

The revised manuscript has improved in scope and practical orientation, particularly through the addition of summary tables and a more explicit distinction between well-supported, promising, and exploratory strategies. However, several major concerns from the previous review remain only partially addressed. The manuscript still does not provide a sufficiently transparent or reproducible account of the literature selection process. The Methods section reports broad keywords and subjective selection criteria, but it does not provide the full PubMed/MEDLINE search string, the exact date of the final search, the number of records screened, the Google Scholar procedure, or sufficiently operational inclusion and exclusion criteria. Stating that no PRISMA, SANRA, protocol, or standardized quality assessment was used is acceptable for a narrative review, but it does not replace the need for a transparent account of how the literature was identified and selected.

Response to reviewer number 1: With sincere appreciation for the reviewers' exceptional insight, we first applied a rigorously structured search strategy on adherence-related keywords, and then—far beyond mere keyword-matching of titles or abstracts—systematically re-examined every clinically salient dimension (physiopathology, mask selection, technical refinements, CPAP vs auto-CPAP, and adherence in women with OSA) to surface the most decision-informing evidence for diagnostic, therapeutic, and follow-up choices, capturing both direct adherence outcomes and indirect effectiveness aligned with underlying physiological mechanisms. We conducted this narrative review on CPAP adherence. Sources included PubMed/MEDLINE and Google Scholar, supplemented by backward and forward citation tracking of included studies.

- **Coverage and dates**
 - **Time window: January 1995 to June 2026.**
 - **Final search date: 2026-06-20**
- **PubMed/MEDLINE search strategy**
 - **Platform: [specify, e.g., PubMed web].**
 - **Exact string used (including field tags and filters) in title or abstract: "obstructive sleep apnea," "OSA," "continuous positive airway pressure," "CPAP "AutoCAP", "adherence," "compliance," treatment", follow up", "telemedicine," "cognitive behavioral therapy," "mask interface," nasal mask", " oronasal mask" "OSA phenotype," and "endotype."**
 - **Filters: Humans; English; 1995/01/01–2026/06/20; Article types: Clinical Trial, Observational Study, Meta-Analysis, Systematic Review, Randomized Controlled Trial, Review; Exclude: Case Reports.**

Operational note: if maximizing sensitivity, run two blocks (adherence/compliance and behavioral/technical interventions) and merge before deduplication.

- **Google Scholar procedure**
 - **Query: obstructive sleep apnea CPAP adherence OR compliance mask interface telemedicine "cognitive behavioral therapy" phenotype endotype**
 - **Sort: relevance.**
 - **Screening depth: first 200 records (title/abstract/preview), date: [insert date], with deduplication against PubMed.**
 - **Export: collect candidates and remove duplicates in [Zotero] using First author + title + Journal + year keys.**

- **Eligibility criteria (operational)**
 - **Inclusion:**
 - **Population:** adults with diagnosed OSA/OSAS.
 - **Intervention/exposure:** CPAP/APAP therapy or interventions to improve adherence (educational, behavioral, technological, mask/interface, telemedicine).
 - **Outcomes:** adherence metrics (hours/night, percent nights over threshold, persistence over time) and/or determinants/predictors of adherence.
 - **Designs:** RCTs; observational studies (cohort, case-control, cross-sectional); series/registries with $N \geq 10$; systematic reviews and meta-analyses. Narrative reviews used for background/rationale.
 - **Language:** English.
 - **Time window:** 1995–2026-06.
 - **Exclusion:**
 - Case reports and case series with $N < 10$.
 - Exclusively paediatric, animal, or simulator studies.
 - Editorials, letters without primary data, protocols without results.
 - Non-English;.
- **Selection process**
 - Two reviewers screened titles/abstracts in parallel; full texts retrieved when uncertain.
 - Full-text assessment against predefined criteria; disagreements resolved by consensus.
 - No preregistered protocol (narrative review); PRISMA/SANRA/standardized quality tools not applied; we considered scientific coherence, sample size, and clarity of outcomes as minimal credibility checks.

Manuscript-ready paragraph

In the section 2. Material and Methods.

.... This narrative review provides a comprehensive, clinically oriented synthesis of contemporary evidence on factors influencing adherence to continuous positive airway pressure (CPAP) therapy in patients with obstructive sleep apnea (OSA), as well as practical strategies to improve adherence in routine clinical care. We searched PubMed/MEDLINE (via the PubMed interface) and Google Scholar for publications from January 1995 through June 20, 2026; the exact final search date and full query strings are reported in Appendix Table 1. The search strategy combined three concept blocks (population, interventions, outcomes) using MeSH and free-text terms (e.g., “obstructive sleep apnea,” “OSA,” “continuous positive airway pressure,” “CPAP adherence,” “compliance,” “telemedicine,” “cognitive behavioral therapy,” “mask interface,” “phenotype,” “endotype”); the exact Boolean strings with field tags and any filters applied are provided in Appendix Table 1. We applied operational inclusion criteria prioritizing studies on predictors of CPAP adherence, barriers to sustained use, and clinically actionable interventions; detailed inclusion and exclusion rules (population, study designs, outcomes, time frame, language) are specified below. Priority was given to recent original investigations and meta-analyses; clinically oriented reviews were included when they synthesized actionable evidence, whereas case reports and non–data-driven commentaries were excluded. Particular attention was paid not only to identifying factors associated with higher

or lower CPAP adherence, but also to the clinical interpretability of those findings. Studies and meta-analyses limited to a purely descriptive listing of variables associated with adherence were considered less informative for the purposes of this review than those offering a broader interpretive framework through which the observed associations could be understood in clinical practice. Accordingly, preference was given to studies that, beyond reporting statistical associations, also explored the potential behavioral, physiological, and practical mechanisms underlying those results. This approach was intended to support a more clinically meaningful discussion of adherence as a multidimensional and dynamic process rather than the simple sum of isolated predictors.

