https://doi.org/10.5664/jcsm.11858

JCSM | Journal of Clinical Sleep Medicine

SPECIAL ARTICLES

# Treatment of central sleep apnea in adults: an American Academy of Sleep Medicine clinical practice guideline

M. Safwan Badr, MD, MBA[1]; Rami N. Khayat, MD[2,3]; J. Shirine Allam, MD[4,5]; Suzanne Hyer, PhD, RN[6]; Reem A. Mustafa, MD, MPH, PhD[7,8]; Matthew T. Naughton, MBBS, MD, FRACP, ATSF, FERS[9]; Susheel Patil, MD, PhD, FAASM[10,11]; Grace W. Pien, MD, MSCE[12]; Winfried Randerath, MD, FAASM[13]; Christine Won, MD, MSc[14]

*[1]Department of Internal Medicine, University Health Center, Wayne State University School of Medicine, Detroit, Michigan; [2]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, Penn State University College of Medicine, Hershey, Pennsylvania; [3]Penn State Sleep Services, Milton S. Hershey Medical Center, Penn State Health, Hershey, Pennsylvania; [4]Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia; [5]Department of Medicine, Sleep Medicine Center, Atlanta Veterans Affairs Medical Center, Atlanta, Georgia; [6]American Academy of Sleep Medicine, Darien, Illinois; [7]Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS; [8]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada; [9]Alfred Hospital & School of Translational Medicine, Monash University, Melbourne, Victoria, Australia; [10]Sleep Medicine Program, University Hospitals of Cleveland, Cleveland, Ohio; [11]Case Western Reserve University School of Medicine, Cleveland, Ohio; [12]Division of Sleep Medicine, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; [13]Clinic of Pneumology and Allergology, Center for Sleep Medicine and Respiratory Care, Bethanien Hospital, Solingen, Germany; [14]Section of Pulmonary, Critical Care and Sleep Medicine, Yale University School of Medicine, New Haven, Connecticut*

**Introduction:** This guideline establishes clinical practice recommendations for treatment of central sleep apnea (CSA) syndromes in adults.

**Methods:** The American Academy of Sleep Medicine (AASM) commissioned a task force of experts in sleep medicine to develop recommendations and assign strengths based on a systematic review of the literature and an assessment of the evidence using the Grading of Recommendations Assessment, Development and Evaluation methodology. The task force provided a summary of the relevant literature and the certainty of evidence, the balance of benefits and harms, patient values and preferences, and resource use considerations that support the recommendations. The AASM Board of Directors approved the final recommendations.

**Good Practice Statement:** The following good practice statement is based on expert consensus, and its implementation is necessary for the appropriate and effective management of patients with CSA. The optimal approach to CSA treatment should incorporate clinical features, comorbid conditions, and polysomnographic findings in an individualized manner. Specifically, clinicians must prioritize optimizing therapy for the conditions contributing to central apneas and improving patient-reported outcomes rather than solely focusing on eliminating disordered breathing events. Once therapy for CSA has been initiated, persistence of central respiratory events should prompt re-evaluation of the underlying risk factors and consideration of alternative treatment options.

**Recommendations:** The following recommendations are intended as a guide for clinicians in choosing a specific treatment for adults with CSA. Each recommendation statement is assigned a strength ("Strong" or "Conditional"). A "Strong" recommendation (ie, "We recommend … ") is one that clinicians should follow under most circumstances. A "Conditional" recommendation (ie, "We suggest … ") is one that clinicians should offer to most patients if clinically appropriate. Some recommendations include remarks that provide additional context to guide clinicians with the implementation of this recommendation.

1. The AASM suggests using continuous positive airway pressure over no continuous positive airway pressure in adults with CSA due to the following etiologies: primary CSA, CSA due to heart failure, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)
2. The AASM suggests using bilevel positive airway pressure *with a backup rate* over no bilevel positive airway pressure with a backup rate in adults with CSA due to the following etiologies: primary CSA, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, very low certainty of evidence)
3. The AASM suggests against the use of bilevel positive airway pressure *without a backup rate* in adults with CSA due to the following etiologies: primary CSA, CSA due to heart failure, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, very low certainty of evidence)
4. The AASM suggests using adaptive servo-ventilation over no adaptive servo-ventilation in adults with CSA due to the following etiologies: primary CSA, CSA due to heart failure, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)
   *Remarks: Prior to initiation of adaptive servo-ventilation, patient-provider shared decision-making is recommended, and treatment decisions should be based on expectations of symptomatic or quality-of-life improvement. Treatment with adaptive servo-ventilation in patients with heart failure with reduced ejection fraction should be limited to centers with experience, along with close monitoring and follow-up.*
5. The AASM suggests using low-flow oxygen over no low-flow oxygen in adults with CSA due to heart failure. (Conditional recommendation, low certainty of evidence)
6. The AASM suggests using low-flow oxygen over no low-flow oxygen in adults with CSA due to high altitude. (Conditional recommendation, very low certainty of evidence)
   *Remarks: Patients with transient and mild CSA symptoms at high altitude may reasonably decline treatment with low-flow oxygen.*

