive risks; Small samples are error-prone and less valid and reliable than large samples, and the small number of surviving patients in the right-hand side of the Kaplan Meier curve leads to less precise survival estimates and greater uncertainty; To obtain reliable results, a study cut-off point must be strictly determined prior to analysis.
Hidden Markov	Changes in individual characteristics when these are not directly observable	N = 40 for transition probabilities and for low to medium overlap in component distributions; Smaller sample sizes (e.g., N ≤ 20) lead to extreme bias in parameter estimates	Flexible and robust approach; Small samples; Imputation of Missing At Random values without loss of information or bias; Obtain the latent clusters of the final model; Efficient; Possible predictions	A priori parameters to avoid overestimation or fail to find occasional clusters; No criteria for selecting optimal number of latent clusters; Impossible non-homogeneous transitions; Small sample better; A priori model parameters on their distribution; Label changes; Lost to follow-up status has no exchange possibilities with the other statuses

(H) AutoRegression Integrated Moving Average (ARIMA) & Cross-correlation

ARIMA and cross-correlation methods were used to analyze time series data and evaluate the correlation between two time series varying over time, whether or not they coincide over time intervals [53–57] (Table 4).

Example – We first compared CPAP adherence (across all time points) with the ESS score, transforming both into time series. For educational purposes, 88 additional ESS scores were simulated and added to the original two ESS observed scores in order to match the length of the CPAP adherence time series. This step was necessary, as cross-correlation analysis cannot be performed with only two data points. Only one patient was included in this example, although the model can be replicated for each individual. Assumptions and validation of the methods are detailed in the Supplementary Material (Appendix H).

For CPAP adherence, the final model was ARIMA (0, 1, 1) indicating a non-stationary time series without trend. In contrast, the ESS score followed an ARIMA (0, 0, 0) model, suggesting random fluctuation around a constant (reference) value. A cross-correlation function was then performed to compare the correlation between these two time series (the variables detrend by the ARIMA model). This analysis revealed a weak correlation ($\rho = -0.07$) between ESS score and CPAP adherence with a lag of 14-time points suggesting that above-average CPAP adherence may be associated with a below-average ESS score approximately 14 time points earlier.

This observed lag could be further incorporated into a regression model to further explore the association between ESS score and CPAP adherence at varying time lags (in Supplementary Material, Appendix H).

(I) Time to event and survival model

The survival model (also known as the time-to-event model) can be used to determine the survival probability or cumulative risk within a population over a defined period of time [58–60] (Table 4). It is also applied in joint modeling, a more advanced method used to analyze the simultaneous evolution of two variables over time.

Example - The aim of the analysis was to estimate the probability of achieving CPAP adherence $\geq$4 h (i.e. the survival probability). In this context, the "event" (analogous to death in traditional survival models) was defined as reaching CPAP adherence $\geq$ 4h at least once during the study period. Patients who never reached this threshold (i.e., adherence $<$ 4h throughout the study) were considered censored (event = 0), while those who did were assigned an event status (event = 1). The time variable corresponded to the first time point at which a patient reached adherence $\geq$4 h or to the 90th time point if the event never occurred. Full model results are available in the Supplementary Materials (Appendix I).

The probability of achieving treatment adherence remained relatively stable from the first time points, at around 35 %. Stratification by baseline sleepiness status at T1, using a binary classification of the ESS score, was also conducted. No significant difference in CPAP adherence survival probability was found between sleep and non-sleep patients ($p = 0.30$). Early in the study, non-sleepy patients showed a slightly higher survival probability (around 40 %) of reading adherence compared to sleepy patients (around 35 %), but both probabilities remained stable throughout the study period.

(J) Hidden Markov model

Hidden Markov model (HMM) was used to assess changes in individual characteristics when these are not directly observable [3,61–63] (Table 4). In other words, this model helps identify the patient's hidden state at any time point by knowing the value of the variable observed at each time point and, consequently, the transition between time points.

Example - The aim of the analysis was to estimate the probability of an individual belonging to a specific CPAP adherence status (adherent or non-adherent) over the 90 time points, based on observed transitions between three defined CPAP adherence categories: highly adherent, adherent and non-adherent. The HMM requires one known categorical variable, in this case CPAP adherence with 3 levels and one hidden categorical variable with a predefined number of hidden states (here set to two: non-adherent and adherent). Parameters and full results are detailed in the Supplementary Material (Appendix J). For the first state, the patient was assigned to the "adherent" status. The transition probability matrix (i.e. the probability to go from one state to another) showed a low probability of switching states: 0.03 for transitioning from Non-adherent to Adherent, 0.02 for Adherent to Non-adherent, 0.98 for remaining in the Adherent state, and 0.97 for remaining in the Non-adherent state. State prediction over the first 200 times points indicated that the patients spent approximately 30.5 % of the time points in the non-adherent state and 60.5 % in the adherent state (detail in Supplementary Material, Appendix J).

7. Discussion

This work summarizes longitudinal data analysis as a four-step analytical framework (Fig. 4): data description, data visualization, definition of the research question, and statistical analysis. Selecting an appropriate statistical method requires aligning the analytical approach with the data type, data source, and study objectives.

Beyond monitoring adherence to continuous positive airway pressure (CPAP) treatment, longitudinal data hold considerable potential for advancing clinical research in sleep medicine. By capturing temporal dynamics rather than isolated measurements, they provide a unique opportunity to study how physiological, behavioral, and environmental factors interact over time to shape sleep health trajectories. This temporal perspective facilitates the identification of early markers of deterioration or recovery, the evaluation of treatment responses in real-life settings, and the characterization of patient subgroups with distinct trajectories.

Integrating longitudinal approaches also supports the assessment of bidirectional relationships—such as those linking sleep quality with cardiometabolic outcomes, mental health, or physical activity—thereby improving causal inference and enabling more personalized care. Advances in wearable sensors and digital health platforms now make it possible to monitor sleep–wake patterns and treatment behaviors continuously and at scale [64,65]. Properly analyzed, such datasets can bridge mechanistic understanding and clinical decision-making, contributing to precision medicine and population-level sleep health improvement.

Analyzing longitudinal data is inherently complex and requires close collaboration between clinicians, biostatisticians, and data scientists. The richness and complexity of repeated-measure data require both a solid clinical understanding of the studied phenomena, good knowledge of data collection and management, and appropriate mastery of analytical methods. While it is unrealistic to expect clinicians to master all statistical techniques in detail, developing a broad understanding of their logic and applications is essential. Such shared knowledge fosters more productive interdisciplinary dialogue, enabling researchers to frame clinically relevant questions, select suitable analytical strategies, and correctly interpret longitudinal patterns. Ultimately, this collaborative approach ensures that statistical sophistication remains anchored in clinical meaning, turning data into actionable insight rather than abstract modeling.

This collaborative perspective highlights the contribution of the present work, which proposes an analytical framework and illustrates ten commonly used methods for longitudinal data analysis. By offering a structured overview rather than an exhaustive review, this paper aims to promote mutual understanding and constructive dialogue between clinical and methodological experts.

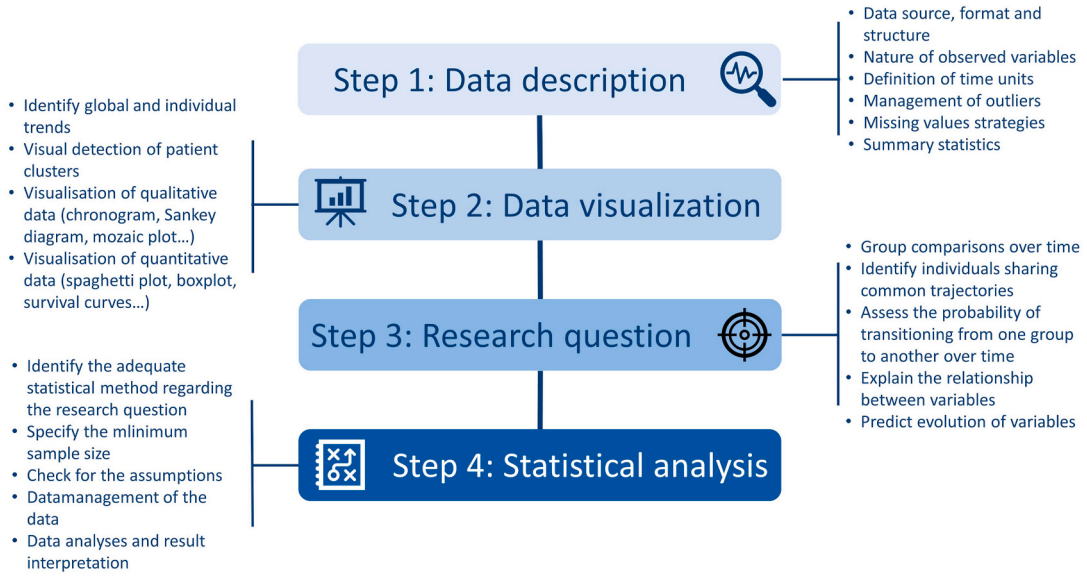

Fig. 4. How to analyze longitudinal data? A comprehensive step-by-step approach. *Abbreviation: CPAP, continuous positive airway pressure.*

However, this overview has limitations that should be acknowledged. It does not address all methodological challenges commonly encountered in longitudinal data analysis. Outliers and missing values are common in such datasets, and require dedicated methods for detection, imputation or exclusion [63]. This important aspect should not be underestimated, as failing to address it could result in biased or false results (Supplementary Material, Appendix B) [66–69]. Data collection also deserve attention, as data collected by connected devices or remote monitoring differs substantially in structure and content from data obtained through clinicians' assessments, questionnaires or other traditional methods.

This study is not intended to compare statistical methods used in sleep research or evaluate their performances. Rather, it emphasizes that the choice of method can strongly influence results and, consequently, scientific and clinical conclusions. Selecting an appropriate approach requires first defining the research question and understanding the data structure—number and timing of measurements, missing data, and within-subject correlations—as well as the intended interpretation of results (e.g., individual vs. subgroup trajectories) and the method's ability to handle incomplete data (Supplementary Material, Appendix B).

Statistical methods also vary in complexity, according to data characteristics and study design. Each approach has specific assumptions, advantages and limitations that must be evaluated before use. Some methods are more suitable for comparisons (e.g., repeated measures ANOVA, χ^2 tests), others for clustering and phenotyping (e.g., LCA, K-means clustering, LTA, GBTM, GMM), and others for modeling and forecasting (e.g., mixed models, ARIMA and cross-correlation, time-to-event models, and Hidden Markov Models).

While this overview focuses on the most commonly applied statistical methods for longitudinal data, many alternative approaches can also exist, incliding Configural Frequency Analysis [38], Latent growth Curve Model [43] and various hierarchical or partitioning methods [18,31,40,70,71] (e.g. Principal Component Analysis, Multiple Correspondence Analysis, Hierarchical Ascending Classification [40,70,72], X-means, DBSCAN, K-medoids). Additional methods have been developed for modeling and forecasting longitudinal trajectories (e.g., Random Intercept - Cross-Lagged Panel Model [73–75], Bayesian Kernel Machine Regression [76]). Finally, more advanced tools such as those based on Bayesian, machine learning or deep learning approaches (e.g., random forest, Long Short-Term Memory) can also be applied to explore longitudinal data, though these lie beyond the scope of this article.

To conclude, while not intended as an exhaustive review, this work provides a structured overview of the most commonly used statistical methods for longitudinal data, illustrated with implementation examples in R and Python (https://github.com/HP2-data/methodo_longitudinal_data). It proposes a comprehensive, step-by-step approach for longitudinal data analysis and highlights the logical links between the different methods. Specifically, descriptive analyses (e.g., ANOVA) can capture average trends, which may then be further explored using clustering approaches to identify distinct adherence phenotypes. Finally, modeling methods allow for a more precise examination of relationships between variables over time.

Longitudinal data are particularly relevant in healthcare research, where they are often frequently collected during follow-up visits, hospitalizations and, increasingly through connected devices (e.g., CPAP treatment for sleep apnea). However, the methodological framework here is broadly applicable to other fields, including climate [55,56], finance [77] or insurance [78,79].

CRediT authorship contribution statement

Ophélie Coiffier: Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Ina Jandric:** Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Christian Caussé:** Writing – review & editing, Resources, Investigation, Funding acquisition. **Jean-Louis Pépin:** Writing – review & editing, Funding acquisition, Conceptualization. **Monique Mendelson:** Writing – review & editing, Conceptualization. **Sébastien Bailly:** Writing – original draft, Supervision, Methodology, Conceptualization.

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Declaration of competing interest

None of the authors have a competing interest directly related to this

work to declare. CC is employed by Bioprojet (Paris, France); all other authors are academics and/or public sector hospital employees or students.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2025.106871.

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Supplementary material

An overview of longitudinal data analyses in sleep research

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Appendix A - Codes in R and Python

https://github.com/HP2-data/methodo_longitudinal_data

Appendix B – Bias in longitudinal data

As mentioned in the manuscript, some bias can occur when analyzing longitudinal data, such as:

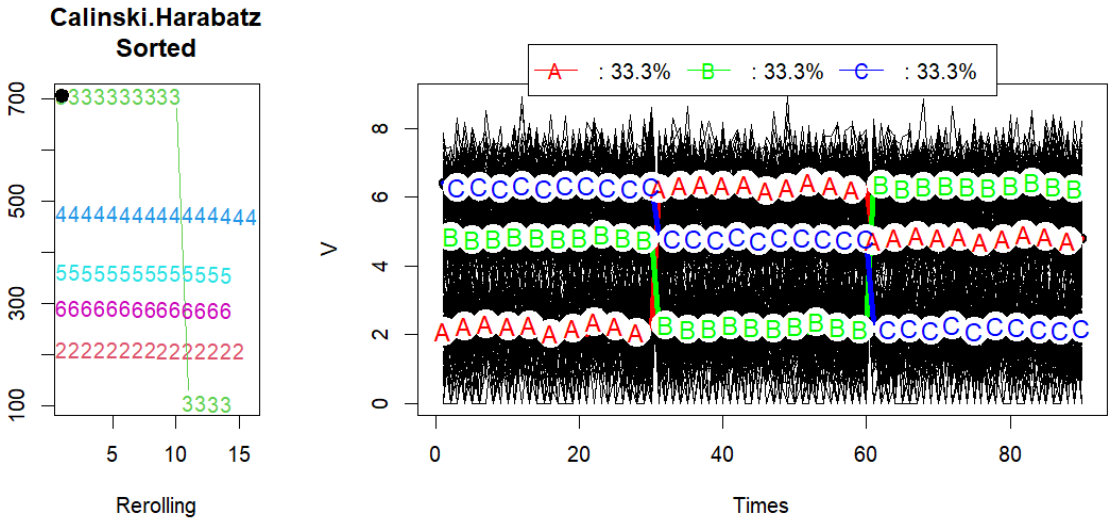
- Selection bias (e.g., non-representative samples, differential dropouts, patients bias such as prevalent user/patient or number of measurements for the comparison between healthy and sick patients) [1-3].
- Measurement bias (e.g., device errors, self-report inaccuracies) [3,4].
- Missing data bias (e.g., non-random missingness leading to distorted trajectories) [3-5].
- Confounding bias (unmeasured or inadequately adjusted covariates) [3,4].
- Information bias (occurring during data collection) [3].

It is not an exhaustive list but these are the most common sources of bias. When defining and selecting the study population, collecting data, or studying the association between different determinants of an outcome in patients, significant biases may arise [3]. Therefore, careful selection of the statistical method can help avoid bias in parameter estimates and outcome predictions.

Appendix C – Additional information on (C) K-means method

The first step was to transform the trajectories (longitudinal data with one line per patient and time points represented as columns) into ClusterLongData format (the original longitudinal data and all partitions found by the kml function) [6-9]. Then, the kml function performed the clustering. In this example, 15 redraws (i.e., the function was re-run with different starting conditions) were conducted for each cluster, as well as tests with 2 to 6 clusters. Finally, based on the Calinski-Harabasz score, the model with 3 clusters was the best one (Figure E1).

Figure E1. Trajectories of clusters obtained using the K-means method*. The K-means method identified three distinct clusters representing CPAP adherence over 90 time points for 300 OSA patients. The Calinski-Harabasz index indicates the optimal number of clusters (the black point in the left graph). The clusters were fairly distributed, with 33% of patients in each. Cluster A increased patients' adherence to a highly adherent status in the second 30 time points, becoming adherent in the last 30 time points. Cluster B decreased patients' adherence from adherent to non-adherent over the second 30 time points, but increased it again over the last 30 time points to become highly adherent. Cluster C decreased patients' adherence from highly adherent to non-adherent over the last 30 time points.*



Appendix D – Additional information on (D) Latent Transition Analysis (LTA) model

Description [6,10,11] – Latent transition analysis (LTA) is a finite, semi-parametric mixture model used to analyze longitudinal categorical data. It examines changes in categorical responses, typically organized as contingency tables, measured across multiple time points. Based on latent class theory, the LTA model identifies homogeneous subgroups of individuals (latent classes) based on their responses over time. At each time point, the LTA defines a latent categorical variable inferred from the observed categorical or discrete data. Reducing categorical variables with many categories is recommended to ensure model stability. Additionally, the LTA model is most appropriate for datasets with no more than six time points.

A key feature of latent class analysis (LCA) is its ability to model transitions in class membership over time. Between time points, each individual may switch from one latent class to another. Transition probability matrices link consecutive time points and capture these transitions.

Model estimation provides the following outputs:

- The probability of latent class membership at the first time point;
- The proportion of individuals in each latent class at each time point;
- The conditional probabilities of transitioning between latent classes over time;
- The conditional response probabilities within each class;
- The posterior probabilities of class membership at each time point.

Parameters can be estimated using maximum likelihood via the expectation-maximization (EM) algorithm or Bayesian methods via Markov chain Monte Carlo (MCMC). However, MCMC is not recommended for small sample sizes (an effective sample size greater than 1000 is sufficient for stable estimates) or when item-response probabilities are very close to 0 or 1.

Covariates can be included in the model, to evaluate how they relate to the profile membership, but the number of latent classes must first be determined. Otherwise, adding covariates may alter the class structure, which complicates interpretation and comparability.

Process – The LTA model follows an iterative process based on a priori decisions relevant to the study's domain knowledge:

1) Choice of the latent class number based on the results of the hypothesis test;

2) Model characterization: decision on the time invariance of item response probability, the invariance of transition probability measures and the inclusion of covariates;

3) Model estimation: the choice of model must be made before the models are applied. Parameters are estimated by maximum likelihood (EM algorithm) or by the Bayesian approach (MCMC algorithm).

4) Model selection: by Akaike Information Criteria (AIC) or Bayesian Information Criteria (BIC) criteria.

Example (additional information) – The model used long format data. For the reproducibility of the analysis, a seed was implemented. We tested the model for 2, 3 and 4 clusters (Table E1). According to the Log-likelihood and the BIC or AIC criteria, the best model identified 3 clusters in our simulated dataset (Table E1).

Table E1. AIC, BIC, log likelihood for model with 2, 3 and 4 clusters*. Red lettering indicates the selected and best-fitting model.*

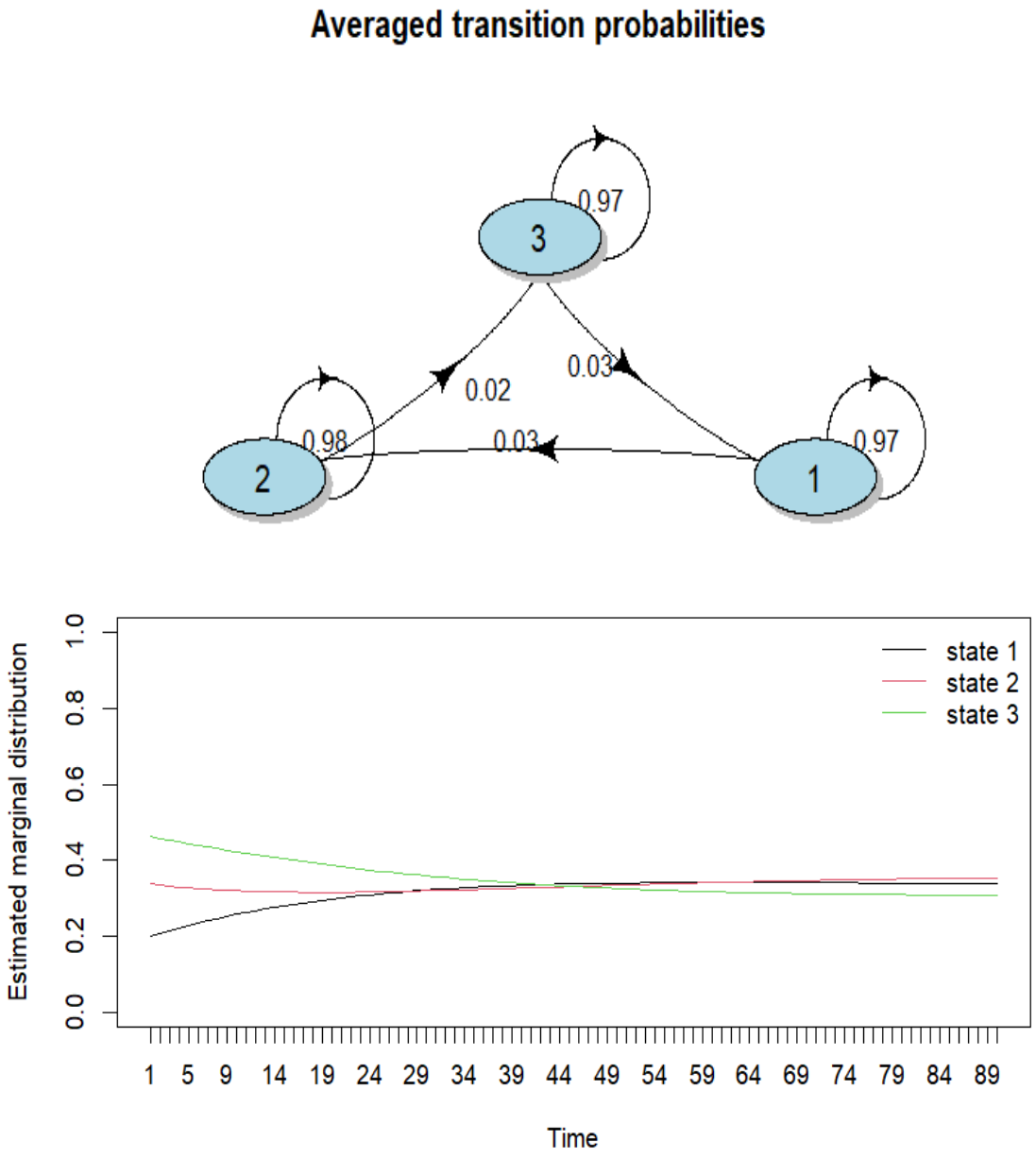
	2 clusters	**3 clusters**	**4 clusters**
AIC	25288.1	24627.5	24516.5
BIC	25314.1	24679.4	24601.7
Log Likelihood	-12637.1	-12299.8	-12235.3

The conditional response probabilities were described below (Table E2), along with the average transition probabilities and the trajectories of the three latent states (Figure E2).