We included randomized trials, prospective and retrospective observational studies, and meta-analyses of adults (≥ 18 years) with OSA evaluating CPAP or auto-CPAP, with adherence outcomes (e.g., nightly hours of use, nights with ≥ 4 h) and/or indirect effectiveness aligned with physiological mechanisms. We excluded in vitro/animal and pediatric studies; editorials or letters without primary data; narrative overviews lacking decision-guiding synthesis; single-case reports; conference abstracts without full text; and duplicate or overlapping cohorts (retaining the most comprehensive or most recent analysis).

Two authors independently reviewed titles, abstracts, and full-text articles to identify studies of greater clinical and methodological relevance. Eligible designs included randomized trials, prospective and retrospective observational studies, and meta-analyses addressing CPAP adherence, its determinants, and strategies for improvement; narrative reviews were considered when they added decision-guiding synthesis. No formal protocol was prospectively registered for this review. Given the narrative nature of the article, no PRISMA-based methodology, SANRA framework, or formal standardized quality assessment tool was applied. Selection and interpretation were based on prespecified relevance, cross-study consistency, and clinical applicability; study-level decisions and reasons are documented in Appendix Table 2. A PRISMA-style flow diagram with counts (identified, deduplicated, screened, full-text assessed, excluded with reasons, included) is provided in the Appendix. Any differences in interpretation were discussed among the authors and resolved by consensus. This article is based exclusively on previously published studies and does not include any new studies involving human or animal subjects conducted by the authors.

In addition to a structured keyword search on adherence, we deliberately re-examined each clinically salient dimension—pathophysiology, mask selection, technical refinements, CPAP versus auto-CPAP comparisons, and adherence in women with OSA—to identify evidence most capable of guiding diagnostic, therapeutic, and follow-up decisions, capturing both direct adherence outcomes and indirect effectiveness aligned with physiological mechanisms.

The citation-to-claim problem remains a major concern. The authors have corrected the previous date inconsistency by extending the search period to May 2026, so that point no longer needs to be raised. The remaining problem is that several claims are still not adequately linked to the cited references. For example, the manuscript states that CBT-I before CPAP significantly increased CPAP adherence in COMISA patients, but the cited references visible in the revised reference list do not correspond to randomized CBT-I adherence trials. Because a citation mismatch was already

noted in the previous round, the authors should now check every citation-to-claim link in the manuscript.

Response to the reviewer. Thank you to the reviewer for the clarification. There must have been an issue with Zotero that recurs when updating the references. We have reviewed and corrected every citation in every sentence, but you will find them corrected only in the final version of the manuscript; given the numerous requested changes, I chose to make the necessary corrections to the text only once, rather than in the response to the reviewers. The English and citations were corrected last. In the tracked-changes version, you can see the specific corrections applied to each reference (punctuation, order, and formatting). Below that section, the reference style has been standardized and aligned with the journal's guidelines, with consistent formatting applied across all entries.

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The revised discussion of the 4-hour adherence threshold is directionally better, but the wording remains imprecise and sometimes overgeneralized. The manuscript should distinguish more clearly between an administrative or reimbursement threshold, a reporting convention used in research, and clinically meaningful CPAP use. Statements implying that shorter nightly use will not improve symptoms or cardiovascular risk should be softened unless supported by specific dose-response evidence. The REM-OSA argument is plausible and clinically relevant, but it should be framed as a subgroup-specific concern rather than as general proof that the 4-hour threshold is clinically inadequate in all patients.

Response to reviewer Thank you for the thoughtful and constructive feedback. We have clarified the distinction between administrative/reimbursement thresholds, research reporting conventions, and clinically meaningful CPAP use; tempered statements about shorter nightly use to align with dose–response evidence; and reframed the REM-OSA discussion as a subgroup-specific consideration while emphasizing individualized adherence targets.