7. The AASM suggests using oral acetazolamide over no acetazolamide in adults with CSA due to the following etiologies: primary CSA, CSA due to heart failure, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)
8. The AASM suggests using oral acetazolamide over no acetazolamide in adults with CSA due to high altitude. (Conditional recommendation, very low certainty of evidence)
9. The AASM suggests using transvenous phrenic nerve stimulation over no transvenous phrenic nerve stimulation in adults with CSA due to the following etiologies: primary CSA and CSA due to heart failure. (Conditional recommendation, very low certainty of evidence)
   *Remarks: Given that transvenous phrenic nerve stimulation requires an invasive procedure, is not universally accessible, and is associated with high costs, it may be more appropriate to consider other treatments first.*

**Keywords:** central sleep apnea, central sleep-disordered breathing, therapy, clinical practice guideline
**Citation:** Badr MS, Khayat RN, Allam JS, et al. Treatment of central sleep apnea in adults: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2025;21(12):2181–2191.

## INTRODUCTION

This clinical practice guideline (CPG) updates the previously published American Academy of Sleep Medicine (AASM) practice parameters on the treatment of central sleep apnea (CSA) syndromes and reflects current recommendations of the AASM.[1,2] Since these publications, the AASM has modified its development of CPGs according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process.[3] Several notable developments have taken place since the publication of the previous guidelines, including newly published studies on adaptive servo-ventilation (ASV) and the introduction of phrenic nerve stimulation as a novel therapy for CSA.

CSA is a form of sleep-disordered breathing in which an absence or reduction in effort is coupled with a corresponding change in airflow.[4] CSA is not a single disorder but represents central breathing instability in various clinical conditions, including heart failure (HF), obstructive sleep apnea (OSA), and opioid analgesic use. The sleep state (specifically, non-rapid eye movement sleep) removes the wakefulness "drive to breathe," rendering respiration critically dependent on the partial pressure of carbon dioxide ($PaCO_2$) and unmasking the hypocapnic apneic threshold. Accordingly, central apnea results from transient cessation of ventilatory motor output, which occurs when inhibitory influences promoting instability predominate over excitatory influences favoring stable breathing. The pathogenesis of CSA can vary depending on the underlying clinical condition. The majority of central apnea is a posthyperventilation phenomenon. Hypoventilation disorders are not considered under the rubric of CSA. The final common pathway involves posthyperventilation hypocapnia, which leads to central apnea. The development and persistence of CSA through multiple mechanisms exemplify the concept of "equifinality," where central apnea can be triggered by distinct etiological pathways. Current classification focuses on components of the ventilatory loop, increased controller gain or plant gain. Opioid-associated CSA may have unique pathways in addition to the ventilatory loop in that the breathing pattern can occur with a depressed central respiratory drive and decreased chemosensitivity, unlike the increased chemosensitivity present in other types of CSA such as hypoxia or HF-related CSA. This pathophysiological heterogeneity may account for the diverse clinical presentations of CSA and the lack of a universally effective treatment for all patients.[5] The management strategy should consider polysomnographic findings, individual patient factors, and the underlying conditions, which should be addressed as a key component of the therapeutic plan.

The *International Classification of Sleep Disorders*, third edition, text revision classifies CSA in adults into 6 categories: primary CSA, CSA with Cheyne–Stokes respiration (frequently due to underlying HF), CSA due to a medication or substance, CSA due to a medical disorder without Cheyne–Stokes, treatment-emergent CSA, and CSA due to high altitude.[4] Though the definition of CSA requires that > 50% of respiratory events be central in nature, in some patients the true nature of the sleep-related breathing disorder (whether central or obstructive) cannot be determined with confidence during routine polysomnography (ie, without the use of esophageal pressure monitoring). This is especially true of patients whose respiratory events are predominantly hypopneas.[6] As such, the true classification of the underlying sleep-related breathing disorder can be challenging in the clinical setting. In addition, patients frequently present with mixed disorders, in which both obstructive and central events occur, and the choice of treatment should address both disorders, if present.

CSA is associated with sleep fragmentation, daytime sleepiness, insomnia, and poor quality of life and may portend a poor clinical outcome. In addition, CSA can be associated with significant adverse clinical consequences, including increased mortality and hospitalization in patients with HF.[7,8] In a recent 21-year retrospective study of the Veterans Health Administration's electronic medical records, almost one fifth of patients with CSA died within 5 years of diagnosis.[9] As the accompanying systematic review[10] demonstrates, treatment of CSA is warranted to mitigate long-term adverse consequences.