Table E2. Conditional response probabilities for each latent state and each observed CPAP adherence categories.

State **Category**	**1**	**2**	**3**
[0h;2h[	0.00	0.41	0.00
[2h;4h[	0.09	0.55	0.00
≥4h	0.91	0.04	1.00

Figure E2. Average transition probabilities and trajectories of the 3 latent states over the 90 time points using the LTA model.



Appendix E – Additional information on (E) Group-Based Trajectory Modeling (GBTM) method

Description [9,10,12-14] – Group-Based Trajectory Modeling (GBTM) is a type of finite mixture model designed for the analysis of longitudinal data—either continuous or categorical—assuming a discrete distribution such as Bernoulli, Poisson, or Normal. The method identifies unobserved (latent) subgroups of individuals who follow similar trajectories over time. It assumes no within-class (intra-group) variation, and constant residual variance across time and between classes. GBTM models the dependent variable as a function of time within each latent class, estimating distinct trajectories for each group. While the subgroups exhibit low within-group variability and high between-group heterogeneity, group membership cannot be fully predicted from observed covariates. Therefore, a categorical latent class variable is introduced to capture unobserved heterogeneity. The model estimates the proportion of the population in each class and computes posterior probabilities of class membership for each individual. Individuals are typically assigned to the class which they have the highest posterior probability for. Model parameters are estimated via maximum likelihood. These posterior probabilities can also be used for further prediction or classification tasks. Time-varying and time-invariant covariates can be included in the model to influence either class membership or the shape of the trajectories.

Process – The GBTM method follows an iterative process based on a priori decisions:

1) Hypothesize the expected number of latent classes and the shape of the trajectory curve for each class (linear, quadratic, cubic, ...);
2) Model characterization: initially, it is necessary to test a model with 1 class, then progressively adjust the maximum number of subgroups. This number must be greater than the expected number of classes. To determine the optimum number, compare models for 1 trajectory (for 1 class) with a quadratic curve and a linear curve. Then, if the quadratic model is good, compare 2 trajectories with quadratic components. To test the models, the BIC criterion is used (differences between 2 adjacent models > 10), while the average a posteriori probability (> 70%) and relative entropy (> 0.8) are evaluated to test the correct number of individual trajectories among the identified classes;
3) Model estimation: by maximum likelihood or Bayesian methods;
4) Model selection: study's domain knowledge is the first step in model selection. It is necessary to opt for a useful and parsimonious model, and to have a close correspondence between the estimated probability of each class and the proportion of individuals attributed to each class according to the rule of maximum membership probability. Specifically, the average of the a posteriori membership probabilities must be greater than or equal to 0.7, and there must be at least 5% of individuals in each class. There must also be a reasonable confidence interval and a BIC difference between 2 models for a different number of class trajectories.

Example (additional information) – First, we performed the GBTM method using the Normal distribution, with linear curve, quadratic curve and cubic curve with 2 clusters to find the best type of curve. The chosen model was the quadratic curve, according to BIC (difference should be > 10) and log-likelihood criteria (Table E3). Then, tests on the number of clusters were applied with a quadratic curve for 2, 3 or 4 clusters. According to BIC, Average Posterior Probability (better if ≥ 0.7) and proportion of assignment parameters, the model with 3 clusters was the best model (Table E3).

Table E3. Information for selecting the best model, according to curve shape (linear, quadratic or cubic) and number of clusters (2, 3 or 4). *Red lettering indicates the selected and best-fitting model.*

	Linear curve – 2 clusters	**Quadratic curve – 2 clusters**	**Cubic curve – 2 clusters**	**Quadratic curve – 3 clusters**	**Quadratic curve – 4 clusters**
BIC	4670.2	4679.6	4690.8	4108.6	4111.2
Likelihood	-2315.1	-2314.1	-2314.0	-2014.4	-2001.4
Average Posterior Probability		Cluster 1 = 1.00 Cluster 2 = 1.00		Cluster 1 = 1.00 Cluster 2 = 1.00 Cluster 3 = 1.00	Cluster 1 = 1.00 Cluster 2 = 1.00 Cluster 3 = 1.00 Cluster 4 = 1.00
Proportion of assignment		Cluster 1 = 0.33 Cluster 2 = 0.67		Cluster 1 = 0.33 Cluster 2 = 0.33 Cluster 3 = 0.34	Cluster 1 = 0.33 Cluster 2 = 0.01 Cluster 3 = 0.33 Cluster 4 = 0.34
Estimate probabilities		Cluster 1 = 0.33 Cluster 2 = 0.67		Cluster 1 = 0.33 Cluster 2 = 0.33 Cluster 3 = 0.34	Cluster 1 = 0.33 Cluster 2 = 0.01 Cluster 3 = 0.33 Cluster 4 = 0.34

Finally, the 3-cluster model presented an equitable distribution of patients with 100 patients in the 1st cluster, 99 in the 2nd and 101 in the 3rd. The 1st cluster was described as non-adherent, the 2nd cluster as adherent and the 3rd cluster as highly adherent over the 5 time points. The clusters remained stable throughout the study.

Appendix F – Additional information on (F) Growth Mixture Modeling (GMM) model

Description [9,10,15-19] – Growth Mixture Modeling (GMM) is a parametric finite mixture model designed to analyze longitudinal data—whether continuous or categorical—by identifying distinct unobserved subgroups that follow different developmental trajectories. Unlike simpler polynomial trajectory models, GMM accommodates complex trajectory shapes and allows for individual-level variation within each latent class. The model estimates the average trajectory for each class and introduces individual-specific random effects, such as random intercepts (initial levels) and slopes (rates of change), which capture within-class heterogeneity. Parameters are estimated by maximizing the log-likelihood function, including fixed and random effects for each class. Latent classes are defined based on differences in trajectory form (e.g., shape, level, scale), and individuals are assigned to the class with the highest posterior probability. Once the latent trajectories are identified, they can be used as dependent or independent variables to explore associations with predictors or to investigate their role in forecasting health outcomes. GMM models are sensitive to initial parameter specifications, and convergence may depend on starting values. Covariates—either time-invariant or time-varying—can be incorporated to explain class membership or trajectory variation, but should be introduced after finalizing the class structure to avoid altering the underlying latent profiles. These predictors can help clarify the determinants of class membership and inform intervention strategies.

Process – The GMM model follows an iterative process based on a priori decisions:

1) Hypothesize the expected number of latent classes and the shape of the trajectory curve for each class (linear, quadratic, cubic, ...);
2) Characterize the model: make decisions on the curve's trajectory parameters (intercept, variance and slope covariance);
3) Model estimation: by maximum likelihood (EM algorithm) or Bayesian methods (MCMC algorithm), where the unobserved class classification variable is treated as a latent variable. These algorithms use an iterative process to obtain parameter estimates and a posteriori estimates of the probability of each individual belonging to each possible class with respect to the observed data. Each individual belongs to the class for which it has the highest probability of membership;
4) Model selection: choose the model giving the best representation of the observed data by various tests (Lo-Mendell Rubin adjusted likelihood ratio test (LRT, $p < 0.05$), Parametric bootstrapped likelihood ratio (BLRT, $p < 0.05$), BIC (minimum BIC corresponds to the best model), AIC (minimum AIC corresponds to the best model), convergence and ability to distinguish the different classes (entropy close to 1.0)) and validation of model parameters (proportion of the population in each class (> 5%), probability of belonging to a class (close to 1.0), frugality and usefulness of latent classes for the study).

Example (additional information) – The model was defined by long format data, a random intercept and slope and a mixture parameter on the time variable. A seed was implemented for reproducibility. The 300 patients were included with 5 time points (faster calculation), which is a fairly small sample. Four tests were performed to find the best number of clusters (1, 2, 3 or 4; Table E4). According to the BIC criteria, the model with 4 clusters was the best model (Table E4). Moreover, the distribution of patients in the clusters was balanced including around 33% in the 1st cluster, 15% in the 2nd, 34% in the 3rd and 19% in the 4th cluster.

Table E4. Information for selecting the optimal number of clusters (1, 2, 3 or 4) according to BIC criteria, Log Likelihood and percentage of patients in each cluster*. Red lettering indicates the selected and best-fitting model.*

	Log Likelihood	BIC	%cluster 1	%cluster 2	%cluster 3	%cluster 4
1 cluster	-2249.1	4617.9	100			
2 clusters	-2125.6	4410.9	34	66		
3 clusters	-2112.4	4424.4	66.7	66.7	26.7	
4 clusters	-1987.4	4214.4	33.0	14.7	33.7	18.7

The mean posterior probabilities of the selected model have been described in the table below (Table E5), and these results validate the final model (average probability to a class, close to 1 and > 0.7 for each cluster).

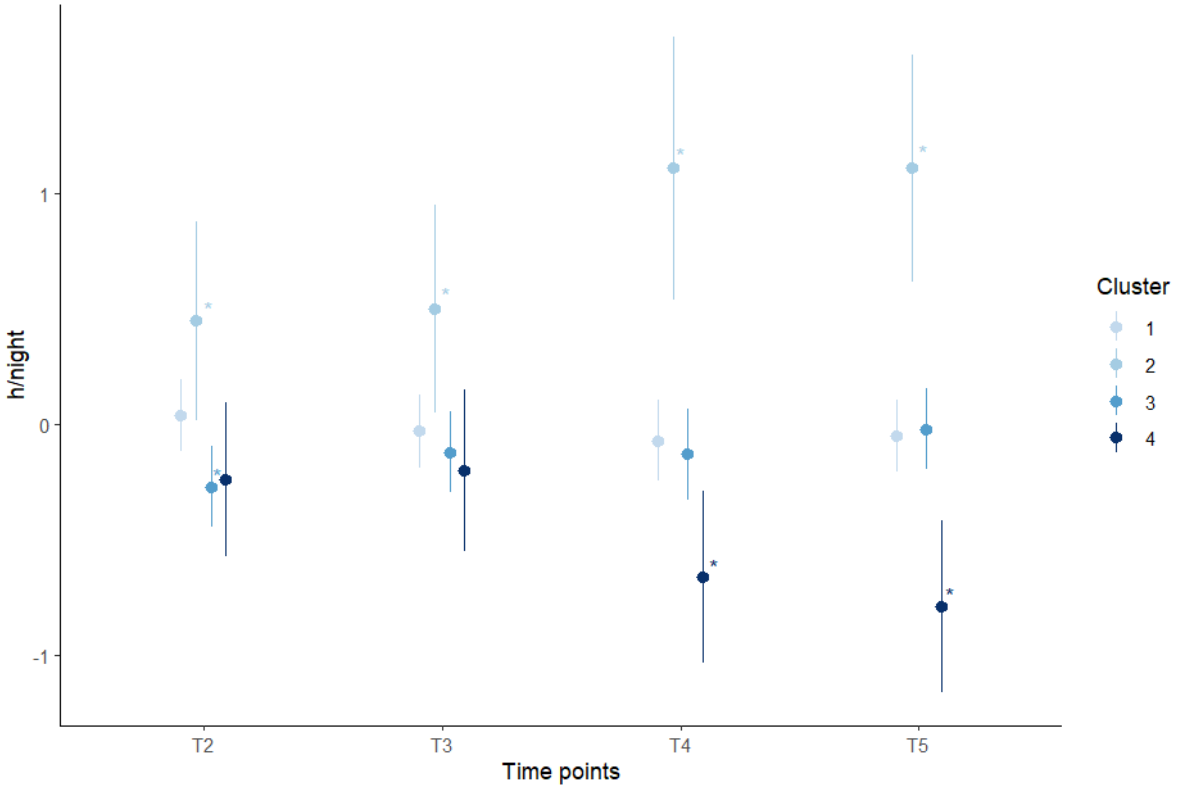
Table E5. Mean posterior probability in each cluster, for the best fitting model.

	Prob1	Prob2	Prob3	Prob4
Cluster 1	0.995	0.000	0.005	0.000
Cluster 2	0.000	0.9031	0.000	0.069
Cluster 3	0.002	0.000	0.998	0.000
Cluster 4	0.000	0.095	0.000	0.905

The probability to belong to a cluster and the posterior probability above a threshold (0.7, 0.8, 0.9) were also available.

The model estimated the fixed effect in the longitudinal model associating CPAP adherence and time depending on patients' adherence (Figure E3). Finally, the 1st cluster, including 99 patients, did not have a significant impact of time on CPAP adherence over the observed 5 time points. The 2nd cluster, including 44 patients, increased CPAP adherence through all 5 time points (T2: β [95%CI] = 0.45 [0.03; 0.88]; T3: β [95%CI] = 0.50 [0.05; 0.95]; T4: β [95%CI] = 1.11 [0.55; 1.67]; T5: β [95%CI] = 1.11 [0.62; 1.60]) compared to the 1st time point. The 3rd cluster, including 101 patients, decreased CPAP adherence at the 2nd time point (β [95%CI] = -0.27 [-0.45; -0.10]) compared to the 1st time point. The 4th cluster, including 56 patients, decreased CPAP adherence at the 4th (β [95%CI] = -0.66 [-1.03; -0.28]) and 5th (β [95%CI] = -0.79 [-1.16; -0.42]) time points compared to the 1st time point.

Figure E3. Trajectories of clusters over 5 time points using GMM model. **Represent a significant association (p<0.05) between the 1st time point and the time point studied in the cluster.*



Appendix G – Additional information on (G) Generalized linear mixed model

Description [12,20,21] – Mixed Models can be linear or generalized, and are commonly used to analyze longitudinal or clustered data. The linear mixed model (LMM) estimates the relationship between dependent variables and both fixed and random effects, accounting for variability in means and covariances. However, when the number of predictors is large, inference and prediction can become computationally infeasible. To address this, penalization techniques can be applied to fixed effects, and variable selection methods can be used for random effects.

Several strategies exist: 1) Simultaneous estimation of fixed effects, random effects, and their covariance structure using a penalized likelihood approach. 2) Two-step procedures where fixed and random effects are selected separately, using proxy matrices to estimate the unknown variance-covariance structure and Bayesian methods for random effect selection. 3) Joint selection and estimation using dual penalty functions within a restricted maximum likelihood (REML) framework.

In high-dimensional settings, dimensionality reduction is often required prior to model fitting to ensure algorithmic stability and convergence, especially when using EM-based estimation procedures. Generalized Linear Mixed Models (GLMMs) extend LMMs by incorporating non-Normal outcomes and relaxing the assumption of independent observations. GLMMs are suited for repeated measures of categorical or mixed data types. They rely on the construction of pseudo-dependent and pseudo-independent variables to model multiple outcome types jointly while maintaining the structure of repeated or clustered data.

Example (additional information) – The model used long format data. The marginal R^2 indicated that the model was not appropriate (near 0). That could be explained by the non-adjustment of the model and the distribution of the population (use of 3 clusters following 3 different Normal distributions over 3 periods of time, so nonlinear association). However, from the educational point of view, the results could be studied. No significant variables were identified (Table E6).

Table E6. Association between CPAP adherence and time adjusting for baseline patients' sleepiness status. Random intercept and slopes at the patient level were included in the model to account for individual differences in patient's' adherence.

	β (CI 95%)	**P-value**
Time	0.00 (0.00; 0.00)	>0.90
Drowsy at baseline - Yes	0.03 (-0.01; 0.06)	0.17

CI: Confident Interval

Appendix H – Additional information on (H) AutoRegression Integrated Moving Average (ARIMA) model & Cross-correlation method

Description [22-26] – ARIMA (AutoRegressive Integrated Moving Average) models are widely used for analyzing non-stationary time series, effectively capturing trends, seasonality, and random fluctuations. When external predictors are included, the model becomes an ARIMAX (ARIMA with exogenous variables), allowing for the inclusion of lagged covariates. To explore the relationship between two time series, cross-correlation analysis can be applied. This involves computing the Pearson correlation between matched measurement vectors from each series, potentially offset by a time lag to capture delayed effects. This method can assess the association between two time-dependent variables, even when their timing differs. If the assumption of stationarity is met (i.e., constant mean and variance over time), windowed cross-correlation can be used to study how the strength and lag of the association evolves across time segments. For non-stationary series, detrended cross-correlation analysis (DCCA) provides a robust alternative by removing local trends, thus avoiding spurious correlations. Detrended partial cross-correlation analysis (DPCCA) extends this approach by combining DCCA with partial correlation techniques, improving the assessment of dynamic associations while controlling for shared variance across multiple time series. The ARIMA model can also be used to predict the evolution of time series trajectories.

Process – The ARIMA model is first defined, then the cross-correlation function is applied:

1) ARIMA model analysis: fit the ARIMA model to the time series, i.e. analyze the stability and seasonality of the data (ACF, PACF), then estimate and test the model (AIC, BIC, Box Ljung statistic);

2) ARIMA model construction and validation: divide the data into 2 parts to perform the train/test and validation method. The first part is used to define the model and the second to validate it;

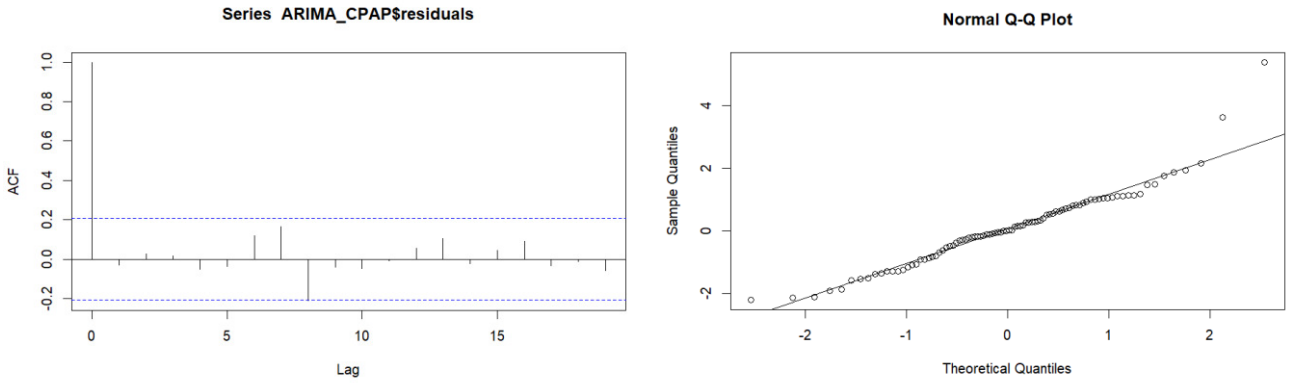
3) Model application: validation of model's prediction and execution by RMSE. The trajectory of the time series evolution can be analyzed and predicted;

4) Evolution of the 2 time series: perform cross-correlation functions.

Example (additional information) –

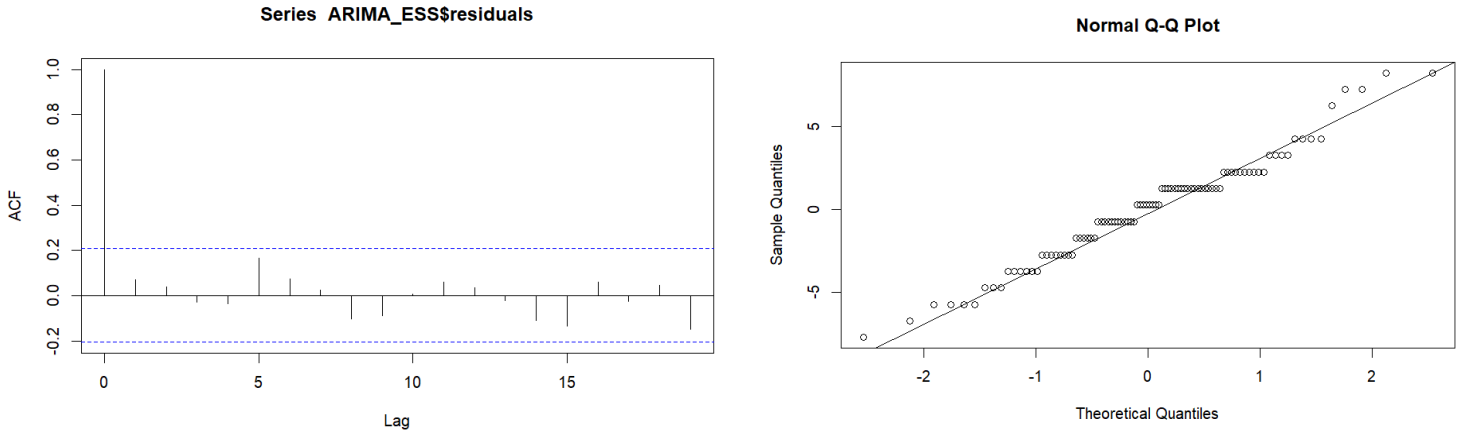
For model validation of CPAP adherence, the p-value of the Box-Ljung test was 0.77 showing that there was no pattern in the residuals. The ACF and QQPlot yielded the same results (Figure E4). Consequently, the time series model of CPAP adherence was validated.

Figure E4. Auto-Correlation Function and QQ plot of the CPAP adherence time series allowing to validate the model.



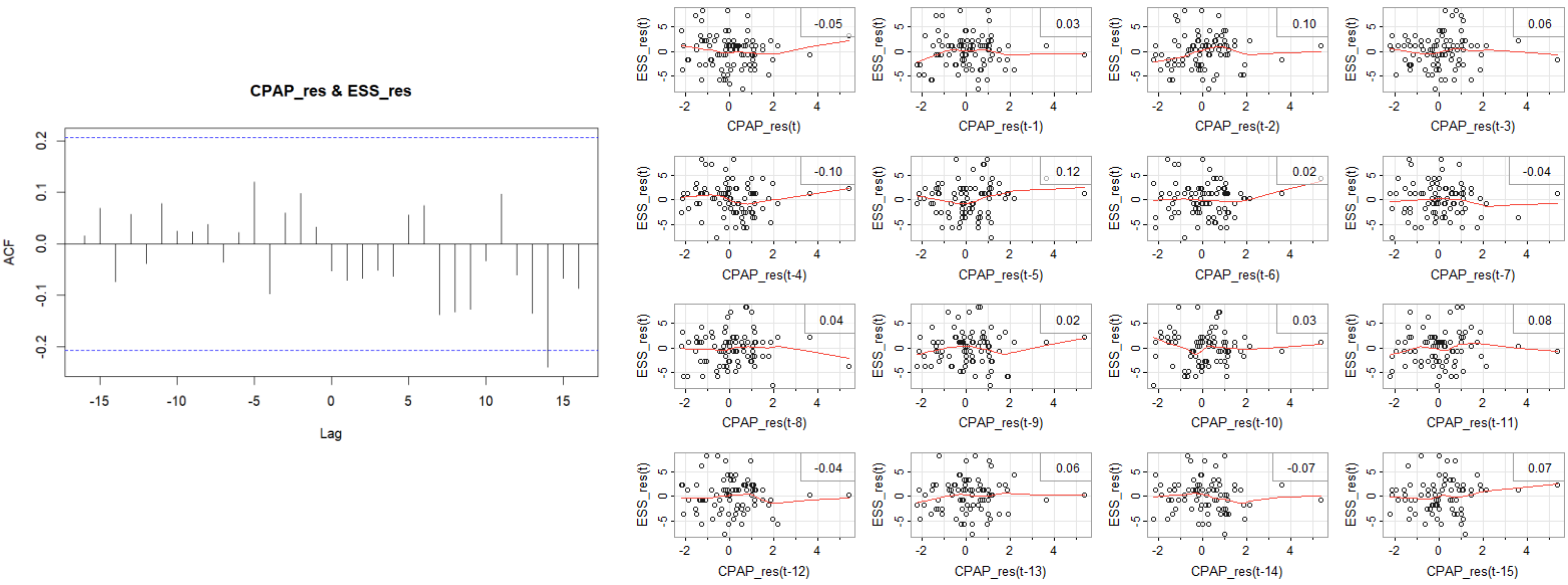
For model validation of ESS score, the p-value of the Box-Ljung test was 0.50 showing that there was no pattern in the residuals. The ACF and QQplot (approximately) yielded the same resu lts (Figure E5). Consequently, the time series model of ESS score was validated.