In the text chapter 3.1 (version with track changes)

In 2009, the Centers for Medicare & Medicaid Services adopted a requirement of minimum 4 hours of Positive Airway Pressure (PAP) use for 70% of nights, or 21 days in a consecutive 30-day period, to continue medical coverage for PAP therapy [15][15]. The use of an economic rather than a clinical definition— is the first CPAP adherence issue to be fixed. Indeed, this is commonly used for reimbursement or coverage purposes but, although it is not clinically ineffective for all patients, the reduction of the AHI could be only partial. [16]. ~~it is not the goal that a clinician could suggest to his patient.~~ A few hours during the night may not improve symptoms, quality of life or reduce cardiovascular risk, with a subsequent reduction in patient motivation. Continuous positive airway pressure (CPAP) adherence using a “≥4 hours on ≥70% of nights” metric represents an administrative or reimbursement threshold used by payers and device monitoring programs and does not, by itself, define clinically meaningful treatment adequacy. First this threshold has been criticized as being too low by some and too strict by others for patients who may sleep less and benefit even less from 4 hours of sleep [17]. Second, it also appears in the research literature as a reporting convention that enables comparability across studies. Third, clinically meaningful CPAP use is better conceptualized as the duration needed to achieve patient-centered outcomes (symptom relief, functional improvement) and risk modification (cardiovascular and metabolic), which may exceed administrative minima for many patients and may vary by phenotype and sleep pattern. Evidence supports a dose–response relationship between nightly CPAP duration and clinical benefit, but this relationship should be articulated carefully to avoid overgeneralization [18]. Observational and experimental data indicate that limited nightly use can reduce disease burden, yet the magnitude of benefit often scales with longer wear times Daytime sleepiness improves after 7 hours of sleep, while seven hours and 30 minutes is the medium time necessary to reach a good performance status [19], [7]. This range could also be different for shorter or longer sleepers and varying during the lifespan. Certainly a cut off and a value is necessary in literature to quantify the adherence and to compare different reports. ~~CPAP treatment, in a clinical point of view, could be applied during sleep without interruption, in particular in patients with REM sleep OSA, in which the second part of the night could be less intentional by the patient. Considering that a physiological hypnogram has a prevalence of REM sleep in the second half of the night and that REM OSA is associated with higher cardiovascular risk. An OSA patient who removes the mask after only the first 4 hours of sleep will not treat the deeper desaturations, the more severe and longer events in REM sleep that prevails in the second part of the sleep and it is associated with an increase in cardiovascular risk and the cardiovascular risk [20], [21]. In addition recent evidences underline that patients with REM related OSA demonstrated significantly lower nightly CPAP use in particular in long term adherence compared with patients with non stage specific OSA. In addition, recent evidence underline that patients with REM-related OSA, with more than 50% events during REM sleep, demonstrated significantly lower nightly CPAP use in particular in long term adherence compared with patients with non-stage-specific OSA [22]. CPAP efficacy have a dose-response effect, suggesting that the ineffectiveness of CPAP in terms of cardiovascular and metabolic health in some trials is partly due to poor or not optimal adherence [23], [1].~~

Heterogeneity in sleep duration, OSA phenotype, comorbidities, and patient priorities further cautions against a one-size-fits-all adherence target. Short sleepers may accrue meaningful benefit at lower absolute nightly hours than long sleepers, though—consistent with dose–response principles—additional hours commonly produce additional gains. Conversely, some patients with severe, non-stage-specific OSA or substantial cardiometabolic risk may require near–full-night use to meaningfully modify outcomes. Real-world data also suggest that adherence patterns and therapy persistence vary across OSA phenotypes and patient profiles, with implications for how thresholds are met—or not met—in practice [24]

Another aspect is the definition of adherence compared to compliance. The term adherence itself underlines the necessity of the active and collaborative treatment acceptance including a self-efficacy meaning, with a no exclusive terminological difference with the most passive compliance. Adherence is also different from the acceptance. Acceptance is defined as willingness to purchase and use a CPAP device and it could be related to financial issue, social stigma or intolerance to CPAP or preference to another therapy [25]. In sleep medicine time issue is also important that defines the short- and long-term adherence. Long term adherence refers to different time horizons (3, 6 or 12

months), while shorter adherence refers to the first month of CPAP treatment and strongly influences the following period [26]

The section on phenotypes and endotypes remains too assertive for the evidence presented. The manuscript acknowledges that routine clinical endotyping is not currently feasible and that validated methods are lacking, but it also states that guidance on endotype-based therapeutic approaches is already “well-established” and that poor CPAP tolerance in low arousal threshold patients has been clearly demonstrated. These statements need further tempering. Phenotype- and endotype-guided titration should be presented as a promising hypothesis or specialized-center approach requiring prospective validation, not as a currently established clinical pathway for everyday care.

Response to reviewer. We appreciate the reviewer’s comment. We have revised the manuscript to temper statements about phenotypes and endotypes. Specifically, we:

- **Removed language implying that endotype-based therapeutic guidance is “well-established” or that poor CPAP tolerance in low arousal-threshold patients is “clearly demonstrated” in routine care.**
 - **Now present phenotype- and endotype-guided titration as a promising, hypothesis-generating approach suitable for specialized centers and research settings, pending prospective validation and standardized clinical tools.**
 - **Clarify that routine clinical endotyping is currently not feasible in everyday care and should not be considered a standard pathway for CPAP initiation or adjustment.**
-
- The response to the request for practical implementation of endotype assessment remains incomplete. The revised text mentions polysomnographic clues for high loop gain and low arousal threshold, but it does not clearly explain which traits can be measured reliably in routine practice, which require specialized methods, and which remain inferential. A short practical paragraph distinguishing routinely available clinical clues, specialized-center measurements, and research-only measures would make the section much more useful and would prevent over translation of mechanistic concepts.