CSA remains a poorly understood and sometimes misinterpreted disorder, particularly in terms of its mechanisms, clinical manifestations, and treatment indications.[11] Significant knowledge gaps in the pathogenesis of the respiratory control instability underlying CSA hinder the development of a pathogenesis-based classification system. This lack of understanding also complicates the identification of clinical and physiological factors that contribute to the onset of CSA across different health conditions.

The aforementioned knowledge gaps present 2 major challenges. First, the current classification relies on clinical presentation rather than underlying pathophysiology. Polysomnographic criteria for CSA classification, particularly hypopnea scoring, are inconsistently applied in clinical practice and were seldom used in the studies reviewed by the task force (TF). Second, treatment

options targeting specific mechanistic pathways of CSA are limited. There is a lack of treatment strategies based on precise pathophysiological traits of individual CSA syndromes. These challenges and limitations have impeded progress in the field for decades, leading to a narrow range of treatment options for patients with CSA.

These guidelines are limited by the quantity, quality, and variability of available studies. CSA is less common and less well understood than OSA, and consequently there are fewer studies and investigations on the disorder. This lack of research has been further compounded by recent clinical trials in both CSA and OSA, which failed to demonstrate survival benefits, though improvement in several intermediate outcomes (eg, quality of life, sleepiness) were reported with treatment and supported these recommendations.[12,13] Considering the limited number of studies available for certain patient populations and the shared pathophysiological mechanisms across various types of CSA, the TF aimed to group studies that evaluated similar treatments across different CSA subtypes (see **Table 1**). When appropriate, the TF reviewed both individual and grouped data to provide a more comprehensive assessment of treatment effectiveness and enhance confidence in clinically relevant recommendations.

This guideline, in conjunction with the accompanying systematic review,[10] provides a comprehensive update of the available evidence and a synthesis of clinical practice recommendations for the treatment of CSA. It is intended to optimize patient-centric care by broadly informing clinicians who care for patients with CSA.

## METHODS

The AASM commissioned a TF of sleep medicine clinicians with expertise in CSA along with guideline methodologists. The TF was required to disclose all potential conflicts of interest, per the AASM's conflicts of interest policy, prior to being appointed to the TF and throughout the research and writing of these documents. In accordance with the AASM's conflicts of interest policy, TF members with a Level 1 conflict were not allowed to participate. TF members with a Level 2 conflict were required to recuse themselves from any related discussion or writing responsibilities. All relevant conflicts of interest are listed in the Disclosures section.

**Table 1**—Summary of recommendations.

| Intervention | Recommendation | Overall Certainty of the Evidence | Population |
|---|---|---|---|
| CPAP vs no CPAP | Conditional for | ⊕⊕◯◯ | • Primary CSA<br>• CSA due to heart failure<br>• CSA due to medication or substance use<br>• Treatment-emergent CSA<br>• CSA due to a medical condition or disorder |
| BPAP *with a backup rate* vs no BPAP with a backup rate | Conditional for | ⊕◯◯◯ | • Primary CSA<br>• CSA due to medication or substance use<br>• Treatment-emergent CSA<br>• CSA due to a medical condition or disorder |
| BPAP *without a backup rate* | Conditional against | ⊕◯◯◯ | • Primary CSA<br>• CSA due to heart failure<br>• CSA due to medication or substance use<br>• Treatment-emergent CSA<br>• CSA due to a medical condition or disorder |
| ASV vs no ASV | Conditional for | ⊕⊕◯◯ | • Primary CSA<br>• CSA due to heart failure<br>• CSA due to medication or substance use<br>• Treatment-emergent CSA<br>• CSA due to a medical condition or disorder |
| Low-flow oxygen vs no low-flow oxygen | Conditional for | ⊕⊕◯◯ | • CSA due to heart failure |
| Low-flow oxygen vs no low-flow oxygen | Conditional for | ⊕◯◯◯ | • High altitude* |
| Acetazolamide vs no acetazolamide | Conditional for | ⊕⊕◯◯ | • Primary CSA<br>• CSA due to heart failure<br>• CSA due to medication or substance use<br>• Treatment-emergent CSA<br>• CSA due to a medical condition or disorder |
| Acetazolamide vs no acetazolamide | Conditional for | ⊕◯◯◯ | • High altitude* |
| TPNS vs no TPNS | Conditional for | ⊕◯◯◯ | • Primary CSA<br>• CSA due to heart failure |

*Recent ascent to high altitude (at least 2,500 m [8,202 feet]). Grading of Recommendations Assessment, Development and Evaluation certainty of evidence: ⊕⊕◯◯ = low, ⊕◯◯◯ = very low. ASV = adaptive servo-ventilation, BPAP = bilevel positive airway pressure, CPAP = continuous positive airway pressure, CSA = central sleep apnea, TPNS = transvenous phrenic nerve stimulation.