Figure E5. Auto-Correlation Function and QQ plot of the ESS score time series allowing to validate the model.



For CPAP adherence, the final model was ARIMA (0, 1, 1) while for ESS score, it was ARIMA (0, 0, 0). Consequently, the time series of CPAP adherence is a non-stationary time series with no trend, while the time series of the ESS score shows a random fluctuation around a constant (reference value). A cross-correlation function was performed to compare the correlation between these two time series (the variables were detrended by the ARIMA model; Figure E6).

Figure E6. Auto-Correlation Function (left) and correlations functions (right) of the Cross-Correlation Function between CPAP adherence and ESS score.

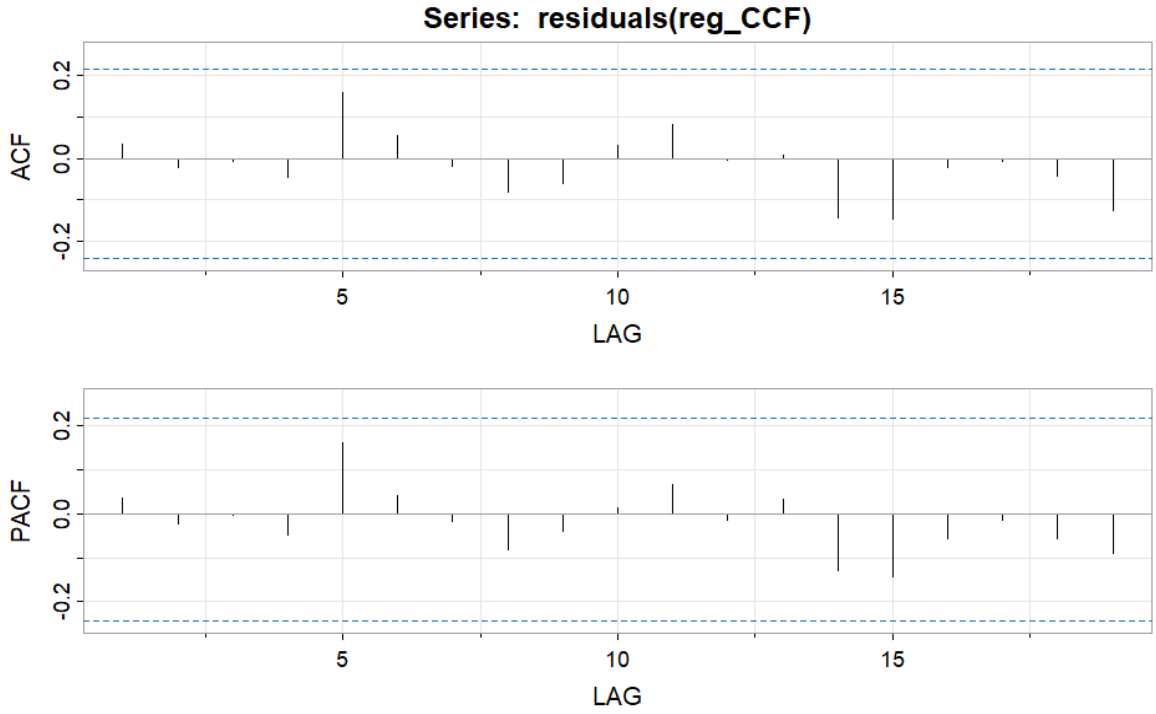


Correlations were observed with a 14-time points lag (Figure E6). This lag could be implemented into a regression to study the association of the ESS score and the CPAP adherence at different lags. For example, a 14-time points lag was chosen (Table E7). Consequently, we found the same result, i.e. an increase of the CPAP adherence was associated with a decrease of 0.8 of ESS score, 14 time points later. Note: the association was not linear in this example, however, the results were presented for educational purposes. The regression model was validated using ACF and PACF plots, which showed that the residuals were not autocorrelated (Figure E7).

Table E7. Coefficient of linear regression between ESS score and CPAP adherence with a 14-time points lag.

	β	**SE**	**Pvalue**
CPAP adherence - lag 14	-0.77	0.31	0.02

Figure E7. Auto-Correlation Function and Partial Auto-Correlation Function of the residuals of linear regression between ESS score and CPAP adherence with a 14-time points lag.



Appendix I – Additional information on (I) Time to event and survival model

Description [27-29] – Survival analysis is used to estimate the survival function or cumulative incidence of an event over time. It determines the time to event occurrence from a defined starting point (e.g., treatment initiation), accounting for censored observations—individuals who are lost to follow-up, drop out, or do not experience the event before the study ends. A key quantity is the hazard function, which represents the instantaneous rate of event occurrence among individuals still at risk. Two main variables are required: (1) a time variable indicating the duration until the event or censoring, and (2) a binary event indicator (1 = event occurred, 0 = censored). A crucial assumption is non-informative censoring: censored individuals are assumed to have the same survival prospects as those who remain under observation. Survival models are appropriate when: 1) Patients enter the study at different times; 2) Follow-up durations vary; 3) The event of interest may or may not occur during the observation window.

The Kaplan–Meier estimator is used to estimate survival in the absence of competing risks. In the presence of competing risks, it may overestimate the incidence function. Kaplan–Meier curves are typically compared using the log-rank test, which evaluates differences in survival across groups by summing time-specific chi-squared statistics. However, this test does not adjust for confounders or quantify effect size.

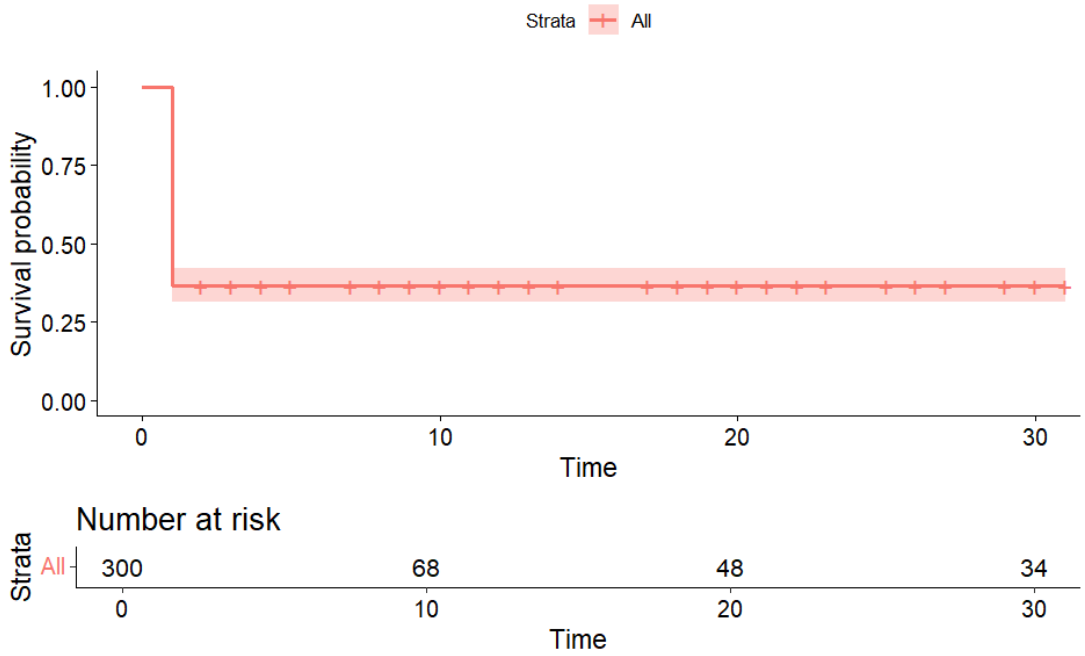
To address this, hazard ratios (HRs) are often derived from the Cox proportional hazards model, which estimates the effect of covariates on the hazard function, not directly on survival time. The Cox model assumes proportional hazards (i.e., constant relative risk over time), an assumption that must be checked. Importantly, it provides valid estimates even in the presence of censoring or independent competing risks.

Process – The survival model follows two general steps:

1) Define the two important parameters: the death variable and the time variable;
2) Apply the log-rank test or hazard ratios and plot the survival curve.

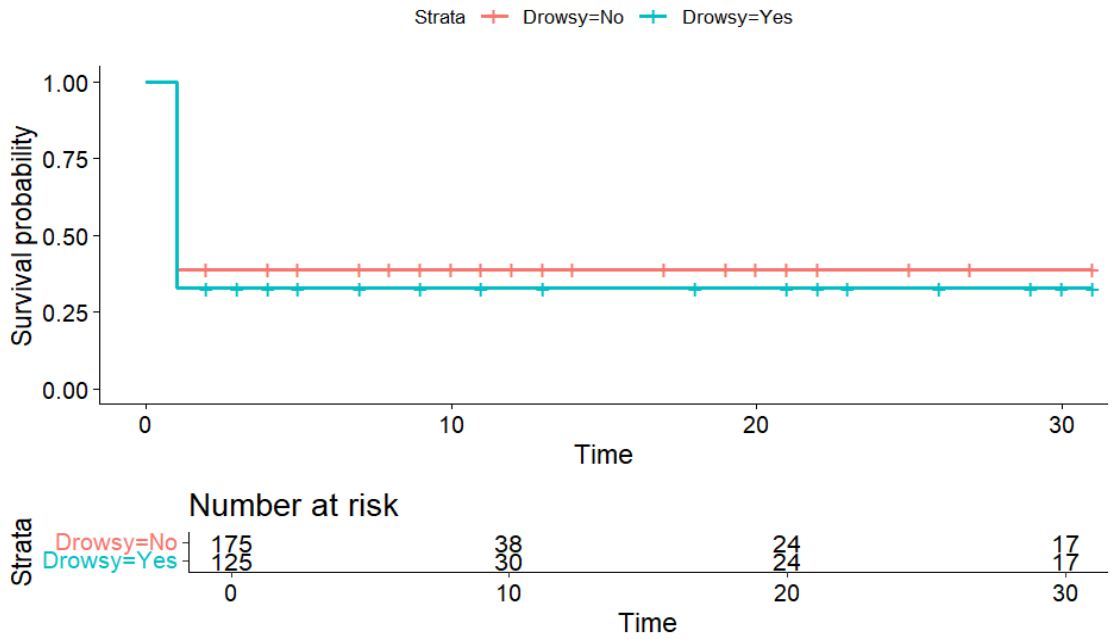
Example (additional information) – The Kaplan-Meier survival model was performed using continuous CPAP adherence. The event variable (i.e. mortality status) is 0 when patients are alive or censored, i.e. they have a CPAP adherence <4h over the study, and 1 when patients are dead, i.e. they have a CPAP adherence ≥ 4h at one time point. The time variable is the first time point that patients have a deceased status or the 90th time point (the end of the study). The probability of treatment adherence has remained relatively stable since the first time points, at around 35% (Figure E8).

Figure E8. Survival probability of becoming adherent to CPAP treatment, over the course of the study.



Stratification according to sleepiness status at T1, using the binary variable ESS score, is also possible (Figure E9).

Figure E9. Probability of becoming adherent to CPAP, according to the drowsy status, over the course of the study.



There is no difference in the survival probability of CPAP adherence according to the patient's sleepiness status, as the p-value of the log-rank test is 0.30. The survival probability is around 40% in the early time points for non-drowsy patients compared with drowsy patients who have a survival probability of around 35%. Both probabilities remain stable over the remaining time points of the study.

Appendix J – Additional information on (J) Hidden Markov model

Description [30-33] – A Hidden Markov Model (HMM) is a generative statistical model used to describe time-varying stochastic processes. It is defined by an initial probability vector, a transition matrix, and the emission densities of hidden states. This method models the interaction between two sequences: The first sequence corresponds to the observed time series, and the second sequence corresponds to the discrete Markov chain and the hidden state. In other words, the model is characterized by a longitudinal response that follows a known distribution, whose density is parameterized by a function of the covariates and the hidden state-dependent "regression" coefficients. For a first-order Markov chain, each value depends exclusively on the preceding values. The aim is to identify the best set of parameters from the set of observable sequences. Using the sequence of observations and the set of hidden Markov model parameters, the Viterbi algorithm estimates the most probable state sequence. This model distinguishes a number of latent classes that differ in terms of model parameters. Within each class, however, no individual differences are allowed. The number of latent classes can be defined a priori and evaluated as the most reasonable and interpretable number of classes using criteria such as AIC and BIC. The transition matrix consists of proportions of transitions from one state to another. The hidden Markov process describes inter-state transitions, and the Markov chain can take into account different types of longitudinal data collected regularly, irregularly, or continuously. In other words, individuals can move from one class to another over time. These dynamics correspond to trajectories. To this end, rather than a single latent variable, a sequence of discrete latent variables is associated with each individual. This gives rise to a hidden process that is assumed to follow a Markov chain. Once this matrix is known, it is applied to the K-means method. After estimating the model using the EM algorithm, the standard error of the estimated parameters can be obtained based on the observed information matrix. The final model must strike a balance between quality and complexity. Latent variables must account for unobserved heterogeneity between individuals that cannot be explained by observed covariates. A train/test and validation method can be used to determine the final model. After defining this model, clustering is performed using the maximum a posteriori (MAP) rule. More specifically, the Latent Markov (LM) model is used for univariate and multivariate longitudinal data analysis based on repeated observations of a sample over time. This model assumes that conditional response probabilities are homogeneous over time.

Process – The Hidden Markov Model follows 3 steps:

1) Markov assumptions: the probability of transition from one state to another must not depend on previously visited states or time spent in the current state, and it assumes that the transition rate must be constant over time and common to all individuals;

2) Estimation of model parameters: estimation of the transition rate from a transition probability that can be directly estimated from the data. A Bayesian method using the MCMC algorithm could be a solution;

3) Inclusion of random effects and individual covariates: assume that transition rates are not fixed but modifiable;

4) Modeling unobserved responses: several scenarios are possible, depending on missing data (Missing At Random, Missing Completely At Random, Missing Not At Random, Last Observation Carried Forward-like missingness) and loss to follow-up.

Example (additional information) – This model fitted the EM algorithm and used the multinomial family for the categorial observations. The independence of observation variable from all covariates were added to the model. A seed was used for reproducibility. A test for another number of hidden states

can be applied and comparisons using BIC, AIC and log likelihood criteria could be performed. However, the interpretation of hidden states must stay possible. For an education point of view, we only included the last 200 patients. Indeed, the results with all patients showed equality of probabilities.

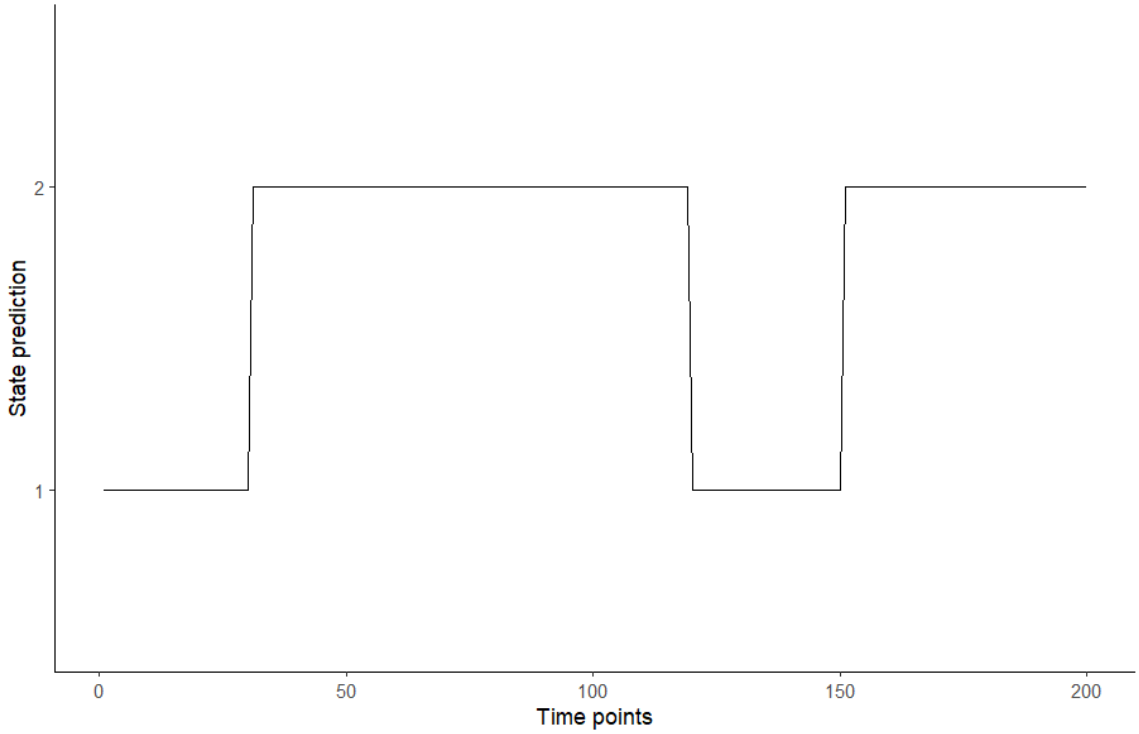
For the first state, the patient was assigned to the "adherent" status. The transition probability matrix (i.e. the probability to go from one state to another) showed a low probability of switching states: 0.03 for transitioning from Non-adherent to Adherent, 0.02 for Adherent to Non-adherent, 0.98 for remaining in the Adherent state, and 0.97 for remaining in the Non-adherent state (Table E8).

Table E8. Matrix of transition probabilities from number of hours to CPAP use to hidden state of CPAP adherence using Hidden Markov model.

	Non-adherent	**Adherent**
Non-adherent	0.97	0.03
Adherent	0.02	0.98

The prediction of the patient's state at each time point was predicted and plotted in the graph below (Figure E10). The state's prediction included 30.5% of time points in the non-adherent state and 69.5% in the adherent state.

Figure E10. Prediction of state changes at each time point, showing only the first 200 time points for a better visualization.



Appendix K - Comparison of R and Python software in the sleep examples

R and Python packages used for application examples of the various statistical methods.

	R	Python
ANOVA	rstatix	statsmodel
X^2	stats	statsmodel
K-means	kml	tslearn
LTA	LMest	-
GBTM	trajeR	-
GMM	lcmm	-
Mixed	lme4	statsmodels
Survival	survival, survminer	lifelines
ARIMA & Cross-correlation	forecast	pmdarima
Hidden Markov	depmixS4	hmmlearn

In Python, there are no packages that allow direct implementation of LTA, GBTM and GMM methods.

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Lettre de recherche, soumise au journal Sleep Medicine, n°1

Introduction

Le suivi à domicile de l'évolution des paramètres de santé tels que la pression artérielle est désormais facilité par la démocratisation des objets connectés. Le tensiomètre connecté, par exemple, permet un suivi régulier de la pression artérielle chez les patients atteints de SAOS, une population particulièrement exposée à un mauvais contrôle de sa pression artérielle et donc à risque d'événements cardiovasculaires[89,138]. Par ailleurs, l'évolution de l'observance au traitement par PPC peut également être suivie grâce au télémonitoring de la PPC qui permet de recueillir en continu différents paramètres dont ceux liés à l'observance[81,88]. Cependant, il y a un fort taux d'abandon d'utilisation des appareils connectés, en particulier de la PPC[21]. Certains patients refusent, ne tolèrent pas ou n'arrivent pas à utiliser l'appareil correctement. Plusieurs facteurs ont été identifiés tels que l'inconfort, la complexité de l'appareillage, le bruit ou encore des freins d'ordre psycho social[76,80]. Toutefois, il a été montré que la pression artérielle, les MACEs et la mortalité diminuent lorsque l'observance à la PPC est suffisante[82,139]. De plus, l'utilisation d'un tensiomètre connecté a également été associée à une meilleure observance des traitements médicamenteux antihypertenseurs[140–145] ; cette technique de prise de mesure de PA devenant progressivement un standard de soin pour le diagnostic de l'hypertension et le suivi de la réponse de la PA au traitement. Cependant, à notre connaissance, il n'existe pas d'étude évaluant l'évolution respective de l'utilisation d'objets connectés pour la mesure de la pression artérielle et l'observance à la PPC chez un même patient atteint de SAOS.

Objectifs

L'objectif de cette étude est de déterminer l'évolution respective du taux de complétion de l'utilisation du tensiomètre connecté à domicile et du taux d'observance à la PPC au cours des 6 premiers mois de traitement sous PPC.

Méthodes

Les données de cette étude proviennent des deux cohortes observationnelles prospectives, e-Meuse (Verdun, France) et Sleep Connect (Lille et Grenoble, France) présentées auparavant. Les patients inclus devaient être diagnostiqués pour un SAOS, par PSG ou polygraphie respiratoire, et être traités par PPC. Ils devaient, de plus, avoir au moins une automesure de la pression artérielle et au moins une mesure d'observance à la PPC au cours des 6 premiers mois de traitement.
Les taux de complétion pour l'utilisation du tensiomètre et l'observance à la PPC ont été définis pour cette étude et calculés mensuellement sur une période de 6 mois. Des analyses comparatives ont permis d'étudier leur évolution dans le temps (tests statistiques de Mann-Kendall) et leur association mutuelle (modèles linéaires mixtes ajustés).