We are sincerely grateful for this thoughtful suggestion. To keep the review practical while avoiding over-translation, we added a concise, tiered clarification within the text distinguishing (i) routine clinical clues (with concrete examples for each predominant endotype, including apnea-predominant events/CPAP level for collapsibility, central instability for high loop gain, Edwards’ criteria for low arousal threshold, and REM-dominant OSA for reduced dilator responsiveness), (ii) specialized-center assessments using validated model-based inference from routine PSG (e.g., Terrill et al., 2015), and (iii) definitive research-level measurements requiring esophageal pressure and CPAP dial-down protocols. This framing makes explicit what is feasible in routine care versus what requires advanced testing, consistent with the practical scope of the review.

In the text we added:

In the Chapter 3.3 you could see the modified part about endotype as follow

“To avoid over-translation while preserving clinical utility, we clarify three practical tiers. First of all, routine clinical clues from standard PSG/Home sleep apnea test, which we illustrate for each predominant endotype: apnea-predominant events or higher therapeutic CPAP levels suggesting increased collapsibility (anatomical factor); coexisting or mixed central events, periodic/waxing–waning breathing, or Cheyne–Stokes–like instability suggesting high loop gain; the Edwards composite criteria (AHI < 30 events/h, nadir SpO₂ > 82.5%, fraction of hypopneas > 58.3%; score ≥ 2 indicating a low arousal threshold) to screen for low arousal threshold; and REM-dominant OSA as a clinical marker of reduced dilator muscle responsiveness [58], [20]. Second, specialized-center assessments that estimate traits from routine full PSG using validated model-based inference, notably the mathematical framework described by Terrill et al, which computes ventilatory-control endotypes from standard signals without invasive instrumentation [59]. Finally, research-level measurements requiring full laboratory protocols, including esophageal pressure monitoring and CPAP platforms permitting dial-down pressure CPAP manipulations (and, where applicable, targeted gas perturbations), which remain outside the practical scope of this review [59], [60]. Phenotype/endotype-informed strategies to improve adherence are discussed as promising and research-oriented, not yet feasible for routine care, and requiring prospective validation.”

The mask/interface section has improved, but it still contains unsupported or overly categorical statements. The recommendation that retrognathic patients “should be treated with the nasal mask first” requires either a specific supporting citation or removal. The manuscript should consistently state that nasal interfaces are often preferable when feasible, but that mask choice must be individualized according to nasal patency, mouth leak, facial anatomy, comfort, previous intolerance, and patient preference.

We appreciate the reviewer’s further clarification regarding mask/interface selection. We agree that interface choice must be individualized and that evidence is heterogeneous across settings and patient subgroups. We have revised the text to avoid categorical statements and to emphasize that nasal interfaces are preferred when feasible, given signals of better comfort, lower leak, and adherence in several comparative analyses, while oronasal masks remain appropriate in clearly defined scenarios (e.g., persistent relevant nasal obstruction, predominant mouth breathing despite optimization). We also state explicitly that early reassessment and switching interface if problems persist are integral to care. These changes align our wording with the available evidence and the need for patient-centered selection, while preserving the practical message for everyday clinics.

“Interface selection should be individualized and reassessed early. When feasible, a nasal interface (nasal mask or nasal pillows) is generally preferred as a first option because multiple studies suggest better comfort, lower leak, and a signal of improved adherence compared with oronasal masks. However, this advantage is not universal and depends on patient factors and clinical context. Oronasal masks remain appropriate in selected situations, notably in patients with persistent relevant nasal obstruction or predominant mouth breathing despite targeted optimization (e.g., nasal therapies, humidification, chin strap). Our practical approach is to start with a nasal interface when reasonable, actively manage nasal symptoms and humidification, and switch interface if leaks, discomfort, or efficacy issues persist. This stepwise, patient-centered strategy avoids categorical claims while preserving the clinical importance of nasal masks in routine care.”

The added tables are useful, especially the table summarizing adherence strategies, evidence type, target subgroup, expected outcome, and limitations. However, Table 3 needs refinement because some categories appear inconsistent. For example, CBT-I for COMISA is placed under evidence-based recommendations, whereas psychological support programmes are categorized as preliminary. In addition, the terminology used for telemedicine and digital health interventions should be consistent across the text and tables. The authors should ensure that each strategy is categorized consistently with the strength and type of evidence cited in the text.

Response to reviewer. We thank the reviewer for this helpful observation. We have revised Table 3 to ensure internal consistency across categories and alignment with the strength and type of evidence cited in the text. Specifically, we harmonized the placement of psychological/behavioural interventions (CBT-I for COMISA and broader psychological support), standardized terminology for technology-enabled care as “telemedicine/remote monitoring (digital health)” across text and tables, and verified each strategy’s category against the cited evidence. These changes improve clarity without altering our conclusions.

Categorization was aligned to intervention specificity and trial maturity: protocolized, trial-supported interventions (e.g., CBT-I for COMISA; routine telemonitoring) are listed as evidence-based; non-protocolized psychological support and advanced digital tools with heterogeneous data are placed under expert opinion or preliminary evidence.