The TF conducted a systematic review of the published scientific literature, focusing on patient-oriented, clinically relevant outcomes. The key terms, search limits, and inclusion/exclusion criteria specified by the TF are detailed in the supplemental material of the accompanying systematic review.[10] The purpose of the review was to determine whether the interventions provided clinically meaningful improvements in relevant outcomes in relation to no treatment. The TF set a clinically meaningful threshold (CMT) for each outcome to determine whether the mean differences between treatment and control or before and after treatment in the outcomes assessed were clinically meaningful.[10] The following critical outcomes were identified for decision-making: (1) excessive sleepiness; (2) disease severity (in order of importance: apnea-hypopnea index [AHI], central apnea index [CAI], central apnea-hypopnea index [CAHI], oxygen desaturation index [ODI]); (3) cardiac outcomes (6-minute walk distance, New York Heart Association class); (4) patient-reported sleep quality; (5) hospitalizations; and (6) mortality. Adverse events within the accepted literature were included in assessing the balance of beneficial and harmful effects. When the available evidence was not sufficient, other important outcomes were considered for decision-making. The clinical practice recommendations were then developed according to the GRADE process.[3,14] The TF assessed the following 4 components to determine the direction and strength of a recommendation: certainty of evidence, balance of beneficial and harmful effects, patient values and preferences, and resource use. Additionally, the impact on equity, feasibility, and acceptability was discussed. There was no direct evidence regarding health equity. Details of these assessments can be found in the accompanying systematic review. Taking these major factors into consideration, each recommendation statement was assigned a strength ("Strong" or "Conditional"). Additional information is provided in the form of "Remarks" immediately following the recommendation statements, when deemed necessary by the TF. Remarks are based on the evidence evaluated during the systematic review and are intended to provide context for the recommendations and to guide clinicians in the implementation of the recommendations in daily practice.

This CPG reflects the evidence and state of knowledge at the time of the last literature search, February 2025. Scoping literature searches are performed every 1 to 2 years on all published AASM CPGs to review new evidence. Based on this review, updates may be made if there are significant changes in areas such as the available interventions, outcomes of interest (or values placed on outcomes), or evidence regarding the existing benefits and harms. The ultimate judgment regarding the suitability of any specific recommendation requires the clinician to use clinical knowledge and experience and strongly consider the individual patient's values and preferences to determine the best course of action.

## RECOMMENDATIONS

The following clinical practice recommendations are based on a systematic review and evaluation of evidence using the GRADE process. The implications of the strength of recommendations for guideline users are summarized in **Table 2**. Remarks are provided to guide clinicians in the implementation of these recommendations.

## GOOD PRACTICE STATEMENT

The following good practice statement is based on expert consensus, and its implementation is necessary for the appropriate and effective management of patients with CSA. The optimal approach to CSA treatment should incorporate clinical features, comorbid conditions, and polysomnographic findings in an individualized manner. Specifically, clinicians must prioritize optimizing therapy for the underlying condition and improving patient-reported outcomes rather than solely focusing on eliminating disordered breathing events. Once therapy for CSA has been initiated, persistence of central respiratory events should prompt re-evaluation of the underlying risk factors and consideration of alternative treatment options.

**Table 2**—Implications of strong and conditional recommendations for users of American Academy of Sleep Medicine clinical practice guidelines.

| User | Strong Recommendations: "We Recommend …" | Conditional Recommendations: "We Suggest …" |
|---|---|---|
| Clinicians | Almost all patients should be offered the recommended course of action. Adherence to this recommendation could be used as a quality criterion or performance indicator. | Most patients should be offered the suggested course of action; however, different choices may be appropriate for different patients. The clinician must help each patient determine if the suggested course of action is clinically appropriate and consistent with their values and preferences. |
| Patients | Almost all patients should be offered the recommended course of action, although a small proportion of patients would not choose it. | Most patients should be offered the suggested course of action, though some may not choose it. Different choices may be appropriate for different patients. The patient should work with their clinician to determine if the suggested course of action is clinically appropriate and consistent with their values and preferences. |
| Policy makers | The recommended course of action can be adopted as policy for most situations. Adherence to the recommended course of action could be used as a quality criterion or performance indicator. | The ultimate judgment regarding the suitability of the suggested course of action must be made by the clinician and patient together, based on what is best for the patient. This decision-making flexibility should be accounted for when establishing policies. |

## ADULTS WITH CSA

Recommendations with sufficient evidence for specific interventions for the treatment of adults with CSA are presented below and summarized in **Table 1**. Remarks are provided to guide clinicians in the implementation of these recommendations. The TF assessed effectiveness for the treatment of CSA in adults based on the following critical outcomes: excessive sleepiness, disease severity (AHI, CAI, CAHI, ODI), cardiac outcomes, hospitalizations, mortality, daytime functioning, and quality of life. Consistent with patients' values, the TF placed a high importance on symptom relief and improvement in quality of life even in instances of no direct evidence to show improvement in mortality. Therefore, treatment with the following modalities should be considered. Hypoventilation disorders were not addressed by this guideline.