Résultats

98 patients ont été inclus et 36 600 mesures de pressions artérielles étaient disponibles. Une diminution moyenne significative (25%) du taux de complétion de l'utilisation du tensiomètre connecté a été observée alors que le taux d'observance à la PPC a légèrement mais significativement augmenté (6%) au cours des 6 mois de mesure. Une diminution de l'utilisation du tensiomètre connecté a été observée indépendamment des caractéristiques des patients : patients observants à la PPC, hypertendus ou non-hypertendus à l'entrée dans l'étude, chez les patients plus jeunes, avec un IAH modéré, sévère et très sévère, chez les femmes et chez les patients somnolents à l'entrée dans l'étude. Cependant, il existe une association significative positive entre l'utilisation des deux objets connectés. Ainsi, lorsque le taux d'observance à la PPC augmente de 1%, le taux de complétion de l'utilisation du tensiomètre connecté augmente de 0.17% [0.08 ; 0.25] ($p < 0.01$). Cette augmentation de taux de complétion du tensiomètre connecté lorsque le taux d'observance à la PPC augmente est modeste et cliniquement non-significative montrant ainsi une interaction limitée entre les taux d'observance des objets connectés au cours du temps.

Cette lettre de recherche a été soumise au journal Sleep Medicine en avril 2026.

Perspectives

Le premier article original (partie III) montre que l'analyse de la pression artérielle des patients atteints d'un SAOS est une problématique intéressante du fait du fort taux de patients SAOS ayant une hypertension non diagnostiquée ou insuffisamment contrôlée. L'article de revue et la première lettre de recherche (partie IV) proposent une procédure générale d'analyse des données longitudinales et une mise en garde concernant l'impact des données manquantes. Nous avons montré également que le taux de complétion des mesures de PA diminue au cours du temps pour une population atteinte de SAOS contrairement au taux d'observance de la PPC qui augmente légèrement. Il existe, de plus, une association modeste positive entre observance à la PPC et taux de complétion du tensiomètre connecté. En prenant en compte ces trois problématiques liées à l'étude de la PA chez des patients atteints de SAOS, il est intéressant de regarder l'évolution de la réponse au traitement par PPC en termes de PA mesurée à domicile via un tensiomètre connecté.

Article

Short communication

Respective evolution of the completion rate of home self-measurements of blood pressure and continuous positive airway pressure adherence rate in obstructive sleep apnea

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Keywords: Telemonitoring, home blood pressure monitoring, obstructive sleep apnea, continuous positive airway pressure, completion rate

Highlights:

- HBPM completion rates decreased over the first six months of CPAP treatment
- CPAP adherence rates slightly increased over the first six months of treatment
- The use of HBPM device decreased regardless the patients' clinical phenotype
- Limited interaction between the use of the two connected devices was found

Abstract

Objective/Background – Home blood pressure monitoring (HBPM) has become the standard of care for diagnosing hypertension - the most prevalent comorbidity of obstructive sleep apnea (OSA) - and for monitoring blood pressure response to treatment. Connected devices have been used in recent studies to monitor blood pressure in patients with OSA initiated on continuous positive airway pressure (CPAP). We compared the respective evolution of HBPM completion rate and CPAP adherence rate in the first six months of treatment.

Patients/Methods – 98 patients were prospectively included, and were asked to record 6 daily HBPM measurements. CPAP adherence was obtained using telemonitoring. HBPM completion rates and CPAP adherence rates were monthly calculated. A Mann-Kendall test was performed to describe the changes in rates and adjusted linear mixed models were used to assess the association between these two rates.

Results - HBPM completion rate significantly decreased from 44% during the 1st month to 19% at six months. CPAP adherence rate significantly increased from 35% the 1st month to 41% at six months. A similar decrease of HBPM completion rate was shown among different patients' profiles. Linear mixed models showed that an increase in CPAP adherence rates of 1% was associated with an increase in HBPM completion rates of 0.17% [0.08; 0.25].

Conclusion - The use of HBPM device decreased regardless the patients' clinical phenotype, whereas adherence to CPAP increased slightly. The positive association between the two rates was modest and non-clinically significant suggesting a limited interaction between the use of the two connected devices.

Introduction

Hypertension is the most prevalent comorbidity of obstructive sleep apnea (OSA) and is strongly related to prognosis [1–3]. Home self-measured blood pressure monitoring (HBPM) is increasingly becoming a standard of care for diagnosing hypertension and monitoring blood pressure response to treatment [4–6]. HBPM dissemination in routine practice has been facilitated by using connected devices for collecting and transmitting blood pressure measurements [7,8].

Continuous positive airway pressure (CPAP), the first line primary therapy for OSA, is also a connected device allowing telemonitoring of various parameters of adherence and treatment efficacy [9,10]. As hypertension is difficult to control in OSA patients and blood pressure reduction under CPAP is heterogeneous and unpredictable [11,12] recent studies have included connected devices for monitoring blood pressure in OSA patients initiated on CPAP [13,14].

However, no study to date has addressed the respective evolution of completion rates of HBPM measurements and CPAP adherence rates in OSA patients. Our study aimed to compare, in the six first months after CPAP initiation, the respective evolution of HBPM completion rates and CPAP adherence rates.

Methods

Adult patients suffering from OSA initiated on CPAP from the e-Meuse (NTC04963192) and Sleep Connect (NCT04054180) observational prospective cohorts were included in the study. Patients with at least one HBPM measurement and one CPAP adherence measurement during the first six months of CPAP therapy were selected.

During the first six months of CPAP therapy, patients were instructed to self-measure their BP six times a day (3 in the morning, 3 in the evening) and CPAP adherence was assessed every night by device remote monitoring. As no standardized definition of HBPM adherence currently exists, HPBM completion rate was designed to reflect patient engagement in performing scheduled BP self-measurements. Each month, the HBPM completion rate was computed for a patient, as follow:

$$\text{HBPM completion rate (\%)} = \frac{Number\ of\ HBPM\ measurements\ actually\ recorded\ per\ month}{Number\ of\ HBPM\ measurements\ expected\ per\ month} * 100$$

with number of HBPM measurements expected to the monitoring protocol calculated by multiplying the number of days per month and the number of six daily measurements expected per day, i.e. 180 expected measurements for the months with 30 days and 186 expected measurements for the months with 31 days.

The CPAP adherence rate was computed monthly for a patient by considering the number of nights with adherence ≥4h, as follow:

CPAP adherence rate (%) = $\frac{Number\ of\ night\ with\ CPAP\ adherence \geq 4h\ per\ month}{Total\ number\ of\ nights\ per\ month} * 100$

A Mann-Kendall test was performed to describe the changes in HBPM completion rates over the 6 months of the study. Sub-group analyses were performed depending on CPAP adherence status (defined by calculating the mean adherence over the 6-month period, adherent patient defined with a mean adherence ≥4 hours per night) and regarding baseline patients' characteristic subgroups: age (≥ 56 years vs. < 56 years), sex (men vs. women), hypertension status (yes vs. no), sleepiness status (defined by Epworth score >10 vs ≤10) and Apnea-Hypopnea Index (AHI) categories (moderate: 15 ≤ AHI < 30, severe: 30 ≤ AHI < 45, and very severe: AHI ≥ 45). Linear mixed regression models were used to assess the association between the HBPM completion rates and the CPAP adherence rates using a random effect (intercept and slope) on patient and adjusted for months of CPAP treatment (continuous). All analyses were conducted with R-4.3.0 and a threshold of 0.05 indicated a statistical significance.

Results

98 patients were prospectively included with a median age of 56 years (interquartile range (IQR) = (49; 64)), a median AHI of 38 events/h (IQR = (27; 56)) and a median Epworth Sleepiness Scale score of 9.5 (IQR = (5.0; 13.0)) (Table 1). There were 55 (56%) of patients with baseline hypertension. There was a median number of measurements of HBPM per patient of 250.5 (IQR = (110.3; 451.3)). Mean (standard deviation) CPAP adherence over the six months was 4.2 (2.4) h/night.

The HBPM completion rate significantly decreased from 44% during the 1st month to 19% at six months (p = 0.02). CPAP adherence rate significantly increased from 35% the 1st month to 41% at six months (p = 0.02; Figure 1A, Table S1). This increase was also observed comparing the median of CPAP adherence for each month (p = 0.01) with a median (IQR) of 3.2 (1.8; 5.5) h/night the first month while the median (IQR) of the sixth month was 4.0 (2.4; 6.3) h/night (Table S2). In subgroups analyses no specific clinical or anthropometric profile was clearly associated with different evolutions in HBPM completion rates, i.e. HBPM completion rates significantly and similarly decreased in hypertensive and non-hypertensive patients, in younger patients, in patients with moderate, severe and very severe AHI, in women and in sleepy patients (Figures 1B-1C, Table S3).

In the mixed linear regression model, a significant positive association was found between CPAP adherence rate and HBPM completion rate: when CPAP adherence rates increased by 1%, HBPM completion rates increased by 0.17% [0.08; 0.25] ($p < 0.01$, Table S4).

Discussion

During the six months following CPAP initiation, there was a significant decrease in the HBPM completion rate compared to a slight increase in CPAP treatment adherence rates. A similar decrease of HBPM completion rate was shown among different patients' profiles (i.e hypertensive and non-hypertensive patients, younger versus elderly patients, patients with moderate, severe and very severe AHI, women versus men and sleepy versus non-sleepy patients). A slight increase in the HBPM completion rate was associated with an increase in CPAP adherence rates. This increase was modest and non-clinically significant suggesting a limited interaction between the use of the two connected devices.

The decrease of completion rates with HBPM measurements has been investigated in the literature to finally identify three clusters [15,16] defined by high adherence, gradual decline and early discontinuation. The first study was conducted in older adults with ischemic heart disease [15] and our study is the first to address this question prospectively in OSA patients. In Paul et al. study [16], patients generally adhered well to HBPM, particularly among women with hypertension which not consistent with our results. However, although the definition of HBPM adherence and statistical methods differed between studies, results are uniform in showing a decline in HBPM engagement in the majority of individuals. This decrease was also observed by Unly et al. who assessed HBPM engagement among uncontrolled hypertensive patients [17]. In this study, four HBPM adherence groups were defined (no engagement, low engagement, intermediate engagement, and high engagement) and overall engagement was suboptimal, with 65% of patients exhibiting intermediate or lower level of engagement. Unlu et al. suggested that low HBPM engagement may be explained by the burden of monitoring and the need for more accessible approaches [17].

The use of connected devices and remote monitoring for treatment adherence has been widely studied in the literature, although results were inconsistent. Franke et al. reported that digital tools and telemonitoring improved adherence to CPAP [18]. Our group has reported that in OSA patients with high cardiovascular risk, multimodal telemonitoring including HBPM was not superior to usual CPAP care for improving home BP; however, telemonitoring improved adherence and patient-centered outcomes [19]. Further studies evaluating adherence to HBPM and CPAP are needed to

94 better understand their respective and combined effects, as well as to establish a standardized
95 definition of HBPM adherence.

96 One limitation of our study was the absence of a usability questionnaire to assess patients'
97 feelings about using the CPAP and HBPM device respectively, as well as a questionnaire to document
98 reasons for discontinuing BP measurements. Patients only received an educational visit before the
99 treatment informing them about the use of devices, followed by clinical visits at 3 and 6 months
100 dedicated to CPAP follow-up and probably a more limited interest of respiratory physicians directed
101 to HBPM measurements. Another limitation was the intensive burden of measurements asking for six
102 measurements per day. On the opposite CPAP telemonitoring is not associated with any constraints
103 for the patients.

104 In conclusion, the use of HBPM device decreased during the first six months of CPAP therapy
105 regardless the patients' clinical phenotype, whereas adherence to CPAP increased slightly.

Table 1. Participant characteristics at baseline

	Overall (N = 98)
Body Mass Index, kg/m²	31 (27; 35)
Age, yr	56 (49; 64)
Male sex	59 (60)
Current smoker	15 (15)
Former smoker	38 (39)
Epworth Sleepiness Scale score	9.5 (5.0; 13.0)
Diagnostic polysomnography	
ODI, events/hr	19 (10; 41)
AHI, events/hr	38 (27; 56)
Comorbidities (ICD-10)	
History of hypertension	55 (56)
Arrythmias	5 (5)
Abnormal lipid profile	25 (26)
Cerebrovascular disease	6 (6)
Coronary heart disease	8 (8)
Type 2 Diabetes	12 (12)
Treatments (ATC codes)	
Agent acting on the renin-angiotensin system	46 (47)
Antihypertensives	2 (2)
Diuretics	14 (14)
β-blocking agents	20 (20)
Calcium channel blockers	15 (15)
Blood pressure measurements	
Number of measurements*	250.5 (110.3; 451.3)
Baseline diastolic BP > 80 mmHg	31 (32)
Baseline systolic BP > 150 mmHg	14 (14)

Values are median (interquartile range) or number of patients (%)
**Median (interquartile range) of the number of HBPM measurements per patient.*
Abbreviations: AHI: apnea-hypopnea index, ATC: anatomical therapeutic chemical, BP: blood pressure, CPAP: continuous positive airway pressure, ICD-10: international classification of diseases 10th revision, ODI: oxygen desaturation index

Figure 1. Evolution of the HBPM completion rates and CPAP adherence rates

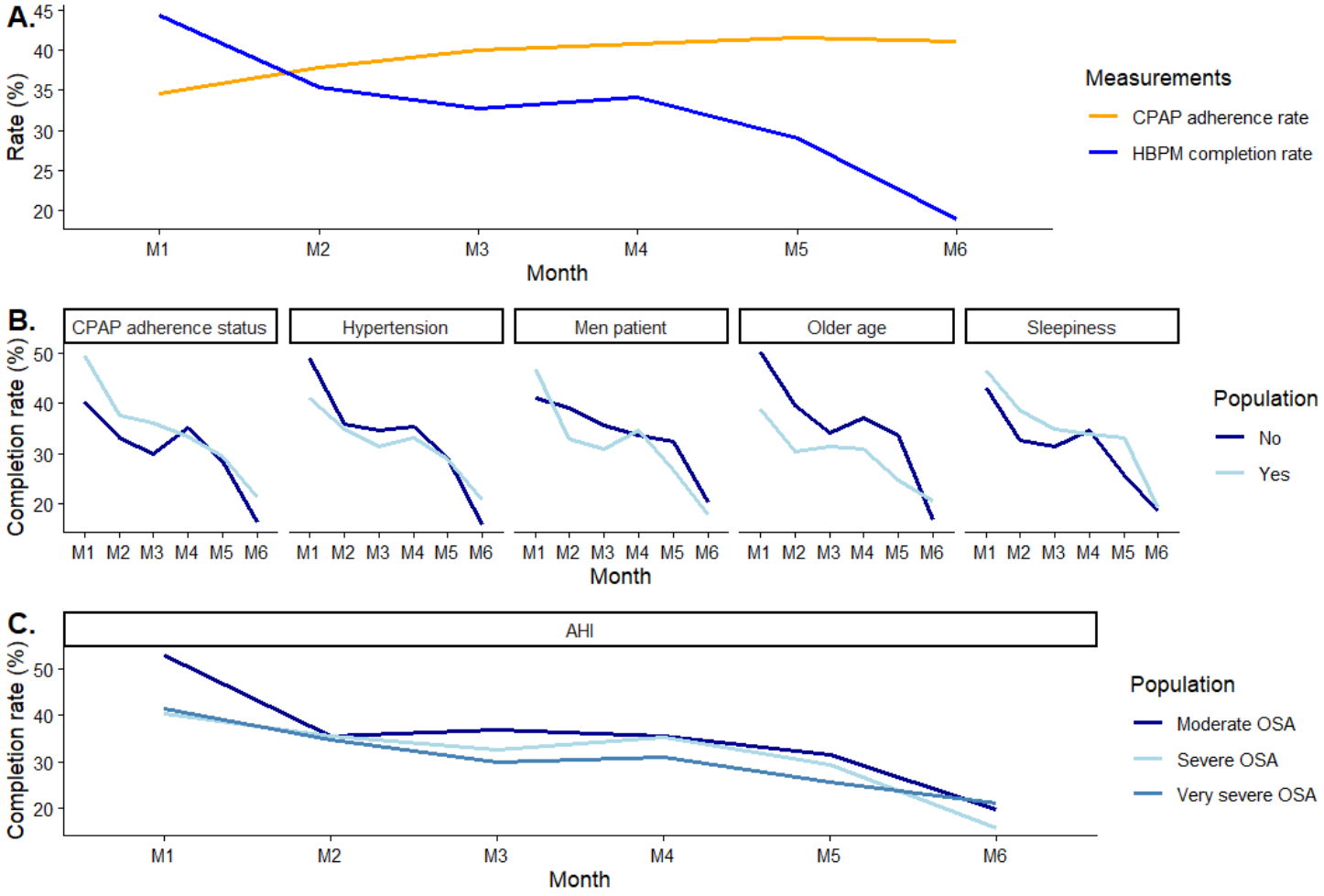

Figure A shows the HBPM completion rates and the CPAP adherence rates, for the overall population (N = 98). Figure B shows the HBPM completion rates depending on CPAP adherent status (mean CPAP adherence ≥ 4h/night vs. < 4h/night over the 6-month period; N = 45 adherent patients), baseline hypertension status (having history of hypertension vs. not having history of hypertension; N = 55 hypertensive patients), sex of the patient (men vs. women; N = 59 men), baseline age (older age refers to age ≥ 56 years; N = 49 patients) and baseline sleepiness status (ESS score >10 vs. ≤ 10; N = 42 sleepy patients) of the patients. Figure C shows the completion rate of HBPM device use depending on baseline AHI (15 ≤ AHI < 30: moderate OSA (N = 29), 30 ≤ AHI < 45: severe OSA (N = 36), 45 ≤ AHI: very severe OSA (N = 33)).

Abbreviation: AHI: apnea-hypopnea index, CPAP: continuous positive airway pressure, ESS: Epworth Sleepiness Scale, HBPM: home blood pressure monitoring, OSA: obstructive sleep apnea

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Supplementary Material

Respective evolution of the completion rate of home self-measurements of blood pressure and continuous positive airway pressure adherence rate in obstructive sleep apnea

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Evolution of HBPM completion rates and CPAP adherence rates

Table S1. HBPM completion rates and CPAP adherence rates

	CPAP adherence rates (%)	HBPM completion rates (%)
Month 1	34.6	44.4
Month 2	37.8	35.3
Month 3	40.1	32.8
Month 4	40.8	34.1
Month 5	41.5	29.0
Month 6	41.1	18.9
P-value*	p = 0.02	p = 0.02

Mean of HBPM completion rates and mean of CPAP adherence rates, per month.
*Mann-Kendall test for the overall population assessing the significance of the evolution over the 6 months
Abbreviation: CPAP: continuous positive airway pressure, HBPM: home blood pressure monitoring

Table S2. Median of CPAP adherence per month

	CPAP adherence (h/night)
Month 1	3.2 (1.8; 5.5)
Month 2	3.6 (2.2; 6.2)
Month 3	3.8 (2.2; 6.3)
Month 4	3.8 (2.3; 6.0)
Month 5	3.9 (2.4; 6.4)
Month 6	4.0 (2.4; 6.3)
P-value*	p = 0.01

Median (interquartile range) of CPAP adherence, per month.
*Mann-Kendall test for the overall population assessing the significance of the evolution over the 6 months
Abbreviation: CPAP: continuous positive airway pressure

Table S3. HBPM completion rates (%) depending on patient's baseline characteristics and CPAP adherence status

	Baseline hypertension‡		Baseline sleepiness$^{\phi}$		Baseline age$^{\gamma}$		Baseline AHI*			Sex		CPAP adherence status**	
	Hypertensive patients (N = 55)	Non-hypertensive patients (N = 43)	Sleepy patients (N = 42)	Non-sleepy patients (N = 56)	Older patients (N = 49)	Younger patients (N = 49)	Moderate OSA (N = 29)	Severe OSA (N = 36)	Very severe OSA (N = 33)	Men (N = 59)	Women (N = 39)	CPAP adherent patients* (N = 45)	CPAP non-adherent patients (N = 53)
Month 1	41.0	48.8	46.4	42.9	38.7	50.1	52.9	40.3	41.5	46.6	41.1	49.3	40.3
Month 2	34.9	35.8	38.6	32.6	30.5	39.5	35.7	35.5	34.8	32.9	39.0	37.6	33.1
Month 3	31.4	34.6	34.8	31.3	31.3	34.2	36.8	32.5	29.9	30.8	35.6	36.1	29.9
Month 4	33.0	35.3	33.8	34.5	30.9	37.1	35.5	35.4	30.9	34.5	33.7	33.3	35.0
Month 5	28.9	29.1	33.1	25.6	24.8	33.7	31.5	29.4	25.8	26.7	32.3	29.4	28.5
Month 6	20.8	15.9	19.2	18.6	20.6	16.9	19.9	15.9	21.1	17.8	20.3	21.2	16.2
p-value* **	0.02	0.02	0.01	0.06	0.06	0.02	0.02	0.02	0.02	0.06	0.01	0.01	0.06

‡ A patient is hypertensive if he had history of hypertension at baseline.

$^{\phi}$ A patient is sleepy if his ESS score at baseline was greater than 10.

$^{\gamma}$ A patient is older if his age is greater than or equal to the median age of the overall population (56 years).

**A patient had moderate OSA if his baseline AHI was between 15 events/h and 30 events/h, had severe OSA if his baseline AHI was between 30 events/h and 45 events/h and had very severe AHI if his baseline AHI was greater than 45 events/h.*

***A patient is adherent if the mean of his CPAP adherence over the 6 months is greater than or equal to 4 hours per night.*

****Mann-Kendall test was performed to assess the significance of the evolution in the completion rate of HBPM device use, over the 6 months.*

Abbreviation: AHI: apnea-hypopnea index, CPAP: continuous positive airway pressure, ESS: Epworth sleepiness scale, HBPM: home blood pressure monitoring, OSA: obstructive sleep apnea

Mixed-effects linear regression models

Table S4. Multivariable mixed-effects linear regressions between HBPM completion rates and CPAP adherence rates, adjusted for time (months) and the baseline characteristics of the patients with random intercept and slope at the patient level

	β (95%CI)	p-value
CPAP adherence rate (%)	0.17 [0.08; 0.26]	<0.01
Months	-5.15 [-6.32; -3.90]	<0.01
Baseline age (years)	2.15 [-1.96; 6.23]	0.31
Sex – Women	3.10 [-4.73; 10.92]	0.45
Baseline hypertension - Yes	-1.05 [-8.73; 6.67]	0.79
Baseline AHI (events/h)	0.05 [-0.11; 0.22]	0.54
Baseline ESS score	-0.08 [-0.89; 0.71]	0.84

The multivariable model assesses the effect of CPAP adherence rates on HBPM completion rates. The model is adjusted for time (months, continuous variable), age of the patients at baseline (continuous), sex of the patient (Men vs. Women), baseline history of hypertension (No vs. Yes), baseline AHI (continuous) and baseline ESS score (continuous).
Abbreviations: AHI: apnea-hypopnea index, CI: confidence interval, CPAP: continuous positive airway pressure, ESS: Epworth sleepiness scale, HBPM: home blood pressure monitoring.