Strategy	Evidence category	Target subgroup	Expected outcome	Limitations
Patient education	Evidence-based	Newly diagnosed OSA; all patients	Improved understanding/acceptance ; modest increase in nightly use	Heterogeneous content and delivery
Early, structured follow-up and troubleshooting	Evidence-based	First 1–4 weeks; early problems	Reduced drop-out; stabilization of use over time	Resource-intensive; protocol variability
Mask/interface optimization (conditional nasal-first; switch if issues persist)	Evidence-based	No persistent relevant nasal obstruction	Lower leaks; better comfort; signal of improved adherence vs oronasal	Advantage not universal; mouth breathing may negate benefit
Treat nasal obstruction; optimize humidification	Evidence-based	Rhinitis/congestion/dry mouth	Comfort gains → increased use	Effect depends on underlying nasal disease
Telemedicine/re remote monitoring (digital health): routine data review + feedback	Evidence-based	Standard care; early maintenance	Small–moderate adherence increase; earlier issue detection	Modest effect sizes; implementation variability
CBT-I for COMISA (protocolized)	Evidence-based	OSA with comorbid insomnia	Better sleep initiation/maintenance; signal of increased CPAP use	Requires trained staff; not for all phenotypes
Shared decision-making for interface selection	Expert opinion	All patients; preference-sensitive	Higher acceptance; fewer early drop-outs	Limited RCTs isolating the effect
General psychological support programs (non-protocolized)	Expert opinion	Low motivation/anxiety/clostraphobia	Engagement support; possible increase in persistence	Heterogeneous content; limited controlled data

Strategy	Evidence category	Target subgroup	Expected outcome	Limitations
Chin strap for persistent mouth leaks (selected cases)	Expert opinion	Nasal interface + mouth leaks despite optimization	Fewer leaks/dry mouth; potential comfort gains	Not universally tolerated; variable benefit
Advanced digital health tools (apps, AI-assisted workflows)	Preliminary	Tech-engaged programs/patients	Early engagement signals; uncertain impact on hours/night	Heterogeneous designs; limited prospective outcomes
Phenotype-/endotype-guided PAP algorithms	Preliminary	Specialized centers; research protocols	Hypothesis-driven personalization; unknown adherence effect	No standardized tools; prospective validation needed
Precision/personalized behavioral interventions beyond CBT-I	Preliminary	Selected behavioral phenotypes	Possible adherence gains in subgroups	Mostly pilot/feasibility data

Table 3. Adherence strategies—classification by evidence, target subgroup, expected outcome, and limitations

The follow-up section has been expanded, and Table 2 now introduces phase-based guidance, including pre-CPAP assessment, titration, early follow-up, and long-term maintenance. However, this structure is not clearly integrated into the main text or into Figure 2. The manuscript should state more concretely what should be assessed at each contact, including nightly use, residual AHI, leak, pressure intolerance, treatment-emergent central apneas, nasal/oral dryness, insomnia, mask-related skin problems, residual symptoms, and patient concerns.

Response to reviewer: We appreciate this helpful suggestion. We have integrated the phase-based framework into the main text and aligned Figure 2 accordingly. For each contact (pre-CPAP assessment, titration, early follow-up, long-term maintenance), we now specify concrete items to review: nightly use, residual AHI, leak, pressure intolerance, treatment-emergent central apneas, nasal/oral dryness, insomnia, mask-related skin issues, residual symptoms, and patient concerns. Table 2 and Figure 2 have been updated to reflect these assessments at each phase

Chapter 3.6 Follow up and practical approach for early problems solutions with track changes