### Conditional recommendations

***Recommendation 1: The AASM suggests using continuous positive airway pressure (CPAP) over no CPAP in adults with CSA due to the following etiologies: primary CSA, CSA due to HF, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)***

The TF identified 11 randomized controlled trials (RCTs) ranging from 1 night to 6 months. The pooled results demonstrated clinically meaningful improvements in disease severity (AHI). The pooled results for excessive sleepiness, disease severity (CAI), cardiac outcomes, hospitalizations, and mortality did not meet the CMT. The potential benefits of CPAP had a small effect size. No serious adverse events were reported in the studies included. The undesirable effect size was deemed trivial. The TF judged the potential benefits of CPAP outweigh the potential harms.

The overall certainty of evidence was low due to imprecision. The cost of CPAP was determined to be moderate. There was no direct evidence of the impact of CPAP on health equity, because cost varies depending on insurance coverage and access to sleep centers. The intervention was determined to be acceptable and feasible to implement.

***Recommendation 2: The AASM suggests using bilevel positive airway pressure (BPAP) with a backup rate over no BPAP with a backup rate in adults with CSA due to the following etiologies: primary CSA, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, very low certainty of evidence)***

The TF identified 6 RCTs and 3 observational studies ranging from 1 night to 6 months of treatment. The pooled estimates demonstrated clinically meaningful improvements in excessive sleepiness, disease severity (AHI, CAI, CAHI), and cardiovascular disease with a small effect size. Small undesirable effects related to the mask interface were reported anecdotally in a few patients, and 1 patient (of the 128 total participants who enrolled and completed treatment in the 9 studies) was reported to have died due to cardiovascular causes. The TF judged that the potential benefits of BPAP with a backup rate outweigh the potential harms.

The overall certainty of evidence was very low due to imprecision. The cost of BPAP with a backup rate was considered moderate. There was no direct evidence that the BPAP with a backup rate would affect health equity; however, due to payor coverage variability, the intervention might reduce health equity. Treatment with BPAP with a backup rate was found to be acceptable and probably feasible to implement.

***Recommendation 3: The AASM suggests against the use of BPAP without a backup rate in adults with CSA due to the following etiologies: primary CSA, CSA due to HF, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, very low certainty of evidence)***

The TF identified 1 RCT of bilevel without a backup rate. However, this study used a very modest level of pressure support to provide comfort that can be considered more similar to present-day CPAP with modified pressure relief settings. The results demonstrated clinically meaningful improvements in disease severity (AHI, CAI) and cardiac outcomes after 3 months of treatment, with a small effect size. However, extensive literature shows that BPAP without a backup rate can induce CSA and periodic breathing if excessive pressure support is provided.[15–17] Although these studies were conducted in healthy individuals or those with OSA, they provide indirect evidence regarding the potential harms of BPAP without a backup rate in adults with CSA. Thus, the undesirable effect size was deemed to be large.

The TF judged that the potential harms of BPAP without a backup rate outweigh the potential benefits. The certainty of the evidence was rated as very low due to indirectness and imprecision. The cost of the treatment was considered moderate. BPAP was determined to be feasible to implement. There was no direct evidence that the treatment would reduce health equity, but it may not be acceptable.

***Recommendation 4: The AASM suggests using ASV over no ASV in adults with CSA due to the following etiologies: primary CSA, CSA due to HF, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)***

*Remarks: Prior to initiation of ASV, patient–provider shared decision-making is recommended, and treatment decisions should be based on expectations of symptomatic or quality-of-life improvement. Treatment with ASV in patients with HF with reduced ejection fraction (HFrEF) should be limited to centers with experience, along with close monitoring and follow-up.*

The TF identified 12 RCTs ranging from 1 night to 5 years. The pooled estimates demonstrated clinically meaningful improvements in disease severity (AHI, CAI, CAHI). The TF reviewed the pooled estimate on all-cause mortality and cardiovascular mortality in all RCTs, specifically in patients with HFrEF. There was no change in mortality with ASV. The pooled results for excessive sleepiness, cardiovascular disease,

hospitalizations, and patient-reported sleep quality did not meet the CMT. The TF also considered the effect of ASV on polysomnographic sleep architecture parameters and found a clinically meaningful effect on the arousal index. The potential benefits of ASV had a moderate effect size. The undesirable effect size was deemed small. The TF judged the potential benefits of ASV to outweigh the potential harms.