V. Hétérogénéité de la réponse au traitement par PPC en termes de pression artérielle – Article original publié n°2[126]

Introduction

Le SAOS et l'hypertension sont des comorbidités connues[5,8] mais comme nous l'avons montré dans l'article original n°1, son diagnostic est difficile et cette comorbidité est associée à une surmortalité[146]. Cela pourrait justifier un monitoring longitudinal avec des mesures plus fréquentes et régulières au cours du temps qui sont rendues possible grâce à l'automesure à domicile de la pression artérielle[79,147,148]. Comme nous l'avons indiqué, l'emploi des objets connectés permet un suivi et une prise en charge des patients plus personnalisés et probablement plus efficace[89,90,138]. De plus, l'utilisation d'objets connectés permet une granularité de collection des données que les méthodes classiques de recueil n'ont pas. L'usage du tensiomètre connecté, par exemple, permet de mesurer l'évolution de la PA au cours de la journée et de prendre en compte la variabilité de la PA sur les 24 heures et au cours du temps contrairement aux mesures cliniques isolées associées à des consultations épisodiques[89,124,125]. L'avantage de ces tensiomètres connectés est également de pouvoir faire des mesures répétées sur plusieurs jours, prenant en compte la variabilité entre les jours de mesures, ce que les mesures ambulatoires sur 24h ne permettent pas[124] ; le dispositif connecté étant, de plus, facile à utiliser, moins contraignant et non inconfortable contrairement à celui utilisé pour des mesures ambulatoires sur 24 heures[125] qui perturbent également la qualité du sommeil.

Chez le sujet sain, la PA varie au cours de la journée avec un pic de pression matinale (morning surge) juste avant le réveil et une augmentation progressive de la PA jusque 12h-13h puis une diminution progressive jusqu'à atteindre son point bas au cours de la nuit, vers 5h-6h (Figure 11). Cette évolution nycthémérale de la PA est modulée par la présence d'une hypertension ou d'un SAOS. Un patient hypertendu aura une pression artérielle beaucoup plus élevée tout au long de la journée par rapport à un patient normo tendu (sain) mais pourra, dans certains cas, garder les mêmes variations au cours de la journée que le patient normo tendu (Figure 11) ; l'hypertension par automesures à domicile étant définie par une PA systolique supérieure ou égale à 135 mmHg et/ou une PA diastolique supérieure ou égale à 85 mmHg[149]. Tandis que le patient atteint de SAOS a des profils de pression artérielle particuliers avec soit un pic de pression matinale trop élevé mais possiblement une variation de la PA au cours de la journée équivalente à un patient normo tendu, soit il n'aura pas de pic de pression matinale mais une élévation de la PA qui débutera pendant son sommeil avec une période de diminution de PA nocturne réduite par rapport à un patient normo tendu (Figure 12).

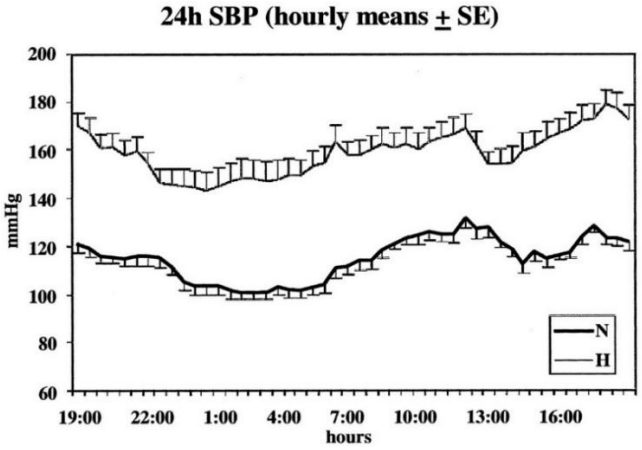

Figure 11. Evolution de la pression artérielle au cours des 24 heures chez des patients sains et hypertendus

Source: Mancia et al., 2003[150]

N correspond à l'évolution de la PA chez des patients normo tendus et H correspond à l'évolution de la PA chez des patients hypertensifs.

Abréviations : SBP : pression artérielle systolique

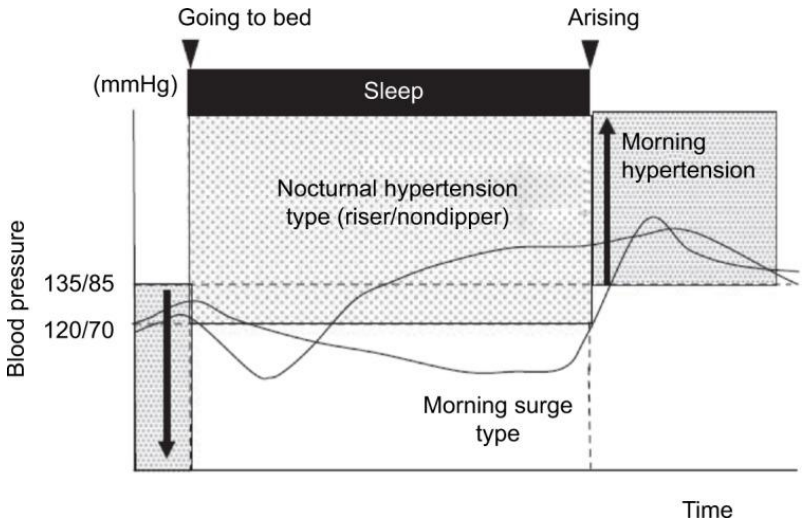

Figure 12. Evolution de la pression artérielle au cours des 24 heures chez des patients atteints de SAOS

Source : Marrone et al., 2018[124]

Alors que des mesures de pressions cliniques ou sur les 24 heures ont été assez fréquemment réalisées [110,125,148,151], l'évolution de la pression artérielle par automesures, chez les patients atteints de SAOS traités par PPC au cours des premiers mois d'utilisation de leur traitement, est très peu documentée.

Objectifs

L'objectif principal de cette étude est de décrire la trajectoire d'évolution de la pression artérielle au cours des 6 premiers mois de traitement par PPC en se basant sur des mesures longitudinales répétées d'automesures de pression artérielle à domicile. L'objectif secondaire est d'évaluer plus spécifiquement l'impact de la PPC sur la pression artérielle du matin et du soir. Enfin, le troisième objectif est d'identifier les prédicteurs de l'évolution de la pression artérielle sous PPC.

Méthodes

Les données utilisées proviennent des deux cohortes observationnelles prospectives, e-Meuse (Verdun, France) et Sleep Connect (Lille et Grenoble, France). Les patients inclus devaient souffrir d'un SAOS diagnostiqué par PSG ou polygraphie respiratoire et être traités par PPC. Ils devaient, de plus, avoir complété des questionnaires multidimensionnels avant traitement et avoir au moins une automesure de la pression artérielle et une mesure d'observance à la PPC au cours des 6 mois de traitement. Les pressions artérielles de référence étaient établies au cours d'une semaine sans traitement.
Dans un premier temps, des tests de comparaison statistique (Wilcoxon et ANOVA) ont été utilisés pour comparer les valeurs de pression artérielle avant traitement par PPC et au cours des 4ème, 12ème et 24ème semaines de traitement. Ensuite, un modèle linéaire mixte ajusté a été appliqué afin de déterminer l'évolution de la pression artérielle systolique et diastolique du matin et du soir relative au temps de traitement, au sexe, âge et changement de poids du patient pendant la durée de l'étude, aux antécédents d'hypertension, à l'indice de désaturation en oxygène, à l'observance à la PPC et au statut tabagique du patient.

Résultats

98 patients ont été inclus dans cette étude qui est exceptionnelle car proposant 36 600 automesures de pression artérielle pour les analyses de la pression artérielle systolique et diastolique, du matin et du soir. Les pressions artérielles systoliques et diastoliques, du matin et du soir, étaient significativement décroissantes au cours des 6 mois après l'initiation de la PPC avec une réduction plus importante pour la pression artérielle du soir comparée à celle du matin. La pression artérielle du matin, que ce soit diastolique ou systolique, était également plus élevée que celle du soir quelle que soit la période de mesure ; c'est-à-dire avant traitement, ou sous traitement par PPC. Enfin, un statut fumeur régulier, un âge avancé, des antécédents d'hypertension et un gain de poids au cours de l'étude étaient des facteurs associés à une réponse limitée de la PPC sur la pression artérielle ; ces résultats étant ajustés sur la sévérité du SAOS à l'entrée de l'étude et l'observance à la PPC des patients.

Cette étude a été publiée sous forme d'article original dans Annals of ATS en septembre 2025 et a été présentée sous forme de poster au congrès Sleep and Breathing et au congrès de l'ERS en 2025.

Perspectives

La PPC améliore la pression artérielle à domicile au cours des 6 premiers mois de traitement, mais la réponse est hétérogène et moins marquée pour les valeurs de pression artérielle du matin. Le pic de pression artérielle du matin est difficile à prendre en charge dans la pratique clinique. La chronothérapie antihypertensive pourrait constituer une approche prometteuse. Il serait pertinent de comparer les effets de la prise de médicaments antihypertenseurs le matin versus la prise au coucher sur la réduction de la pression artérielle du matin et de la nuit au cours du SAOS.

Par ailleurs, le symptôme de somnolence, mesuré principalement par le score d'ESS, est un symptôme important dans le SAOS et une réduction de la somnolence grâce à la PPC a bien été démontrée[51,83,152,153]. La caractérisation de l'évolution de la pression artérielle sous PPC en fonction des niveaux de somnolence avant PPC a très peu été étudiée. La réponse de la pression artérielle sous PPC est-elle la même chez les patients somnolents au diagnostic par rapport aux patients non-somnolents ?

Article

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ORIGINAL RESEARCH

Home Blood Pressure Trajectories during 6 Months of Continuous Positive Airway Pressure Therapy

Results from the eMEUSE-SANTE and SLEEPCONNECT Clinical Trials

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Abstract

Rationale: Obstructive sleep apnea (OSA) and hypertension are common comorbidities and are associated with poor prognosis. Blood pressure (BP) trajectories using home BP monitoring after initiation of continuous positive airway pressure (CPAP) therapy for OSA are poorly documented.

Objectives: To describe BP trajectories in the first 6 months after CPAP therapy initiation based on repeated longitudinal measurements of home BP, to evaluate the impact of CPAP on morning and evening home BP, and to identify predictors of home BP evolution during CPAP.

Methods: This prospective cohort study enrolled patients with OSA. Home BP monitoring was used to assess morning and evening home BP values over a 7-day period at baseline and over the first 6 months after starting CPAP therapy.

Results: A total of 98 patients were enrolled, and 36,600 home BP measurements were available for analysis. Morning and evening systolic/diastolic home BP decreased significantly during the first 6 months of CPAP therapy ($P < 0.05$ vs. baseline). Morning home BP was significantly higher than evening home BP throughout the study ($P < 0.01$). After adjustment for OSA severity at baseline and CPAP adherence, factors associated with limited home BP response to CPAP were older age, weight gain during CPAP therapy, current smoking, and previous hypertension.

Conclusions: CPAP improved home BP trajectories during the first 6 months, but the response was heterogeneous and less marked for morning BP values. Based on the predictors of BP response during CPAP therapy, weight control appears key to the effective management of patients with OSA and hypertension.

Clinical trial registered with www.clinicaltrials.gov (NCT04963192 and NCT04054180).

Keywords: continuous positive airway pressure; blood pressure; home blood pressure monitoring; obstructive sleep apnea

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Author Contributions: O.C., S.B., and J.-L.P. developed the study concepts, performed the data analysis, and drafted the manuscript. M.J.-F., R. Tamisier, K.A., J.-C.C., T.G., and R. Terrail performed the data collection. O.C., S.B., C.C., C.L., M.F.P., and G.P. provided insight on data interpretation and contributed to the final version of the manuscript. All authors contributed to the reviewing of the manuscript. J.-L.P. had full access to all study data and assumes responsibility for the accuracy and completeness of the analyses and for the fidelity of this report to the trial protocol.

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Obstructive sleep apnea (OSA) is characterized by the recurrence of partial (hypopneas) or complete (apneas) pharyngeal collapses during sleep (1, 2), which in turn produce repeated oxygen desaturation–reoxygenation sequences (intermittent hypoxia). Cardiovascular comorbidities, including hypertension, arrhythmias, stroke, and heart failure (3), are common in people with OSA. Hypertension is a particularly common comorbidity, and there are clear links between OSA and the occurrence of prevalent and incident hypertension, as summarized in a 2024 review by Kwon and colleagues (4).

Comorbidities, including hypertension, are the main drivers for poor prognosis and mortality in OSA (5). More than half of all patients with OSA have hypertension, and common patterns/phenotypes include diastolic, nocturnal, resistant, or poorly controlled hypertension (6, 7). Effective blood pressure (BP) reduction is central to risk management in these individuals with multimorbidities.

Continuous positive airway pressure (CPAP) is the first-line therapy choice for treating moderate to severe OSA and has been reported to lower 24-hour systolic BP (SBP), with a mean effect size of 2–2.5 mm Hg (8, 9). The overall effect is modest, and the range of BP reduction after CPAP initiation is highly variable between individuals and difficult to predict for a given patient with OSA (8, 9).

Assessments of BP trajectories after CPAP initiation to date have used a limited number of BP measurements at specific time points before and after CPAP initiation. This approach limits the potential to fully describe BP trajectories in the first months of CPAP therapy. Home BP monitoring (HBPM) is endorsed by current guidelines for the diagnosis and management of hypertension (10) and facilitates the collection of repeated longitudinal BP measurements. HBPM provides better prognostic information than office BP for target organ damage, occurrence of major adverse cardiovascular events, and mortality (11). HBPM also provides data on morning and evening BP, which is relevant in people with OSA because morning increases in BP have been reported in this group (12).

We hypothesized that high-dimensional longitudinal HBPM data would better capture the dynamics of BP evolution during the first 6 months of CPAP therapy. This prospective cohort study described home BP trajectories in patients with OSA during the first 6 months of CPAP using longitudinal HBPM data, evaluated the specific impact of CPAP on morning and evening home BP values, and identified predictors of home BP evolution during CPAP therapy.

Methods

Study Design and Participants

All patients with OSA diagnosed using polysomnography (PSG) or respiratory polygraphy who had an indication for CPAP treatment were included in two observational prospective cohort studies evaluating integrated care combining CPAP telemonitoring and use of wearables at home to measure BP (eMEUSE: NCT04963192; and SLEEPCONNECT: NCT04054180). Participants were recruited between September 2021 and February 2024 in three centers in France. The eMEUSE study and the SLEEPCONNECT study protocols were approved by the relevant ethics committees (2021-043B and 2019-A00076-51, respectively). All participants signed written informed consent before inclusion in the studies. Only patients who completed baseline questionnaires and performed at least a single home BP measurement and had one CPAP adherence measurement were included. The apnea–hypopnea index (AHI) threshold for defining moderate to severe OSA was 15 events/h.

Data Collection Process

Patient characteristics (age, sex, body mass index, smoking status), treatment history (based on Anatomical Therapeutic Chemical codes: antihypertensives [C02], diuretics [C03], β-blocking agents [C07], calcium channel blockers [C08], agents acting on the renin-angiotensin system [C09] [13]), comorbidities (based on International Classification of Diseases 10th Revision codes; see Table E1 in the data supplement), sleep and depression symptoms, and PSG variables (AHI, oxygen desaturation index [ODI], sleep stages) were stored as deidentified data in the secure Multimorbidity Apnea Respiratory failure Sleep database (Figure 1). Data were validated by study investigators during face-to-face consultations.

Home BP Measurements and CPAP Usage

Home BP was measured using a validated oscillometric automated BP monitor (iHealth Feel BP5; Andon [14]). Patients were instructed to take three home BP measurements 1–2 minutes apart in the morning and evening of each day during the 7 days before CPAP initiation (baseline). It was recommended that patients continue to similarly record three morning and three evening home BP measurements during the 6 months after CPAP initiation.

A previous diagnosis of hypertension, ongoing antihypertensive drug treatment, or average home SBP ⩾135 mm Hg and diastolic BP (DBP) ⩾85 mm Hg during baseline BP measurements was defined as indicating the presence of arterial hypertension (15).

We documented daily CPAP adherence via remote telemonitoring of device data. The weekly homecare package fees for homecare providers in France cover the CPAP device, mask and other consumables, mandatory home visits for device/interface set-up and adjustment, patient education, confirmation of tolerability, adherence monitoring, call centers, and support to improve adherence. Three visits during the first 4 months of CPAP therapy are mandatory, with annual visits thereafter for patients using telemonitoring. Homecare providers also need to provide a call center service 24 hours a day, 7 days a week; a telemonitoring platform; and human resources to check telemonitoring data and

Data availability: The data that support the findings of this study are available on reasonable request to the corresponding author.

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This article has a data supplement, which is accessible at the Supplements Tab.

Artificial Intelligence Disclaimer: No artificial intelligence tools were used in writing this manuscript.

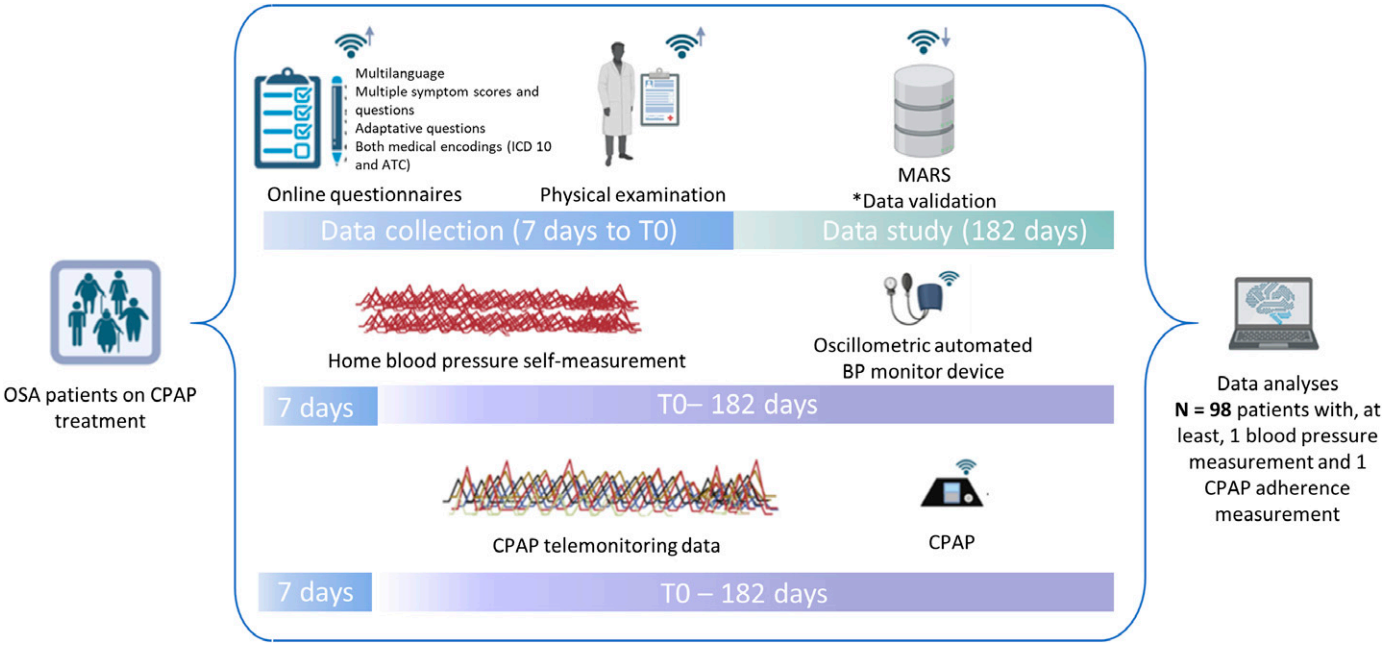

Figure 1. Data collection. ATC = Anatomical Therapeutic Chemical; BP = blood pressure; CPAP = continuous positive airway pressure; ICD-10 = International Classification of Diseases 10th Revision; MARS = Multimorbidity Apnea Respiratory Failure Sleep database; OSA = obstructive sleep apnea; T0 = baseline.

inform the physician if adherence is poor (16). Data were then transmitted to a secure platform linked to the Multimorbidity Apnea Respiratory failure Sleep database.

BP Outcomes

SBP readings <70 mm Hg and >250 mm Hg and DBP measurements <40 mm Hg and >150 mm Hg were excluded (17), which represented <0.2% of the data. For each measurement time, at least two home BP readings were required for analysis, which used the average of two to three SBP and DBP readings in the morning and evening. Values at 1 month, 3 months, and 6 months after CPAP therapy initiation were taken from home BP measurements in the week preceding the end of that month. Time in therapeutic range analysis was used to report the percentage of BP measurements in the normal range, with an SBP threshold of 135 mm Hg and a DBP threshold of 85 mm Hg (Figure E1):

$$\frac{\sum_{i=1}^{m}\frac{\sum_{j=1}^{n}1_{\{x_{ij}<\alpha\}}}{n}}{m}*100$$

where x_{ij} is the mean of measured values on day j by patient i, n is the number of measured days, m is the number of patients, and α is the BP thresholds (reported above).

Statistical Analysis

The study population was described using descriptive statistics: median (interquartile range) for continuous variables and number (percentage) for categorical variables. Wilcoxon and analysis of variance tests were used to compare BP values between different time periods. *P* values from multiple tests were corrected using the Benjamini and Hochberg method.

Because of the number of missing values in the adjustment factors, multiple imputations were performed using *mice* (R; m = 20; Table E2). We used multivariate mixed-effects regressions (*lmer*, *lme4 package*; R) with a random effect on patient (intercept and slope) to determine the evolution of SBP and DBP relative to other factors that were selected based on expert advice. These included follow-up time in days (continuous), sex (male vs. female), age (continuous), change in body weight (measured by connected scale, mean value [kg] over Months 1–3 and Months 4–6, continuous), history of hypertension (no vs. yes), baseline ODI on PSG (continuous), CPAP adherence (continuous, h/night), and smoking status (former or never vs. current). The model was also stratified on BP measurement period (morning vs. evening). The time variable was scaled. Additional analyses included a univariate model and multivariate analyses stratified by baseline hypertension status.

A threshold of 0.05 was considered to indicate statistical significance. All analyses were conducted with R-4.3.0.

Results

Study Population

A total of 98 patients with OSA who started CPAP treatment were included in the analysis (median age, 56 yr) (Table 1). Baseline OSA was severe (median AHI, 38 events/h; median 3% ODI, 19 events/h). More than half of the participants had a history of hypertension at baseline, and nearly all (95%) were receiving antihypertensive drug therapy (Table 1). Six patients (6%) stopped using CPAP during the study period. Mean CPAP adherence was 4.0 ± 2.4 h/night at 1 month and 4.7 ± 2.5 h/night at 6 months.