During the pre-CPAP period or baseline, a rapid evaluation of adherence predictors and barriers is performed first. In particular, comorbidities such as insomnia, depression, anxiety and other sleep disorders were investigated. If insomnia is present, CBT-I therapy may need to be started before CPAP assessment [77]. Nasal obstruction or allergic rhinitis are also taken into account, and specialistic evaluation or specific treatment may be [78]. Immediately prior to titration, a careful review of the polygraphic or polysomnographic recording may be helpful to characterize the sleep architecture and pattern, identify the endotype, and detect the presence of REM-predominant OSA or a more severe oximetric profile that warrants close monitoring once obstructive apneas have been corrected [57][79][20]. Decisions about treatment at this stage are shared with patients regarding home or laboratory titration, the latter being considered when comorbidities are present. Personalized education about the disease and CPAP treatment is required and strongly recommended. The first step in CPAP treatment is to arrange a clear follow-up schedule with the patient. The titration phase days 0 to 7 or 0 to depending on the outpatient clinic workflow. Early follow-up represents one of the most effective interventions for improving long-term PAP adherence and should be regarded as a dynamic, patient-centered adaptation process rather than simply the identification of an effective therapeutic pressure [5]. Current guidelines emphasize that the first days and weeks of therapy are crucial for identifying and correcting factors that may compromise treatment acceptance before they lead to treatment discontinuation. ~~The titration pathway should be adapted not only to the patient's clinical characteristics but also to the organization of the sleep center.~~ In centers where PAP initiation is performed on an outpatient basis, an acclimatization period with auto-adjusting PAP may allow optimization of the pressure range, minimum and maximum pressure settings, and ramp activation and duration according to the patient's sleep-onset latency, as well as overall treatment tolerance ~~ramp activation and duration according to the patient's sleep onset latency, and overall treatment tolerance~~ before defining long-term settings [7]. The most commonly reported side effects within the first month include dry mouth and nasal symptoms, such as congestion or mucosal irritation [80]. Nasal or oral dryness may improve with heated humidification and, when appropriate, heated tubing, whereas mask-related skin lesions usually respond to interface refitting, reduction of strap tension, interface replacement, or protective dressings. Additional issues may include mask leaks, skin lesions related to the interface, airflow-related discomfort, and sleep fragmentation [81]. In these cases, a careful management of mask fitting, circuit leaks and air humidification may improve patients' adherence [82]. Pressure intolerance can often be improved by optimizing pressure settings, ramp duration, or expiratory pressure relief (EPR), while persistent treatment-emergent central sleep apnea may require closer follow-up and, in selected patients, modification of the ventilatory strategy [7]. - During each follow-up visit, clinicians s the following objective metrics: nightly use (hours per night; percentage of nights with ≥4 hours of use), residual AHI (with obstructive vs. central breakdown), leak (median and 95th(th) percentile), pressure profile (median and 95th(th) percentile), flags for treatment-emergent central apneas, and symptoms of relief or persistence, as well as any adverse effects such as residual sleepiness, insomnia/sleep fragmentation, nasal/oral dryness, aerophagia, mask-related skin issues and patient-reported intolerance. Mask, size and cushion adjustments should be made to mitigate leaks. If TECSA are present or pressure variability is poorly tolerated, the APAP range should be narrowed or a fixed CPAP trial conducted [82], [83]. Comorbidity-targeted co-interventions (weight management, positional therapy and insomnia treatment) are different strategies to take into account. If there are persistent residual events with high treatment pressure, a shift to BiPAP or EPR may be required but a significative increase in adherence has not been demonstrated [52]. Provide brief adherence support in the form of coaching and troubleshooting. Another important aspect of each phase is the evaluation of clinical outcomes, such as residual symptoms, blood pressure, cardio-metabolic comorbidities and bed partner feedback regarding snoring and awakenings. After excluding secondary causes of residual sleepiness, the persistent symptom can be managed pharmacologically. Although initiating a specific wake-promoting therapy has not been shown to improve treatment adherence, leaving the patient with residual sleepiness worsens quality of life and undermines perceived treatment efficacy, thereby becoming a driver of non-adherence [84][85].

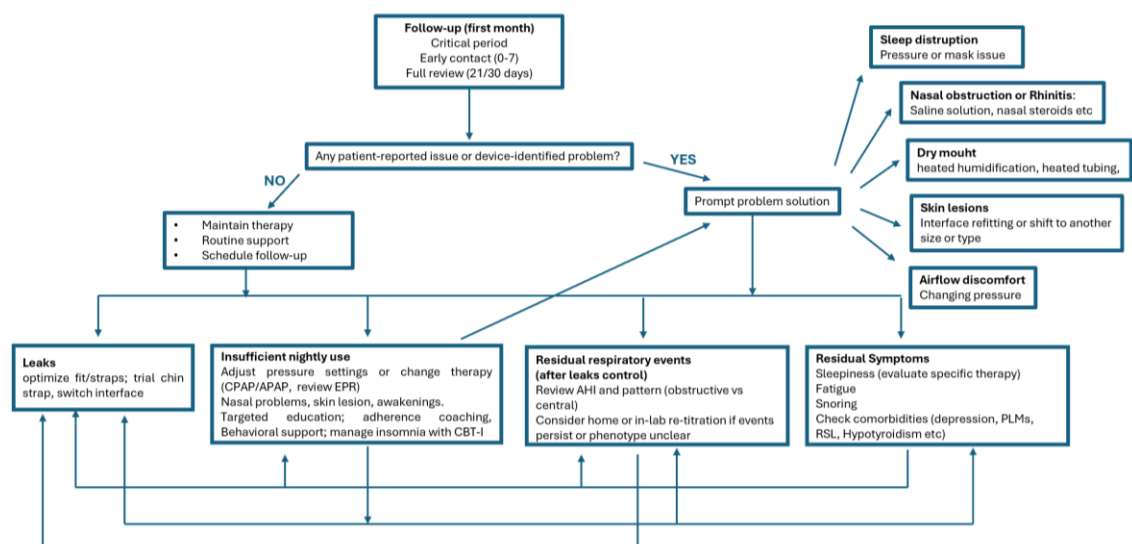
Educational and behavioral interventions have been shown improvements in adherence. Continuous support with telemedicine, telephone follow-up, group-based interviews and cognitive-behavioral therapy may improve CPAP adherence by enhancing patients' engagement [86],[87]. The patient should first be re-evaluated shortly after starting CPAP therapy. ~~Depending on the specific characteristics of the various centers and their workflow—for example, whether titration is performed via telemedicine—the decision regarding when to schedule the first visit may vary. A longer interval is appropriate when titration is performed via telemedicine, which allows for day-to-day monitoring of leaks and fit; a shorter interval is recommended for those not yet using telemedicine to prevent certain problems from going unresolved and the patient from discontinuing therapy. In centers equipped with telemedicine, remote review of PAP downloads allows clinicians to rapidly detect poor adherence, excessive leaks, or persistent residual respiratory events and implement timely corrective measures before these issues become barriers to long-term treatment. In centers where telemonitoring is unavailable, proactive telephone contact during the first days of treatment or an early structured follow-up call may be equally valuable to identify technical difficulties, reinforce education, explore patient concerns, and arrange earlier clinical reassessment when necessary. Clinicians should always evaluate emerging conditions during initial CPAP therapy phase, including insomnia, depressive symptoms or sleep-related movement disorders because these issues can cause CPAP interruption.~~ Depending on center characteristics and workflow—for example, the use of telemedicine—the timing of the first visit may vary. Where telemedicine is available, day-to-day remote review of PAP downloads enables rapid detection of poor adherence, excessive leaks, or persistent residual events and timely corrective actions, allowing for a longer initial interval. In settings without telemonitoring, a shorter interval is advisable; proactive telephone contact or an early structured follow-up call can similarly identify technical issues, reinforce education, explore concerns, and prompt earlier reassessment when needed. Clinicians should also evaluate emerging conditions during the initial CPAP phase—such as insomnia, depressive symptoms, or sleep-related movement disorders—as these can precipitate CPAP interruption [88] [89]. Finally, follow-up intensity should be individualized according to the patient's estimated risk of poor adherence. Patients presenting with anxiety, depression, comorbid insomnia, sleep-related movement disorders, advanced age, cognitive impairment, limited social support, or previous negative experiences with PAP therapy may benefit from a more intensive follow-up schedule during the adaptation phase. ~~Finally, follow-up intensity should be individualized according to the estimated risk of poor adherence. Patients with anxiety, depression, comorbid insomnia, sleep-related movement disorders, advanced age, cognitive impairment, limited social support, or prior negative experiences with PAP may benefit from a more intensive schedule during the adaptation phase~~ [3], [7]. Overall successful long-term PAP adherence relies on a personalized strategy integrating individualized titration, careful interpretation of PAP waveforms rather than device metrics alone, prompt troubleshooting of side effects, patient-centered education, and a risk-stratified follow-up adapted to both the patient's needs and the organizational resources of the sleep center. A table with common barriers to CPAP adherence and practical management strategies and a figure with a work flow diagram have been added to this chapter (Table 1 and Table 2 and Figure 2).