The overall certainty of evidence was low and was downgraded due to imprecision and risk of bias. The cost of ASV was considered moderate. There was no direct evidence that ASV would affect health equity; however, due to payor coverage variability and the need to access a sleep lab, the intervention might reduce health equity. Treatment with ASV was found to be acceptable and probably feasible to implement.

### *Recommendation 5: The AASM suggests using low-flow oxygen over no low-flow oxygen in adults with CSA due to HF. (Conditional recommendation, low certainty of evidence)*

The TF identified 7 RCTs and 3 observational studies. The study duration varied from 1 night to 1 year. The pooled estimates demonstrated clinically meaningful improvement in disease severity (AHI, CAI). The pooled results for excessive sleepiness and cardiovascular disease (6-minute walk distance) did not meet the CMT. There were reduced hospitalizations and improvements in patient-reported sleep quality, as measured by outcomes without prespecified CSTs. Though limited effects were seen on patient-related outcomes, a small effect size was seen on sleep-disordered breathing events. The TF identified 2 RCTs that reported on the presence of adverse events related to cardiac events. The undesirable effect size was deemed trivial. The TF judged that the potential benefits of low-flow oxygen outweigh the potential harms.

The overall certainty of evidence was low due to imprecision in both randomized and observational studies. All judgments were based on the studies evaluating low-flow oxygen treatment. The recommendation was limited to CSA in HF given the insufficient evidence in other forms of CSA. The cost of low-flow oxygen was considered moderate. There was no direct evidence that the low-flow oxygen would affect equity. However, it may not be covered by all payors and might reduce health equity. Treatment with low-flow oxygen was found to be acceptable and feasible to implement.

### *Recommendation 6: The AASM suggests using low-flow oxygen over no low-flow oxygen in adults with CSA due to high altitude. (Conditional recommendation, very low certainty of evidence)*

*Remarks: Patients with transient and mild CSA symptoms at high altitude may reasonably decline treatment with low-flow oxygen.*

The TF identified 1 randomized cross-over study of healthy volunteers at 3,800 m ascension and found a single night of low-flow oxygen therapy led to a clinically meaningful improvement in disease severity (ODI) after a single night of treatment. There were improvements in daytime functioning and quality of life for which there were no prespecified CMTs. However, there was no clinically meaningful improvement in excessive sleepiness. The potential benefits of low-flow oxygen had a moderate effect size. No adverse events were reported. The undesirable effect size was deemed trivial. The TF judged that the potential benefits of low-flow oxygen outweigh the potential harms.

The overall certainty of evidence was very low due to imprecision and risk of bias. The cost of the treatment was considered moderate. There is no direct evidence that the treatment would affect equity. However, low-flow oxygen may not be covered by all payors and might reduce health equity. There may be important uncertainty and variability about the value of outcomes depending on time spent and activities planned at altitude. The intervention was determined to be acceptable and probably feasible to implement.

### *Recommendation 7: The AASM suggests using oral acetazolamide over no acetazolamide in adults with CSA due to the following etiologies: primary CSA, CSA due to HF, CSA due to medication or substance use, treatment-emergent CSA, and CSA due to a medical condition or disorder. (Conditional recommendation, low certainty of evidence)*

The TF identified 3 RCTs where the study duration varied from 3 to 6 nights. The participants in the studies received a dosage of acetazolamide ranging from 250–1,000 mg. The pooled estimates showed clinically meaningful improvements in excessive sleepiness and disease severity (AHI) with no meaningful improvement in cardiovascular parameters. The potential benefits of acetazolamide had a moderate effect size. The undesirable effects were considered trivial and included paresthesia of hands and feet, impaired taste, and increased diuresis. The TF judged that the potential benefits of acetazolamide outweigh the potential harms.

The overall certainty of evidence was low due to imprecision. The cost of medication was considered negligible; the intervention was determined to be feasible to implement and acceptable. There was no direct evidence that the treatment would affect equity.

### *Recommendation 8: The AASM suggests using oral acetazolamide over no acetazolamide in adults with CSA due to high altitude. (Conditional recommendation, very low certainty of evidence)*

The TF identified 2 RCTs that demonstrated a clinically meaningful improvement in disease severity (AHI, desaturation index) and sleep architecture following 1–2 nights of treatment with 250 mg of acetazolamide. The potential benefits of acetazolamide had a moderate effect size. The undesirable effects were considered trivial and included paresthesia of hands and feet, impaired taste, and increased diuresis. The TF judged that the potential benefits of acetazolamide outweigh the potential harms.

The overall certainty of evidence was very low due to imprecision and indirectness. The cost of medication was considered negligible. There was no direct evidence that the treatment would affect health equity. The intervention was determined to be acceptable and feasible to implement.