Home BP Trajectories

A total of 19,300 morning BP measurements and 17,300 evening BP measurements were available. Morning home BP measurements were taken between 4:00 A.M. and 8:00 A.M. (±1.5 h) for 89% of data, and evening home BP measurements were taken between 5:00 P.M. and 8:00 P.M. (±1.5 h) for 84% of data. At the end of the 6-month follow-up,

Table 1. Participant characteristics at baseline, overall, and in subgroups with and without hypertension

	Overall (*N* = 98)	Patients with Hypertension (*n* = 55)	Patients without Hypertension (*n* = 43)
Body mass index, kg/m^2	31 (27–35)	32 (29–36)	30 (26–34)
Age, yr	56 (49–64)	58 (49–65)	52 (47–64)
Male sex	59 (60.2)	32 (58.2)	27 (37.2)
Current smoker	15 (15.3)	10 (18.2)	5 (11.6)
Epworth Sleepiness Scale score	9.5 (5.0–13.0)	9 (5–13)	10 (5–13)
Diagnostic polysomnography			
ODI, events/h	19 (10–41)	23 (9–41)	19 (11–37)
AHI, events/h	38 (27–56)	39 (31–55)	34 (24–51)
Comorbidities (ICD-10)			
History of hypertension	55 (56.1)	—	—
Arrythmias	5 (5.1)	2 (3.6)	3 (7)
Abnormal lipid profile	25 (26)	18 (32.7)	7 (16.3)
Cerebrovascular disease	5 (5.1)	3 (5.5)	2 (4.7)
Coronary heart disease	8 (8.2)	6 (10.9)	2 (4.7)
Type 2 diabetes	15 (15)	13 (23.6)	2 (4.7)
Treatments (ATC codes)			
Agents acting on the renin-angiotensin system	46 (46.9)	43 (78.2)	3 (7)
Antihypertensives	2 (2)	2 (3.6)	0 (0)
Diuretics	14 (14)	14 (25.5)	0 (0)
β-blocking agents	20 (20)	17 (30.9)	3 (7)
Calcium channel blockers	15 (15.3)	15 (27.3)	0 (0)

Definition of abbreviations: AHI = apnea–hypopnea index; ATC = Anatomical Therapeutic Chemical; ICD-10 = International Classification of Diseases 10th Revision; ODI = oxygen desaturation index.
Values are median (interquartile range) or number of patients (%).

36 patients continued to adhere to home BP measurement schedules. The home BP trajectory showed a significant reduction in mean morning and evening BP from baseline at 1, 3, and 6 months after CPAP therapy initiation (Figures 2 and E2 and Table 2). All home BP values showed variation over time, but morning SBP and DBP remained higher than evening SBP and DBP during CPAP therapy ($P < 0.01$) (Figure 3). In the time in therapeutic range analysis (Figure 4), there was a significant increase in the number of morning and evening SBP/DBP readings that were below the hypertension thresholds after 3 months of CPAP use compared with baseline.

The results of the analysis stratified by hypertension status at baseline were consistent with the main analysis (Table E3).

Factors Associated with Home BP Trajectories

In the mixed-effects regressions adjusted for OSA severity at baseline and CPAP

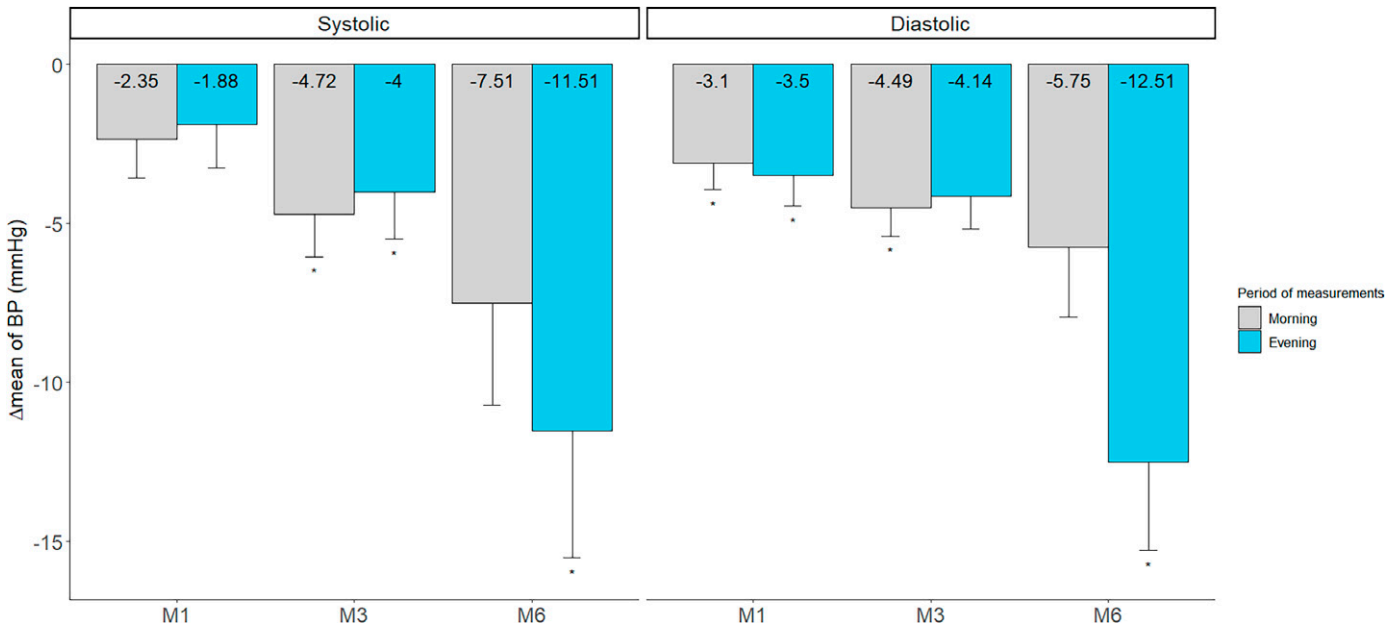

Figure 2. Change from baseline in mean morning and evening diastolic and systolic home BP values during the first 6 months of continuous positive airway pressure therapy. *Wilcoxon test; $P \leq 0.05$ versus baseline. BP = blood pressure; M1 = 1 month; M3 = 3 months; M6 = 6 months.

Table 2. Mean blood pressure values over time

	Baseline	CPAP		
		1 mo	3 mo	6 mo
Systolic blood pressure, mm Hg				
Morning	135.8 ± 15.9	133.4 ± 14.8	131.0 ± 14.5*	128.3 ± 13.3
Evening	134.0 ± 16.2	132.2 ± 16.8	130.0 ± 15.5*	122.5 ± 11.2*
Diastolic blood pressure, mm Hg				
Morning	86.3 ± 10.6	83.2 ± 10.2*	81.8 ± 10.4*	80.6 ± 11.2
Evening	83.0 ± 11.3	79.5 ± 11.2*	78.8 ± 10.8	70.5 ± 13.3*

Definition of abbreviation: CPAP = continuous positive airway pressure.
Values are mean ± standard deviation.
*Wilcoxon test; $P \leq 0.05$ vs. baseline.

adherence, morning and evening DBP values decreased to a greater extent in nonsmokers versus current smokers and in patients who did not gain weight during the 6-month study period. Time (in days) influenced the trajectories of decreases in evening SBP. Older age, weight gain during the study period, and a history of hypertension were associated with poor control of morning and evening home SBP (Table 3 and Figure E3). The results of additional analyses, including a univariate model (Table E4) and multivariate model stratified by baseline hypertension status (Table E5), were consistent with the main analysis.

Discussion

An original feature of our study is that we used data from thousands of HBPM readings to show improvement in morning and evening home BP trajectories during the first 6 months of CPAP therapy in patients with severe OSA. We also highlight a heterogeneous home BP response to CPAP and that the evolution of home BP during CPAP therapy was modulated by hypertension status, body weight stability, and age (after adjustment for sleep apnea severity [ODI] and CPAP adherence).

The link between OSA and hypertension is supported by robust evidence. Mechanistically, in rodent models, intermittent hypoxia (a key feature of sleep apnea) was associated with significant increases in mean SBP and DBP, and the change in BP was associated with the severity and duration of exposure to intermittent hypoxia (18). Chronic intermittent hypoxia exposure in healthy humans was associated with baroreflex inhibition and sustained elevation of sympathetic activity, both of which synergistically increased BP (19, 20). CPAP has both acute and chronic impacts on these pathophysiological mechanisms (21, 22) and would therefore be expected to reduce BP in patients with comorbid OSA and hypertension.

This pathophysiological rationale is supported by data from meta-analyses of randomized controlled trials (RCTs), which reported that the use of CPAP reduced 24-hour ambulatory SBP by 2–2.5 mm Hg (9, 23). However, these data come from studies with relatively short-term follow-up (mean, 15 wk [23]), and data collected during RCTs are also influenced by repeated interactions between participants and investigators during the studies. This limits the generalizability of the findings and might

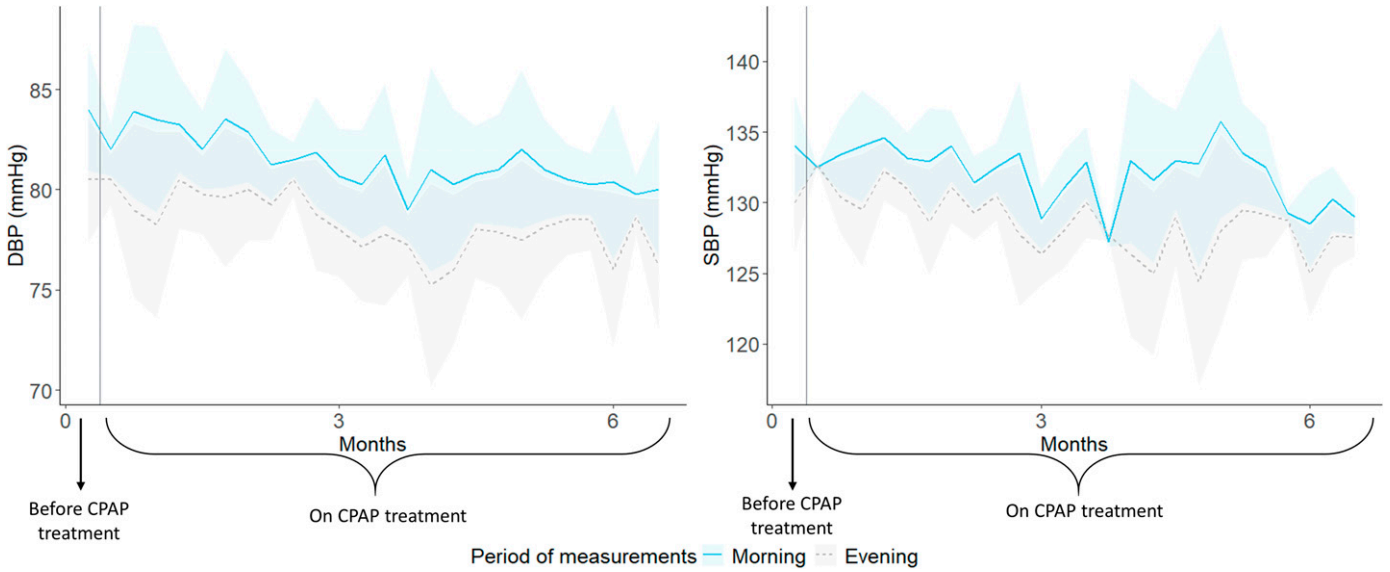

Figure 3. Progressive decrease and variations of median diastolic (left) and systolic (right) morning and evening home blood pressure values during the first 6 months of continuous positive airway pressure therapy. Shaded areas indicate the confidence interval. CPAP = continuous positive airway pressure; DBP = diastolic blood pressure; OSA = obstructive sleep apnea; SBP = systolic blood pressure.

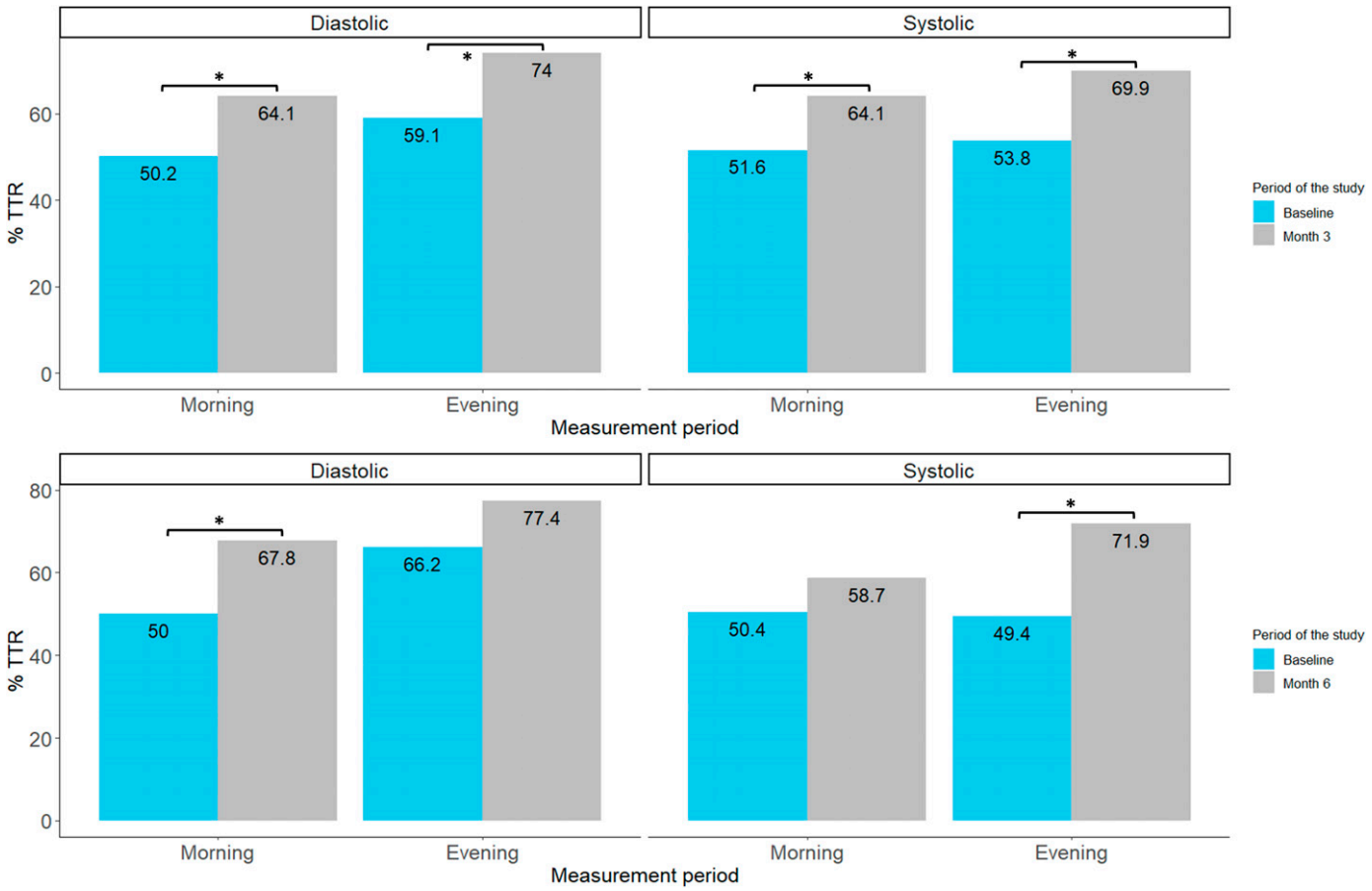

Figure 4. Time in therapeutic range (TTR) for diastolic and systolic morning and evening home blood pressure measurements after 3 months (top) and 6 months (bottom) of continuous positive airway pressure therapy. *Wilcoxon test; significant differences between the %TTR of each time period.

not reflect the real-life impact of CPAP on BP. Also, the RCTs collected BP data at specified sequential time points (usually before and after several months of CPAP therapy). This does not provide much granularity regarding the trajectories of the BP response to treatment with CPAP. In contrast, our analysis used thousands of HBPM values taken regularly during the first 6 months of therapy. The findings therefore indicate that CPAP therapy reduces home BP in real-life settings.

Another feature of our data is the separate reporting of morning and evening home BP values during CPAP. A morning BP increase is a classical pattern in patients with OSA due to the frequent non-dipping pattern of nocturnal BP in this population (24) and to elevated sympathetic tone in the early morning secondary to repeated acute surges in sympathetic activity and BP elevations that occur in association with repeated apneas and hypopneas during sleep (25). Our finding of consistently higher home BP values in the morning than the evening suggests that morning home BP is more difficult to control in people with OSA who are treated with CPAP. These data are clinically relevant, because morning BP is a strong predictor of stroke, major adverse cardiovascular events, and mortality (11, 26, 27).

Finally, our data confirm heterogeneous BP responses to CPAP in individuals with OSA. The question of which OSA phenotypes are more likely to have a positive response to CPAP has been addressed in previous meta-analyses (8, 9, 23). Baseline OSA severity and CPAP adherence are contributors to the variation in BP response during CPAP and were adjusted for in our analysis. Control of body weight and appropriate antihypertensive drug therapy are also expected modulators of the BP response to CPAP, and our findings are consistent with this. On that basis, there is significant interest in the use of combination therapies in this multimorbid population. In adults with obesity and OSA, the combination of CPAP with a weight-loss intervention resulted in incrementally greater reductions in BP than either intervention alone (28). Also, data from an RCT showed that valsartan and CPAP had a synergistic effect on BP compared with either intervention alone (29).

Limitations

Some limitations need to be considered when interpreting our findings. The study design was observational, without a control or comparator group, and therefore longitudinal changes in BP may have been influenced by other confounding factors (30, 31). This study was not designed to support causal inference. Therefore, the results represent associations rather than causal effects. Furthermore, the number of

Table 3. Predictors of the change in home blood pressure during the first 6 months of continuous positive airway pressure therapy using multivariate mixed-effect regressions

	Morning		Evening	
	β (95% CI)	*P* Value	β (95% CI)	*P* Value
Diastolic blood pressure				
Time, d	−0.15 (−0.42 to 0.12)	0.28	−0.27 (−0.65 to 0.11)	0.17
CPAP adherence, h/night	−0.07 (−0.18 to 0.04)	0.19	−0.05 (−0.18 to 0.08)	0.43
Age, yr*	1.68 (−0.09 to 3.44)	0.06	1.20 (−0.76 to 3.16)	0.23
Sex, female vs. male	−2.91 (−6.71 to 0.90)	0.13	−0.78 (−4.86 to 3.30)	0.71
Change in body weight, kg	0.20 (0.14 to 0.27)	<0.001	0.17 (0.10 to 0.25)	<0.001
History of hypertension, yes vs. no	1.44 (−1.99 to 4.87)	0.41	1.41 (−2.26 to 5.07)	0.45
Smoking status				
Former vs. current	−4.37 (−9.80 to 1.05)	0.11	−3.53 (−9.51 to 2.45)	0.25
Never vs. current	−5.30 (−10.45 to −0.14)	0.04	−6.57 (−11.99 to −1.15)	0.02
Baseline PSG ODI, events/h†	0.01 (−0.04 to 0.06)	0.80	0.02 (−0.04 to 0.08)	0.45
Systolic blood pressure				
Time, d	−0.12 (−0.62 to 0.39)	0.65	−0.57 (−1.13 to 0.00)	0.05
CPAP adherence, h/night	−0.05 (−0.20 to 0.11)	0.55	0.04 (−0.14 to 0.23)	0.67
Age, yr*	5.35 (2.99 to 7.71)	<0.001	3.51 (0.91 to 6.10)	0.01
Sex, female vs. male	−3.13 (−8.22 to 1.95)	0.23	−2.64 (−7.99 to 2.71)	0.33
Change in body weight, kg	0.38 (0.30 to 0.47)	<0.001	0.24 (0.14 to 0.35)	<0.001
History of hypertension, yes vs. no	5.00 (0.41 to 9.58)	0.03	5.23 (0.40 to 10.06)	0.03
Smoking status				
Former vs. current	−4.52 (−11.76 to 2.72)	0.22	−2.56 (−10.42 to 5.30)	0.52
Never vs. current	−4.07 (−10.95 to 2.80)	0.25	−3.78 (−10.89 to 3.34)	0.30
Baseline PSG ODI, events/h†	0.04 (−0.02 to 0.10)	0.22	0.07 (−0.01 to 0.16)	0.10

Definition of abbreviations: CI = confidence interval; CPAP = continuous positive airway pressure; ODI = oxygen desaturation index; PSG = polysomnography.
Mixed-effects regressions were performed with a random effect on patient (intercept and slope) and the time (in days) variable was scaled. Time is the variable of interest, whereas confounders included CPAP adherence, age, sex, change in body weight, history of hypertension, smoking status, and baseline PSG ODI variables.
*A 10-year increase in age was associated with an increase of 1.68 mm Hg in morning diastolic blood pressure and an increase of 1.20 mm Hg in evening diastolic pressure.
†An increase of 1 event/h in ODI was associated with an increase of 0.01 mm Hg in morning diastolic blood pressure and an increase of 0.02 mm Hg in evening diastolic blood pressure.

home BP readings decreased over time, reducing the statistical power of comparisons using 6-month follow-up data. This is consistent with previous studies of long-term home BP monitoring that have reported a loss of 16% of patients over 12 months of follow-up (32) and a loss of 30% and 38% of patients over 12 and 24 months of follow-up, respectively (33).

Conclusions

CPAP was shown to generally improve home BP trajectories over time, but the response was heterogeneous and less marked for morning home BP values. Based on the identified predictors of home BP reduction during CPAP, we suggest that weight control could play an important role in the management of patients with coexisting OSA and hypertension. Future studies should continue to use HBPM to monitor BP control in this specific population, who are at high risk of elevated morning BP values. Upcoming studies in the field would be wise to include HBPM among the outcomes. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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Online Data Supplement

Home blood pressure trajectories during 6 months of continuous positive airway pressure therapy

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Table E1. ICD-10 codes for comorbidities

	ICD-10 codes
Arrythmias	I440, I441, I442, I443, I444, I445, I446, I447, I450, I451, I452, I453, I454, I455, I456, I458, I459, I460, I461, I469, I470, I471, I472, I479, I48, I490, I491, I492, I493, I494, I495, I498, I499
Abnormal lipid profile	E780, E781, E782, E783, E784, E785, E786, E787, E788, E789
Cerebrovascular – disease, stroke	I210, I2100, I21000, I2108, I211, I2110, I21100, I2118, I212, I2120, I21200, I2128, I213, I2130, I21300, I2138, I214, I2140, I21400, I2148, I219, I2190, I21900, I2198,
Coronary heart disease	I220, I2200, I22000, I2208, I221, I2210, I22100, I2218, I228, I2280, I22800, I2288, I229, I2290, I22900, I2298, I230, I252
Type 2 diabetes	E110, E111, E112, E113, E114, E115, E116, E117, E118, E119, E120, E121, E122, E123, E124, E125, E126, E127, E128, E129, E130, E131, E132, E133, E134, E135, E136, E137, E138, E139, E14, E140, E141, E142, E143, E144, E145, E146, E147, E148, E149, E15, E160

Table E2. Values for imputed variables

	Before imputation	After imputation
Sex	No missing values	-
Age, years	No missing values	-
Change in body weight, kg	89.8 (77.4; 105.6) (8% missing values)	88.0 (77.4; 102.8)
History of hypertension	No missing values	-
Baseline ODI on PSG, events/h	17.2 (9.9; 39.3) (5% missing values)	18.5 (10.1; 40.9)
Smoking status	No missing values	-

Values are median (interquartile range).