	Pre-CPAP assessment		Titration (days 0-7)		Early follow-up (weeks 1-4)		Long-term maintenance (>=3 months)	
Disease-related	Baseline OSA severity (AHI) or polysomnographic phenotype, endotype/phenotype, craniofacial anatomy, stable comorbidities. Identify COMISA (plan CBT-I before/with CPAP) screen/treat rhinitis or congestion; plan management for depression/anxiety. Other sleep disorders to investigate (PLMS, RLS e)	Modified? No Yes	Tailored and efficacious pressure by sleep stage/position if needed add positional therapy when indicated. Check the optimal pressure to resolve all the events: apnea, hypopnea, flow limitations. Symptoms relief	Modified? Yes	Reassess residual AHI/leak by stage/position; treat rhinitis, asthma, or GERD limiting tolerance. Symptoms relief	Modified? Yes	Fixed anatomy, baseline severity. Persistent symptoms unaffected by treatment (sleepiness). Manage weight change; track new comorbidities/medications affecting sleep/airway; re-evaluate as needed.	Modified? No Yes
Treatment-related	Education on OSA risks/benefits and expectations Identify key symptoms Personalized education approach in What OSA is and its consequences What CPAP is and how it works Establish a schedule follow up plan. Identify barrier to CPAP use: nasal rhinitis or obstruction , claustrophobia etc. Choose home/laboratory titration adjuncts/alternatives via shared decision-making	Modified? Yes	Optimize pressures/ramp/EPR; refine humidification/temperature; swap mask for leaks or claustrophobia; provide rapid-access support. initial mask selection humidification plan comfort features (ramp/EPR); Check: residual AHI, leaks and nightly use Check adverse effects skin lesions, pressure intolerance, awakenings	Modified? Yes	Adjust pressure range; change mask/cushion size; add chinstrap for mouth leak; tweak humidifier/temperature; consider BiPAP for persistent intolerance. Check: residual AHI, leaks and nightly use Check adverse effects skin lesions, pressure intolerance, awakenings.	Modified? Yes	Supply replacement schedule; periodic refit, re-tilt after weight change/surgery; travel solutions. Polysomnographic or polygraphic trace with CPAP treatment Check: residual AHI, leaks and nightly use Check adverse effects skin lesions, pressure intolerance, awakenings Persistence of treatment emergent central sleep apnea (TECSA)	Modified? Yes
Patient-related	Age, sex/gender, socioeconomic constraints. Health literacy/readiness; claustrophobia desensitization plan; engage bed partner/care giver; address work/travel constraints.	Modified? No Yes	Sleep quality and satisfaction Sleep-hygiene coaching; graded exposure for claustrophobia; teach-back to reinforce skills; involve partner/care giver Telemedicine or phone calls during this initial phase to monitor adherence, resolve problems early on, and provide educational support to the patient	Modified? Yes	Sleep quality and satisfaction Problem-solve barriers (time, stigma, intimacy concerns); motivational interviewing; review adherence reports together; accommodate shift work/travel. provide educational and motivational support to the patient	Modified? Yes	Sleep quality and satisfaction Prevention plan; reinforce benefits; partner/peer support; telemonitoring nudges. provide educational and motivational support to the patient	Modified? Yes
Actions: personalized approach in education. Set goals with the patient, treat nasal symptoms, check comorbidities and any CPAP adherence obstacle. Define a scheduled follow up		Actions: mask/humidification; limit the APAP range or try fixed-pressure CPAP if variable pressure causes intolerance/TECSA Telemedicine or phone calls for resolve problems or give a motivational support		Actions: Escalate if <4 h/night average, persistent residual AHI/leaks, or severe insomnia/anxiety; consider behavioral sleep medicine, ENT/OME review, or alternatives.		Actions: Review every 3-6 months, then annually, or sooner with symptoms or data flags. Global evaluations. Persistent symptoms specific therapy		