### *Recommendation 9: The AASM suggests using transvenous phrenic nerve stimulation (TPNS) over no TPNS in adults with CSA due to the following etiologies: primary CSA and CSA due to HF. (Conditional recommendation, very low certainty of evidence)*

*Remark: Given that TPNS requires an invasive procedure, is not universally accessible, and is associated with high cost, it may be more appropriate to consider other treatments first.*

The TF identified 1 RCT, 4 observational studies, and 5 subgroup post hoc analyses and long-term follow-ups stemming from the RCT. The follow-up period was 6 months in the original RCT and 1 night to 12 months in the observational studies. Subgroups of the RCT were followed for 1, 3, and 5 years. The results demonstrated clinically meaningful improvement in excessive sleepiness, disease severity (CAI), and cardiac outcomes (6-minute walk distance) but no effect on mortality and left ventricular ejection fraction. The potential benefits of TPNS had a moderate effect size. Undesirable effects were considered small and included impending device pocket erosion, implant site hematoma and infection, lead dislodgment, lead displacement, and lead component failure. The TF judged that the potential benefits of TPNS outweigh the potential harms.

The overall certainty of evidence was very low due to imprecision in both randomized and observational studies. Although there was no direct evidence that the treatment would affect equity, due to its high cost, the need for a subspecialty cardiology service, and additional training of sleep technologists and physicians, the intervention might decrease overall health equity or disproportionately affect certain groups. The intervention's feasibility was thought to be low due to the resources needed to build the required infrastructure, including the availability of trained electrophysiologists capable of inserting the devices.

### No recommendations (or knowledge gap)

The TF used "no recommendation" when there was value in the findings but thought further research and innovation for this intervention is needed. There was insufficient and inconclusive evidence to make recommendations for the following: zolpidem or other hypnotics; BPAP with a backup rate in CSA due to HF; low-flow oxygen in primary CSA, CSA due to medication or substance, and treatment-emergent CSA; TPNS in CSA due to medication or substance and treatment-emergent CSA. The evidence is reported in the accompanying systematic review and supplemental materials.

## DISCUSSION

CSA remains a challenge for clinicians in both diagnosis and management.[18] Most forms of CSA, with the possible exception of opioid-induced CSA, share a common mechanism involving oscillatory ventilatory drive. This is typically caused by hyperpnea and increased chemosensitivity to carbon dioxide, which leads to recurrent central respiratory events during sleep.

The paucity of studies in every patient population and the shared pathogenesis necessitated grouping data across CSA subtypes with similar treatments. Safety data from studies on HF–associated CSA were used as a proxy to assess the safety of treatments in other CSA subtypes. The TF found this approach valuable for confirming the safety of interventions and the direction of their impact on specific outcomes. Nonetheless, the recommendations were still tailored to address individual CSA syndromes wherever possible.

In its comprehensive review of the literature, the TF noted that studies evaluating treatment of CSA remain dominated by short-term (weeks to months) studies evaluating positive airway pressure (PAP) devices, especially CPAP and ASV. The TF rarely encountered a trial that addressed long-term multiyear outcome of treatment with any modality. Furthermore, very few studies were powered to address long-term outcomes of interest such as mortality as identified during the planning phase of the systematic review.[10] The TF, therefore, attempted whenever possible to consider the longest available duration of therapy of any evaluable outcome.

Following the GRADE methodology,[3] the overall certainty of the evidence was low or very low across critical outcomes due to risk of bias, indirectness, and/or imprecision. The strength of the recommendations reflected the extent to which the TF was confident that the desirable effects of an intervention outweighed the undesirable effects, or vice versa, across the range of subgroup populations for whom the recommendation is intended. The smaller the net benefit or harm and the lower the certainty of evidence about the net effect, the more likely the TF was to conclude that a conditional recommendation for or against the intervention, as opposed to a strong recommendation, was appropriate. The balance of effect (desirable and undesirable effect) was assessed alongside values of people affected and resource use.

Finally, an important consideration when evaluating the literature and the TF's recommendation is the heterogeneity of the definition used for the classification of CSA and the exclusion of OSA in most studies.[18] Studies used various cutoffs of central to obstructive event ratios, resulting in some studies including patients who would be classified as having OSA under the current scoring criteria.[19] This practice may, to some extent, improve the "real world" relevance of the findings.

Despite the slow progress in CSA research, the period since the last AASM guidelines on CSA was notable for 2 important developments featured in these guidelines. The first is the development of the TPNS, a fully implantable neurostimulator that became approved by the Food and Drug Administration and commercially available (Remede, Zoll) in 2016. The second is the publication of a trial[12] addressing the safety and efficacy of a peak-flow-based ASV device in patients with HFrEF. These 2 developments underpin the major updates to the guidelines and are further discussed below.