ODI, oxygen desaturation index; PSG, polysomnography.

Table E3. Mean blood pressure values over time, depending on hypertension status at baseline

	Baseline	CPAP		
		1 month	3 months	6 months
Patients with hypertension at baseline				
Systolic blood pressure, mmHg				
Morning	139.9 ± 15.6	138.0 ± 13.6	136.1 ± 14.0*	131.5 ± 12.5*
Evening	137.0 ± 16.1	136.3 ± 17.2	133.8 ± 16.0*	122.2 ± 11.4*
Diastolic blood pressure, mmHg				
Morning	87.4 ± 11.0	85.0 ± 9.8	84.1 ± 10.3*	80.9 ± 12.3*
Evening	84.1 ± 11.5	80.5 ± 11.8*	80.8 ± 11.4*	69.6 ± 13.3*
Patients without hypertension at baseline				
Systolic blood pressure, mmHg				
Morning	130.5 ± 14.7	127.6 ± 14.3	125.2 ± 12.8*	116.0 ± 9.0*
Evening	129.3 ± 15.1	127.6 ± 15.1	124.5 ± 13.0*	127.5 ± NA
Diastolic blood pressure, mmHg				
Morning	84.9 ± 9.9	81.0 ± 10.4*	79.2 ± 10.0*	79.7 ± 6.5
Evening	81.6 ± 10.8	78.3 ± 10.4*	75.9 ± 9.3*	84.0 ± NA

Values are mean ± standard deviation.

*Wilcoxon test; P≤0.05 vs. baseline.

CPAP, continuous positive airway pressure; NA, not available (only 1 patient in the category).

Table E4. Predictors of the change in home blood pressure during the first 6 months of continuous positive airway pressure therapy using univariate mixed-effects regressions

	Morning		Evening	
	β (95% CI)	p-value	β (95% CI)	p-value
Diastolic blood pressure				
Time, days	–0.15 (–0.43; 0.12)	0.27	–0.31 (–0.69; 0.07)	0.11
CPAP adherence, h/night	–0.07 (–0.18; 0.04)	0.23	–0.05 (–0.18; 0.07)	0.43
Age, years*	-0.07 (–1.78; 1.64)	0.93	0.08 (–1.67; 1.82)	0.93
Sex, female vs. male	–5.48 (–9.00; -1.95)	<0.001	–3.66 (–7.41; 0.09)	0.06
Change in body weight, kg	0.21 (0.15; 0.26)	<0.001	0.18 (0.11; 0.24)	<0.001
History of hypertension, yes vs. no	3.75 (0.20; 7.29)	0.04	3.24 (–0.40; 6.89)	0.08
Smoking status				
Former vs. current	–3.71 (–9.04; 1.62)	0.17	–2.16 (–7.66; 3.35)	0.44
Never vs. current	–7.16 (–12.37; –1.95)	0.01	–6.59 (–11.97; –1.21)	0.02
Baseline PSG ODI, events/h**	0.03 (–0.03; 0.08)	0.30	0.04 (–0.02; 0.11)	0.15
Systolic blood pressure				
Time, days	–0.12 (–0.62; 0.38)	0.63	–0.61 (–1.18; -0.05)	0.03
CPAP adherence, h/night	–0.03 (–0.19; 0.13)	0.73	0.03 (–0.15; 0.22)	0.72
Age, years*	2.61 (0.25; 4.98)	0.03	1.91 (–0.43; 4.25)	0.11
Sex, female vs. male	–5.58 (–10.67; -0.49)	0.03	-4.56 (-9.64; 0.52)	0.08
Change in body weight, kg	0.38 (0.30; 0.46)	<0.001	0.26 (0.17; 0.36)	<0.001
History of hypertension, yes vs. no	9.88 (5.16; 14.60)	<0.001	8.49 (3.78; 13.21)	<0.001
Smoking status				
Former vs. current	–1.28 (–9.02; 6.45)	0.74	0.87 (–6.81; 8.55)	0.82
Never vs. current	–5.16 (–12.72; 2.40)	0.18	–3.53 (–11.03; 3.97)	0.36
Baseline PSG ODI, events/h**	0.08 (0.02; 0.15)	0.01	0.11 (0.03; 0.20)	0.01

Mixed-effects regressions were performed with a random effect on patient (intercept and slope) and the time (in days) variable was scaled.

*A 10-year increase in age was associated with a reduction of 0.07 mmHg decrease in morning diastolic blood pressure and a 0.08 mmHg increase in evening diastolic pressure.

**A 1-event/h increase in ODI was associated with a 0.03 mmHg increase in morning diastolic blood pressure and a 0.04 mmHg increase in evening diastolic blood pressure.

CI, confidence interval; CPAP, continuous positive airway pressure; ODI, oxygen desaturation index; PSG, polysomnography.

Table E5. Predictors of the change in home blood pressure during the first 6 months of continuous positive airway pressure therapy, using multivariate mixed-effect regressions stratified by hypertension status at baseline

	Morning		Evening	
	β (95% CI)	p-value	β (95% CI)	p-value
Patients with hypertension at baseline	**N = 54**		**N = 52**	
Diastolic blood pressure				
Time, days	–0.21 (–0.60; 0.19)	0.31	–0.29 (–0.82; 0.25)	0.30
CPAP adherence, h/night	–0.05 (–0.20; 0.10)	0.49	–0.16 (–0.33; 0.01)	0.06
Age, years*	2.42 (–0.37; 5.20)	0.09	1.61 (–1.28; 4.49)	0.27
Sex, female vs. male	–0.35 (–6.24; 5.54)	0.91	4.87 (–1.14; 10.88)	0.11
Change in body weight, kg	0.27 (0.18; 0.36)	<0.001	0.22 (0.12; 0.32)	<0.001
Smoking status				
Former vs. current	–5.13 (–12.70; 2.44)	0.18	–5.55 (–13.38; 2.27)	0.16
Never vs. current	–7.97 (–15.04; –0.91)	0.03	–11.99 (–19.30; –-4.67)	<0.001
Baseline PSG ODI, events/h**	0.00 (–0.06; 0.06)	0.94	0.00 (–0.06; 0.07)	0.96
Systolic blood pressure				
Time, days	–0.07 (–0.83; 0.69)	0.86	–0.63 (–1.45; 0.19)	0.13
CPAP adherence, h/night	–0.10 (–0.32; 0.12)	0.36	-0.11 (–0.37; 0.15)	0.41
Age, years*	7.50 (3.69; 11.31)	<0.001	5.28 (1.36; 9.21)	0.01
Sex, female vs. male	0.12 (–7.91; 8.15)	0.98	1.45 (–6.56; 9.47)	0.72
Change in body weight, kg	0.52 (0.40; 0.65)	<0.001	0.27 (0.12; 0.43)	<0.001
Smoking status				
Former vs. current	–7.88 (–18.18; 2.41)	0.13	–5.94 (–16.39; 4.52)	0.27
Never vs. current	–7.62 (–17.24; 2.01)	0.12	–7.91 (–17.68; 1.86)	0.11
Baseline PSG ODI, events/h**	0.02 (–0.05; 0.10)	0.56	0.05 (–0.05; 0.15)	0.34

Patients without hypertension at baseline	N = 42		N = 41	
Diastolic blood pressure				
Time, days	–0.08 (–0.45; 0.29)	0.66	–0.31 (–0.88; 0.25)	0.28
CPAP adherence, h/night	–0.11 (–0.28; 0.06)	0.20	0.11 (–0.08; 0.30)	0.26
Age, years*	1.20 (–1.14; 3.54)	0.31	0.96 (–1.56; 3.48)	0.46
Sex, female vs. male	–5.54 (–10.66; -0.41)	0.03	–5.24 (–10.17; -0.32)	0.04
Change in body weight, kg	0.14 (0.05; 0.23)	<0.001	0.12 (0.01; 0.22)	0.03
Smoking status				
Former vs. current	–1.57 (–10.38; 7.25)	0.73	–1.56 (–10.52; 7.40)	0.73
Never vs. current	–1.20 (–9.79; 7.39)	0.78	–2.78 (–10.49; 4.93)	0.48
Baseline PSG ODI, events/h**	0.05 (–0.05; 0.16)	0.32	0.10 (0.00; 0.20)	0.05
Systolic blood pressure				
Time, days	–0.17 (–0.82; 0.48)	0.61	–0.57 (–1.37; 0.23)	0.16
CPAP adherence, h/night	0.04 (–0.18; 0.26)	0.74	0.25 (–0.01; 0.51)	0.06
Age, years*	3.11 (-0.03; 6.26)	0.05	0.88 (-2.44; 4.19)	0.61
Sex, female vs. male	-6.93 (–13.82; -0.03)	0.05	–5.34 (–11.84; 1.15)	0.11
Change in body weight, kg	0.20 (0.09; 0.32)	<0.001	0.20 (0.06; 0.34)	<0.001
Smoking status				
Former vs. current	2.69 (–9.15; 14.53)	0.66	5.59 (–6.14; 17.31)	0.35
Never vs. current	0.50 (–11.03; 12.04)	0.93	1.22 (–8.86; 11.30)	0.81
Baseline PSG ODI, events/h**	0.11 (–0.03; 0.25)	0.11	0.10 (–0.03; 0.24)	0.12

Mixed-effects regressions were performed with a random effect on patient (intercept and slope) and the time (in days) variable was scaled. Time is the variable of interest, while confounders included CPAP adherence, age, sex, change in body weight, history of hypertension, smoking status, and baseline PSG ODI variables.

*A 10-year increase in age was associated with a 2.42 mmHg increase in morning diastolic blood pressure and a 1.61 mmHg increase in evening diastolic pressure for the analysis of patients with hypertension at baseline.

**A 1-event/h increase in ODI was associated with a 0.02 mmHg increase in morning diastolic blood pressure and a 0.05 mmHg increase in evening diastolic blood pressure for the analysis of hypertension at baseline.

CI, confidence interval; CPAP, continuous positive airway pressure; ODI, oxygen desaturation index; PSG, polysomnography.

Figure E1. Graphical representation of methodology used to determine blood pressure (BP) time in therapeutic range (TTR) during continuous positive airway pressure (CPAP) therapy (example is for diastolic blood pressure)

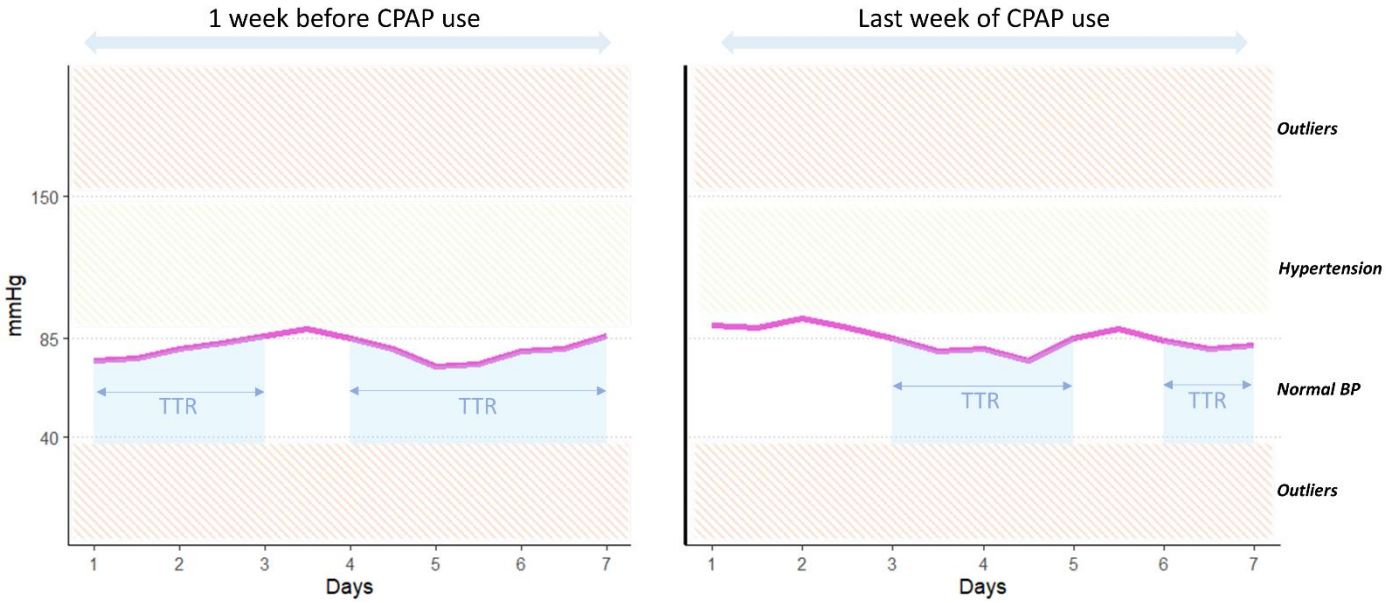
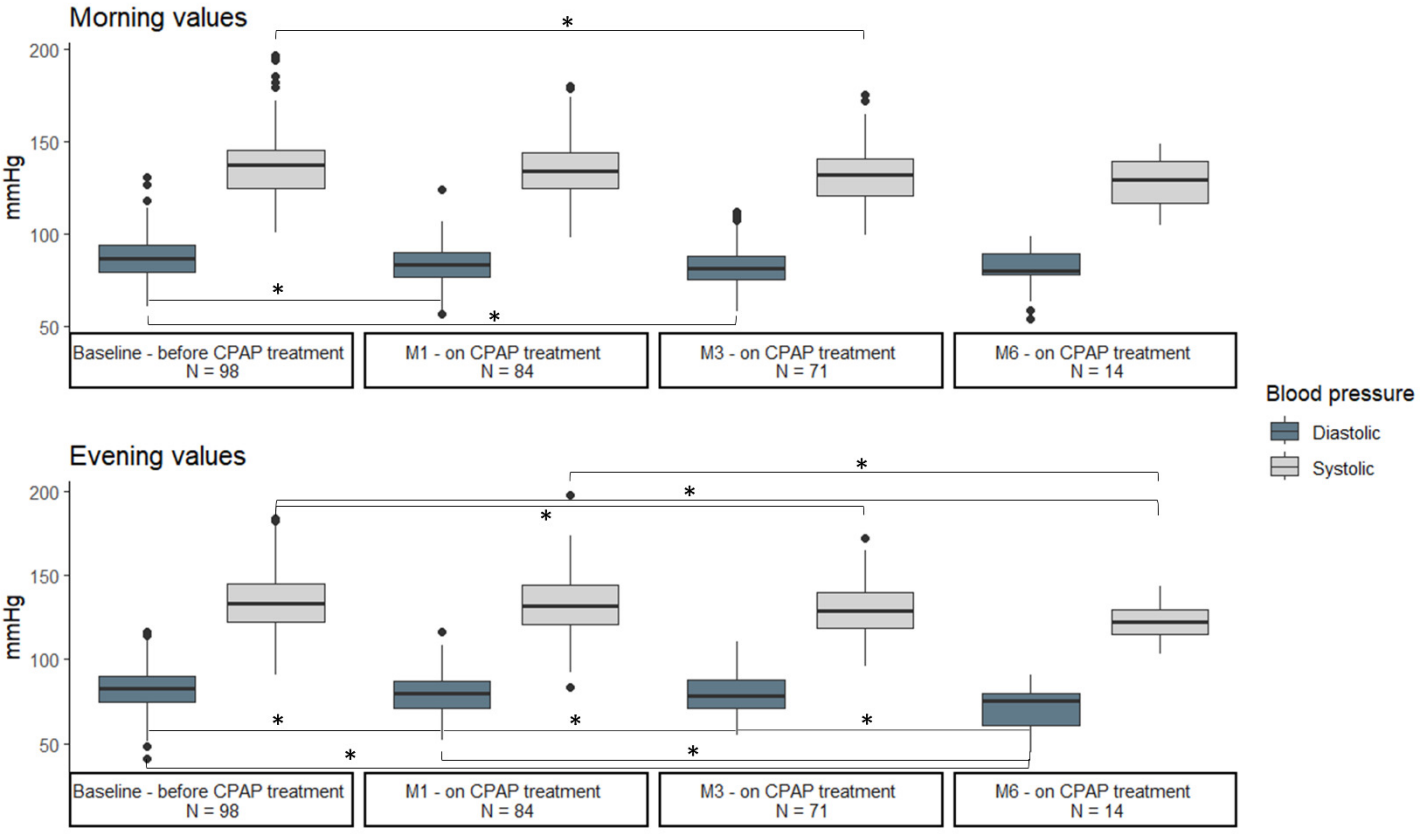
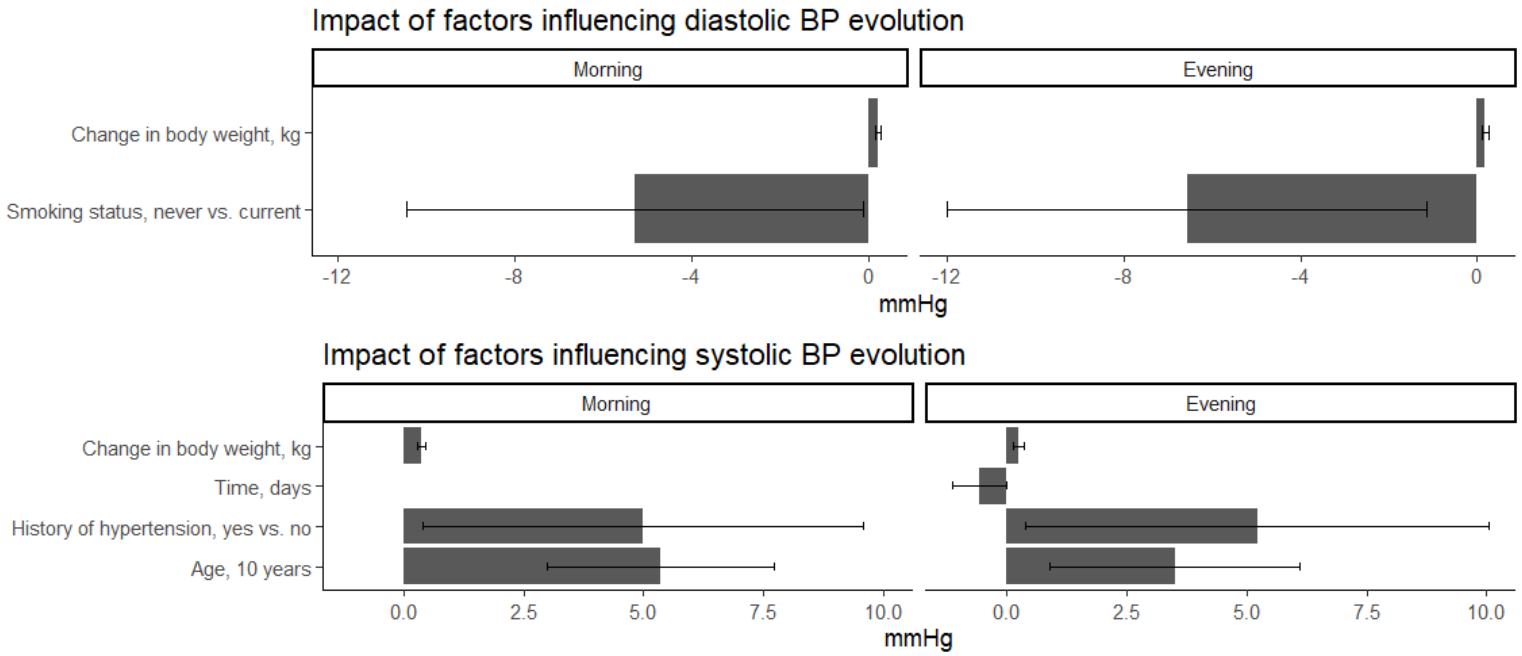


Figure E2. Diastolic and systolic home blood pressure (BP) evolution over the first 6 months of continuous positive airway pressure (CPAP) therapy



**Wilcoxon test corrected by Benjamini & Hochberg method; significant differences (p≤0.05) between each time period.*

Figure E3. Factors that had a significant (p≤0.05) influence on the change in home diastolic and systolic blood pressure (BP) in patients with obstructive sleep apnea during the first 6 months of continuous positive airway pressure therapy



Mixed-effects regressions were performed with a random effect on patient (intercept and slope) and the time (in days) variable was scaled.

VI. Hétérogénéité de la réponse au traitement par PPC en termes de pression artérielle selon la somnolence perçue au moment du diagnostic – Lettre de recherche acceptée n°2

Introduction

Un des principaux symptômes du SAOS est la somnolence qui est associée à un risque plus élevé de survenue d'événements cardiovasculaires incidents[49,102,104] et une meilleure réponse à la PPC pour la réduction de ces événements cardiovasculaires [103]. L'hypothèse est que cette réduction plus significative pourrait être médiée par une meilleure réduction de la pression artérielle sous PPC chez ces patients somnolents. Cependant, la plupart des essais randomisés contrôlés ont essentiellement inclus de patients non-somnolents comme le montre une méta-analyse récente sur les effets de la pression artérielle lorsque le patient est sous traitement PPC[86].

Objectifs

L'objectif de cette lettre de recherche est de déterminer si l'évolution de la pression artérielle systolique et diastolique du matin et du soir mesurée en automesures à domicile, chez des patients atteints d'un SAOS, traités par PPC, était influencée par le statut somnolent du patient avant l'initiation du traitement.

Méthodes

Les données utilisées proviennent des deux cohortes observationnelles prospectives, e-Meuse (Verdun, France) et Sleep Connect (Lille et Grenoble, France), précédemment détaillées. Les patients inclus devaient souffrir d'un SAOS, avoir complété le questionnaire du score d'ESS au diagnostic, avoir réalisé au moins une automesure de pression artérielle et avoir au moins une mesure d'observance à la PPC au cours des 3 premiers mois de traitement.
Le questionnaire du score d'ESS est un questionnaire subjectif de 8 questions appréciant la tendance à somnoler en journée et où la réponse à chaque question est une échelle de 0 à 3. Lorsque le score d'ESS est supérieur à 10, le patient est considéré comme somnolent[49,53,153].
Une stratification des données de PA selon le statut somnolent du patient à l'initiation du traitement a été réalisée en amont des analyses d'évolution de la PA au cours du temps. Afin de comparer les automesures de pression artérielle systolique et diastolique du matin et du soir entre avant traitement et les 4ème et 12ème semaines de traitement, des tests statistiques ont été réalisés (Wilcoxon et ANOVA). Ensuite, un modèle linéaire mixte ajusté, sans stratification de la population, a été effectué afin de déterminer si le temps de traitement, le statut somnolent au diagnostic, l'observance à la PPC, l'âge, le sexe, le poids au cours des 3 mois d'étude, les antécédents d'hypertension, le statut tabagique et l'indice de désaturation en oxygène impactaient l'évolution des pressions artérielles.