Factors influencing CPAP adherence: what to address, when, and what's modifiable

Figure 2 remains below publication quality. Although the concept is useful, the figure still contains informal wording, spelling errors, unclear visual organization, and oversimplified action steps such as “change mask or education,” “Motivation with CBTi or groups work,” and “adherence.” The figure should be redesigned as a clean clinical algorithm with precise wording and a clearer sequence of assessment and management steps. The caption should also match the actual content of the figure.

Thank you the reviewer for the suggestion. You can see figure 2 with changes and improvements.



The conclusion regarding telemedicine has been moderated, but it remains grammatically unclear and still too broad. Telemedicine should be framed as one potentially useful component of structured follow-up, rather than as a general solution for ensuring adherence at scale. The manuscript should briefly acknowledge heterogeneity across telemonitoring interventions, variable long-term effects, infrastructure requirements, and unequal suitability across patient groups.

Thank you for the comment. We have revised the conclusion to avoid overgeneralization and to frame telemedicine as a potentially useful component within structured follow-up pathways rather than a universal solution for adherence. We also added a brief passage acknowledging (i) the heterogeneity of telemonitoring programs and the variable durability of effects over the longer term; (ii) the infrastructure and workflow-integration requirements that condition scalability; and (iii) the unequal suitability across patient groups due to differences in digital access, clinical complexity, and preferences. Finally, we identify as a future priority the clarification of which intervention features, delivery models, and patient profiles are associated with the most sustained benefits, and under what resource conditions.

In the conclusion section we added:

Our findings do not support telemedicine as a universal solution to ensure adherence, but rather as one of several potential components within structured follow-up pathways. Telemonitoring initiatives are heterogeneous in design and intensity, and their effects may wane over the longer term. Effective implementation depends on adequate infrastructure, integration into clinical workflows, and sound data governance, which can limit scalability in some settings. Suitability also varies across patient groups due to differences in digital access, clinical complexity, and preferences. Future research should clarify which intervention features, delivery models, and patient profiles yield the most sustained benefits, and under what resource conditions.

The language still requires extensive revision. This is not a minor stylistic issue: several sentences are difficult to interpret clinically, and errors remain throughout the abstract, methods, results, figures, and conclusions. Examples include incorrect verb agreement, awkward clinical phrasing, repeated wording, spelling errors, and unclear expressions such as “treatment acceptance,” “times frame,” “patient preference or prior intolerance could be considerate,” and “telemedicine... could be useful to ensuring adherence.” The manuscript should undergo a thorough professional language edit after the scientific corrections have been completed.

Response to reviewer. Thank you for this thorough language-focused critique. We agree that the manuscript required substantial linguistic revision beyond minor stylistic edits. Following completion of the scientific corrections, we conducted a comprehensive language edit to improve clarity, precision, and clinical interpretability across the abstract, methods, results, figures, and conclusions. Specifically, we corrected verb agreement, removed repetitive wording, standardized clinical phrasing, and fixed spelling and syntax errors. We also replaced ambiguous expressions with clear terminology, for example: “treatment acceptance” → “treatment acceptance,” “times frame” → “timeframe,” “patient preference or prior intolerance could be considerate” → “patient preference or prior intolerance should be considered,” and “telemedicine...

could be useful to ensuring adherence” → “telemedicine may be one useful component to support adherence.” Where helpful, we adopted field-standard phrasing and simplified complex sentences. We appreciate the guidance and believe these revisions materially improve readability and clinical clarity.

The authors' response letter should be revised to provide a clearer point-by-point account of the changes made. Several responses simply state that the text was rewritten or corrected, without indicating where the change was made or how the concern was addressed. For a revised submission, the response should specify the manuscript section, table, or figure modified, and should clearly justify any recommendation that was not fully changed.

Thank you sincerely for your thoughtful and constructive comments. In this second revision, we have provided a point-by-point response, indicating for each item the exact manuscript location (section/page/paragraph) and the specific changes made, including the revised tables and figures. In the manuscript file, all modifications are highlighted in red to facilitate review. We apologize that our prior response did not specify these details with sufficient precision. Regarding language and style, we did not list individual corrections because the manuscript underwent a comprehensive language edit to standardize terminology, spelling, and usage throughout. We are grateful for your guidance, which has materially improved the clarity and quality of the work.