Résultats

98 patients ont été inclus dans cette étude, avec une répartition des patients somnolents versus non-somnolents au diagnostic plutôt équilibré puisque 42 patients étaient somnolents contre 56 non-somnolents. Les patients SAOS non-somnolents étaient plus âgés avec plus de SAOS sévère par rapport aux patients somnolents. Il n'y avait cependant pas de différence significative en termes de comorbidités et de traitements ni en termes d'observance à la PPC. Avant traitement, les mesures de pression artérielle systolique du matin et du soir étaient plus élevées chez les non-somnolents par rapport aux somnolents. De plus, les trajectoires d'évolution de pression artérielle sous PPC différaient entre les deux groupes de patients, i.e. la pression artérielle systolique et diastolique du matin et du soir décroissaient de manière plus significative après 1 et 3 mois de traitement chez les non-somnolents. Seule la pression artérielle diastolique du matin décroissait à 3 mois de traitement chez les patients somnolents. Enfin, le délai depuis l'initiation de la PPC, l'observance à la PPC et le sexe (les femmes) étaient associés à une réduction plus significative de la pression artérielle. Un gain de poids, les fumeurs réguliers, les patients plus âgés et ayant des antécédents d'hypertension montraient plutôt une augmentation de la pression artérielle. La réduction de la pression artérielle au cours du temps était également significativement plus élevée chez les non-somnolents comparés aux patients somnolents.

Cette lettre de recherche a été acceptée par Annals of ATS en mars 2026 et a été présentée sous forme d'un poster au congrès du sommeil en 2025.

Perspectives

Nos résultats suggèrent que la réponse à la pression artérielle après initiation de la PPC est hétérogène, survient préférentiellement chez les SAOS non somnolents au diagnostic et est plus limitée pour la pression artérielle du matin. D'autre facteurs d'évolution de la pression artérielle mériteraient d'être explorés comme la variabilité de la sévérité du SAOS d'une nuit à l'autre et l'impact de la maladie résiduelle. Certains patients gardent un indice d'événements résiduels sous PPC élevé et cela pourrait limiter l'amélioration de la pression artérielle. A notre connaissance, aucune association entre IAH résiduel et somnolence ou réponse en termes de pression artérielle, n'a été étudiée.

Article

Research Letter

Home blood pressure trajectories during 3 months of continuous positive airway pressure therapy in sleepy vs. non-sleepy patients *Running title: Home blood pressure, sleepiness and CPAP therapy*

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Author contributions: OC, SB, JLP developed the study concepts, performed the data analysis and drafted the manuscript, MJF, R. Tamisier, KA, JCC, TG, R. Terrail performed the data collection, OC, SB, CC, CL, MFP, GP provided insight on data interpretation and contributed to the final version of the manuscript and all authors contributed to the reviewing of the manuscript.

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Descriptor: 15.8 Sleep Disordered Breathing: Management

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To the editor:

We have recently published in the present journal[1] that continuous positive airway pressure (CPAP) improves home blood pressure (HBP) trajectories during the first 6 months after CPAP initiation. The response was heterogeneous and less marked for morning HBP values. The predictors of BP response during CPAP therapy included age, hypertensive status, weight control and CPAP adherence. Excessively sleepy patients with OSA have been demonstrated to be more likely to exhibit incident cardiovascular events[2,3]. In observational cohort studies, a reduction in MACEs was observed with CPAP use >6 h and risk reduction was even stronger in excessively sleepy patients[4]. This reduction in major cardiovascular events might be mediated by a greater reduction in blood pressure under CPAP in the excessively sleepy subtype. A recent individual patient data (IPD) meta-analysis of the BP effects of OSA treatment with CPAP did not question sleepiness at diagnosis as a predictor of BP responses. This is essentially explained by the fact that the majority of RCTS have been conducted in non-sleepy patients. Here, we investigated in the cohort previously published[1], the OSA subgroups with or without sleepiness to depict their respective HBP trajectories

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in the first 3 months after CPAP therapy initiation based on repeated longitudinal measurements of home BP.

Methods

Patients from two observational prospective cohorts (E-Meuse, NTC04963192 and Sleep Connect, NTC04054180) suffering from OSA were included in the study[1]. Patients were recruited and were selected if they completed baseline questionnaires, performed at least one HBP measurement and had one CPAP adherence measurement.

Questionnaires provided information on patient symptom profile and their baseline ESS score (sleepy patient having an ESS score > 10 [5,6]). Using validated automated oscillometric BP monitors, patients were instructed to provide 3 morning and 3 evening HBP self-measurements each day for the 7 days prior to CPAP initiation (baseline) and during the 3 months of CPAP treatment. Finally, CPAP device by telemonitoring provided CPAP adherence information[1].

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To compare HBPM between baseline and the weeks preceding the 1st and 3rd month, Wilcoxon and ANOVA tests were performed following by Benjamini & Hockberg method to correct p-values from multiple tests. Mixed adjusted linear regressions with a random effect on patients were performed to determine the factors affecting BP evolutions[1]. Data analyses were conducted with R-4.3.0 and a threshold of 0.05 corresponded to significant results.

Results

Overall, 98 OSA patients roughly equally divided in sleepy (n=42, median [interquartile range (IQR)] ESS score = 14 [12; 16]) and non-sleepy (n=56, median [IQR] ESS score = 6 [3; 8]) OSA were included. Non-sleepy OSA were older (median [IQR] age 60 [52; 68] years vs. 51 [47; 59] years, $p<0.01$) with more severe OSA metrics at diagnosis (median [IQR] ODI 33 [11; 49] events/h vs. 14 [10; 28] events/h, $p=0.01$; and median AHI 41 [32; 57] events/h vs. 31 [24; 42] events/h, $p<0.01$). No significant difference ($p>0.05$) was observed in terms of comorbidities and drug's treatments. CPAP adherence was also similar between groups, with a median of approximately 3.5

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h/night. At baseline, systolic morning and evening HBP measures were significantly higher in non-sleepy vs. sleepy patients (Table 1).

Home BP trajectories after CPAP initiation differed between sleepy and non-sleepy OSA. Compared to the 1st week of measurements before CPAP initiation, morning and evening diastolic and systolic HBP significantly decreased after 1st and 3rd month of CPAP therapy in non-sleepy patients (Figure 1) (-3.7 mmHg and -5.7 mmHg for morning diastolic BP, -3.6 mmHg and -7.6 mmHg for morning systolic BP, -4.0 mmHg and -5.6 mmHg for evening diastolic BP and -6.9 mmHg for evening systolic BP at 3 months; all $P<0.05$). The only significant decrease in HBP in sleepy patients was a -3.4-mmHg reduction in morning diastolic BP at three months.

In mixed adjusted linear regressions model, time of exposure to CPAP, CPAP adherence and sex (women) were significantly associated with a greater reduction in HBP. Weight gain over the 3 months, current smoking, older age and history of hypertension were associated with an increase in HBP. This adjusted analysis showed that HBP reduction overtime was significantly higher in non-sleepy compared to sleepy OSA patients (Figure 2).

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Discussion

This study mainly showed that beyond classical predictors of BP response in CPAP-treated OSA such as age, sex, weight gain, CPAP adherence, smoking status, and history of hypertension, sleepiness at diagnosis plays a major role.

When targeting OSA-related hypertension, response to CPAP is heterogeneous and a better characterization of relevant influencing factors is crucial for improving cardiovascular risk management in OSA. A recent worldwide individual patient data meta-analysis[7] using RCTs data only identified age and uncontrolled hypertension as significant predictors of BP response to CPAP. Our data provides a new perspective by including sleepy OSA underrepresented in RCTs that were embarking for ethical reasons only minimally symptomatic individuals. There are very few studies addressing the question of different BP responses in sleepy versus non-sleepy OSA. To our best knowledge, the only study available is a retrospective observational work[8] suggesting that higher median sleepiness score (ESS ≥8) is not significantly associated with a difference in BP response compared with those with a lower sleepiness score.

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Outside the OSA field, sleepiness is generally considered as associated with higher blood pressure values [9,10] . Sleepiness in OSA is linked with higher levels of sympathetic activity[11], reduced baroflex sensibility[12] and systemic inflammation[13] that might explain higher blood pressure levels at baseline. Nevertheless, high sympathetic activity has been shown to be inversely correlated with sleepiness[14]. CPAP improves subjective sleepiness, but no changes are observed in inflammatory biomarkers[13,15]. One might speculate that persistent inflammation in this population sleepy at baseline is mitigating BP response to CPAP.

Our analysis has strength and limitations. Prospective data collection using multiple longitudinal home self-measurement of BP over six months is unique. The limitations are sleepiness assessment which was limited to subjective evaluation and relatively low sample size.

In conclusion, our results might have important implications for the decision on how to best manage arterial hypertension associated with OSA depending on sleepiness status at baseline.

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Tables

Table 1: Diastolic and systolic BP evolution over the first 3 months of measurements according to baseline sleepiness score

	Week 1	*Month 1*	*Month 3*
Non-sleepy patients	N = 56	N = 46	N = 40
Systolic (mmHg)			
Morning	138.2 (128.5; 145.8)	134.1 (125.3; 142.5)	129.4 (121.3; 138.5)
Evening	135.1 (125.0; 145.8)	131.5 (122.0; 143.5)	126.5 (118.5; 137.5)
Diastolic (mmHg)			
Morning	86.8 (79.2; 94.0)	83.0 (76.2; 88.9)	79.8 (74.2; 86.6)
Evening	82.1 (74.6; 91.5)	78.8 (71.2; 87.0)	77.0 (70.5; 82.4)
Sleepy patients	N = 42	N = 38	N = 31
Systolic (mmHg)			
Morning	134.2 (118.8; 145.0)	132.9 (122.8; 144.9)	134.5 (120.0; 142.3)
Evening	129.8 (118.4; 143.1)	133.2 (117.4; 144.2)	130.9 (119.1; 145.5)
Diastolic (mmHg)			
Morning	85.7 (78.2; 93.5)	83.5 (77.4; 90.2)	82.1 (76.4; 88.0)
Evening	83.2 (74.2; 89.8)	81.0 (70.3; 87.6)	79.6 (72.3; 88.9)

Non-sleepy patients had an ESS score ≤10 while sleepy patients had an ESS score >10. Morning and evening diastolic and systolic home BP monitoring data were evaluated the week before CPAP treatment (week 1), the week preceding the 1st month (Month 1) and the 3rd month (Month 3) of CPAP use. Median (Q1; Q3) was then assessed for each time point for sleepy group (ESS score > 10) and non-sleepy group (ESS score ≤ 10).

Abbreviations: BP: blood pressure, ESS: Epworth sleepiness scale, Q1: 1st quantile, Q3: 3rd quantile

Figures

Figure 1: Differences in means between diastolic and systolic HBP values over the first 3 months

Mean of HMBP values measured in the week preceding CPAP month 1 (M1) and month 3 (M3) compared to the week preceding CPAP initiation. An ANOVA test was performed to compare the evolution between the 3 time periods including the difference of the mean between these periods and a Wilcoxon test was performed to compare the evolution 2 by 2 of the time periods.

To correct the P values of the multiple tests, the Benjamini & Hochberg method was applied.
* Significant differences between each time period.
Abbreviations: ANOVA: analysis of variance, BP: blood pressure, CPAP: continuous positive airway pressure, ESS: Epworth sleepiness scale, HBPM: home blood pressure monitoring.

Figure 2: BP evolution over time based on patients' sleepiness status using a mixed regression model

Sleepy patients were patients with baseline ESS score >10, indicated by the logo depicting a sleeping figure.
Mixed linear regressions adjusted on CPAP adherence, age, sex, weight over 3 months, history of hypertension, smoking status, baseline polysomnography oxygen desaturation index.
The initial value for ESS was not significantly associated to home blood pressure for DBP and SBP in morning and evening: initial values are similar for both groups.
The Beta coefficient showed in the Figure are the sum of the regression coefficients for time effect, the baseline ESS status and interaction between time effect and baseline ESS status. The symbol * corresponds to significant pvalues for interaction terms. As for example, for morning diastolic blood pressure, there was no significant association between baseline ESS status and DBP over time. Conversely for SBP (morning and evening) and DBP (evening) there was a significant interaction showing a significant decrease for non-sleepy patients compared to sleepy patients as showed by the final Beta regression coefficient.
Abbreviations: BP, blood pressure; CI, confidence interval; ESS, Epworth sleepiness scale.

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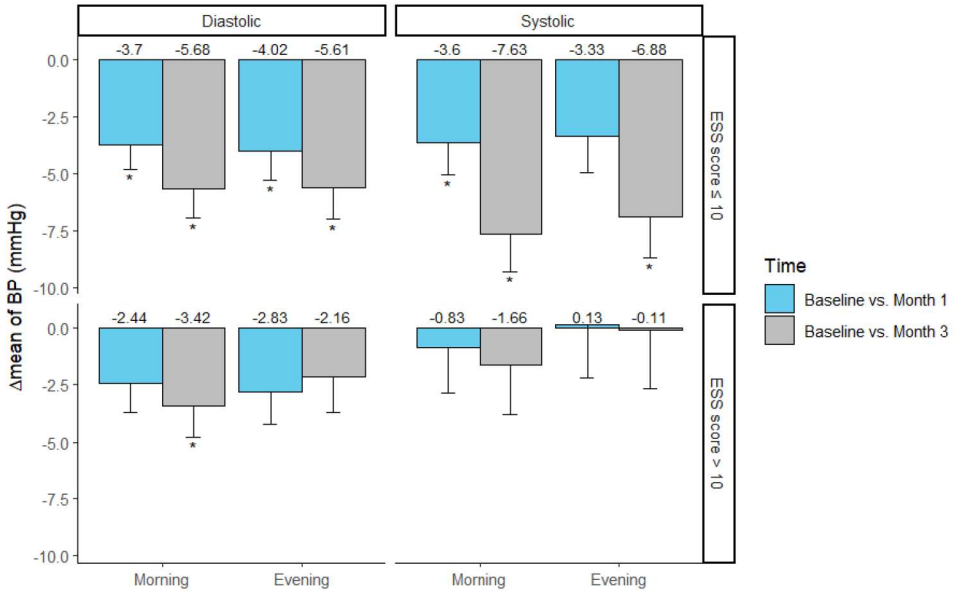

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* Significant differences between each time period.
Abbreviations: ANOVA: analysis of variance, BP: blood pressure, CPAP: continuous positive airway pressure, ESS: Epworth sleepiness scale, HBPM: home blood pressure monitoring.

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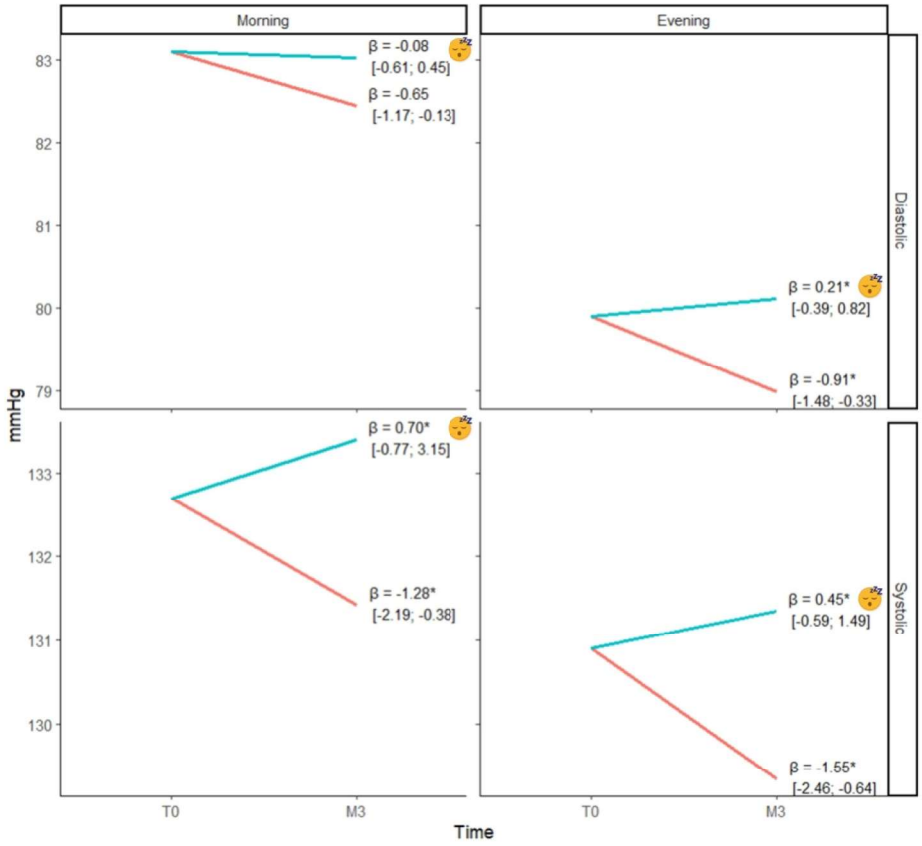

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Abbreviations: BP, blood pressure; CI, confidence interval; ESS, Epworth sleepiness scale.

217x189mm (300 x 300 DPI)

VII. Conclusion générale et perspectives

Cette thèse a permis à la fois de produire des données originales et de tracer des perspectives de recherche dans différents domaines (Figure 13) :

Hétérogénéité du SAOS et caractérisation multidimensionnelle des symptômes.

Cette stratégie de recherche et de collecte de données pourra être déployée pour des phénotypes particuliers du SAOS comme par exemple, le COMISA (coexistence d'un SAOS et d'insomnie chronique comorbide)[161–164], les SAOS chez des patients obèses comparés aux patients non obèses[165,166] ou pour définir précisément les phénotypes respectifs des syndromes d'apnées centrales du sommeil par rapport aux syndromes d'apnées obstructives ou co-existant du sommeil[167,168]. Une perspective de ces travaux serait de proposer et de valider des questionnaires spécifiques au contexte de diagnostic du SAOS en fonction des associations comorbides (overlap entre deux ou plusieurs maladies chroniques). Ce phénotypage multidimensionnel pourra également inclure les données issues d'autres objets connectés comme les montres (sommeil et activité physique) ou les balances connectées permettant une meilleure caractérisation des comorbidités et de leur évolution sous traitement. Ceci ouvrirait la voie à une nouvelle caractérisation du SAOS et des réponses au traitement en clinique.

Importance du choix de la méthode statistique et de la prise en compte de la variabilité des mesures au cours du suivi dans l'analyse de données longitudinales.

La prise en compte de la variabilité des mesures au cours du temps, et en particulier les arrêts, permettra de mieux identifier les profils de patients susceptibles d'arrêter leur PPC et ceux pouvant reprendre secondairement leur traitement (CPAP resumption)[21,76,80,169]. L'implémentation de ces approches dynamiques ouvre comme perspective la possibilité de proposer des algorithmes de prédiction de l'observance à la PPC des patients en s'appuyant à la fois sur leur profil clinique au diagnostic et sur les données de télémonitoring collectées en début de traitement[81]. L'objectif final étant de réaliser un suivi adapté au cours du temps avec, en particulier, un suivi plus intense chez les patients ayant un fort risque d'abandon de la PPC.

L'implémentation de méthodes d'analyse appropriées des données longitudinales permettra également de mieux comprendre l'impact temps-dépendant de l'utilisation de la PPC et sa relation avec les différents pronostics des patients (mortalité, événements cardiovasculaires). La variabilité de l'exposition effective au traitement, qui est temps-dépendante, est actuellement mal caractérisée dans la littérature. L'exposition au traitement est souvent résumée à l'observance à proximité du recueil des outcomes ou à une mesure agrégée sur une période de suivi (moyenne par exemple), ce qui correspond à un résumé imparfait de l'exposition au traitement pendant les mois ou années de suivi.

Une autre perspective est de mieux analyser les interactions longitudinales entre les différents paramètres physiologiques collectés au cours du temps. On peut citer en exemple l'étude de l'interaction dynamique de la PPC avec la pression artérielle, la variabilité glycémique des 24 heures, l'activité physique, etc.

Caractérisation de la réponse en termes de la pression artérielle à l'initiation d'un traitement par PPC.

Cette technique de recueil des données et de suivi de la PA par automesures à domicile pourrait être installée comme un standard de soin dans le suivi du SAOS en particulier chez les patients traités par PPC. Les recommandations internationales orientent de plus en plus les professionnels de santé vers cette technique jugée performante et ayant de nombreux avantages (facilité d'emploi, fiabilité des mesures, etc.) mais la documentation est trop limitée dans le cadre du SAOS et il existe trop peu de données pour établir définitivement l'automesure à domicile comme recommandation pour un suivi de la PA des patients[144,145]. Les recommandations ne s'appliquent pas spécifiquement aux patients atteints de SAOS et/ou somnolents traités par PPC, mais s'appliquent plus généralement aux patients hypertendus.

Notre travail de thèse a également soulevé un questionnement sur la fenêtre horaire de la prise d'antihypertensifs au cours du SAOS. En effet, parmi les patients diagnostiqués comme hypertendus, un fort pourcentage d'entre eux ne sont pas contrôlés pour leur hypertension en particulier matinale. Il serait donc important de construire un essai randomisé contrôlé pour définir le meilleur horaire pour la prise d'antihypertensifs chez les patients atteints de SAOS traités par PPC. La littérature porte principalement sur les effets de l'horaire de la prise de ces médicaments sur la réduction de la PA nocturne mais ne conclut pas sur la réduction de la PA matinale[170–172].

Notre travail sur l'évolution de la PA en fonction du statut somnolent des patients à l'inclusion montre la nécessité d'études supplémentaires sur l'impact d'autres facteurs pouvant limiter ou favoriser la réduction de la PA sous PPC comme les symptômes résiduels (par exemple la somnolence[173]) ou le SAOS résiduel à travers la variabilité de l'IAH résiduel[92]. L'objectif final étant d'optimiser le monitoring et le traitement de l'hypertension dans le cadre de la prise en charge du SAOS.

Pour conclure, cette thèse propose un rationnel solide pour développer une thématique de recherche sur l'intérêt d'une caractérisation et d'un monitoring multidimensionnel du SAOS via l'utilisation d'objets connectés et l'installation d'une médecine numérique et digitale du SAOS en s'appuyant sur une méthodologie robuste.



Figure 13. Conclusions de la thèse et perspectives d'études

Les conclusions et contributions de la thèse correspondent aux textes bleu clair, les perspectives d'études possibles correspondent aux textes bleu acier et les objectifs finaux correspondent aux textes bleu foncé.

Abréviations : COMISA : syndrome d'apnées du sommeil et insomnie chronique comorbide, PA : pression artérielle, PPC : pression positive continue, SAS : syndrome d'apnées du sommeil, SAOS : syndrome d'apnées obstructives du sommeil

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