### PAP therapies

CPAP continues to be widely used for CSA. In its review of the literature, the TF found that available studies investigating CPAP in patients with CSA have shown decreased AHI,[20–25] but only 1 study reported the effect of CPAP on central events specifically. Although CPAP has been used for CSA of varied etiologies, there is no established or widely accepted mechanism of action in any of these settings. A key question is whether CPAP's effects are mediated by the prevention of upper airway obstruction or by stabilizing the ventilatory control system. Overall, the TF found that the level of evidence was weak, which is reflected by the recommendation. Given that CPAP is widely available, and most sleep clinicians and

teams have extensive experience in its administration and management, it is a reasonable first consideration despite the weak evidence. However, given that CPAP is only effective at reducing AHI and has not been shown to consistently reduce the central events, it is critical to confirm responsiveness with sleep testing and review of PAP-generated data if this modality is used. Persistence of central apnea after an appropriate trial period of CPAP may warrant consideration of an alternative treatment modality.

BPAP without a backup rate is often initiated during PAP titration studies when CPAP alone fails to control central apnea. However, this mode is likely to worsen central apnea during sleep.[16] In fact, BPAP is often used as an experimental intervention to induce central apnea and periodic breathing during sleep.[17] Therefore, the TF recommended against using BPAP *without a backup rate* for treatment of CSA. Although BPAP inhibits ventilatory motor output, and hence may trigger central apnea, adding a backup rate renders the device a form of controlled ventilation and prevents the development of CSA. The initiation of BPAP with a backup rate is a pragmatic decision anchored in the need to treat the underlying condition. Expiratory PAP eliminates upper airway obstruction, which commonly coexists with CSA. Adding the combination of inspiratory PAP and a backup rate ensures a minimum level of ventilation, in contrast to BPAP without a backup rate, which may have the potential for exacerbating hyperventilation, central apneas, and hypocapnia.[15,16] BPAP with backup rate should be initiated based on a properly conducted PAP titration study that ensures stable breathing and control of airway patency. Routine monitoring of patients' response with review of device download, along with ventilatory and chemical parameters, is recommended.

Since its introduction, ASV has been highly effective in controlling central apneas in patients with various causes of CSA. However, enthusiasm for ASV decreased following the publication of the SERVE-HF trial,[26] an RCT that evaluated ASV in patients with HFrEF and found evidence of harm. The trial was designed to test the hypothesis that this device would decrease the composite end point that included mortality and cardiovascular events. The trial did not meet the primary end point. Further exploratory analysis showed an increased cardiovascular and all-cause mortality rate in the treatment group, raising concerns about the safety of ASV, and leading to the manufacturer's issuing a field safety notice[27] recommending against using ASV in patients with HFrEF and CSA.[1]

The TF faced the challenge of addressing the duality of a device that combined high efficacy and concern regarding increased mortality. Specifically, several RCTs demonstrate evidence of ASV's efficacy in decreasing disease severity, corroborated by evidence of improved quality of life and patient-reported outcomes in observational studies.[28–30] The TF deliberations were informed by a subsequent study using a different ASV device.[12] However, given the previously reported potential for harm using another type of ASV device, the TF decided to evaluate the class effect of ASV in patients with HFrEF and CSA. The TF approached the question with a hypothesized increased mortality and the expectation to confirm this effect as reported by SERVE-HF. Four published RCTs reported mortality.[10] Meta-analysis using GRADE methodology did not show any effect on mortality in patients with HFrEF and CSA. The finding was corroborated by the evaluated large observational studies.[31–33] Furthermore, the meta-analyses confirmed meaningful improvement in disease severity (AHI, ODI, CAI, CAHI, time with oxygen saturation < 90%, etc), whereas clinically meaningful improvement in daytime sleepiness was noted only in observational cohorts. Thus, it is the TF's assessment that the totality of the evidence warrants a conditional recommendation for ASV.

The systematic review did not support a class effect of ASV on mortality in patients with HFrEF. However, the analysis and the individual trials do not allow an unambitious conclusion regarding each type of ASV modality. The TF cannot therefore recommend a specific ASV device based on the available literature. However, the TF calls on device manufacturers, regulators, and federal funding agencies to sponsor research that can shed light on all aspects of CSA pathophysiology and the efficacy of ASV as well as other devices in patients with CSA. Complex ventilatory assist devices, such as ASV, have been produced by different manufacturers, each using their proprietary algorithm. These devices are rarely subjected to rigorous comparative bench or clinical evaluation. An important recent study[34] highlighted differences in the performance of various ASV devices in response to simulated respiratory events, demonstrating significant variability in delivered therapy based on the device algorithm. One of these ASV devices was used in the ADVENT trial[12] with no associated harm in patients with HFrEF.

Given these evidence gaps, the TF emphasizes caution in using ASV for CSA treatment in patients with HFrEF by recommending regular monitoring in specialized sleep centers with expertise in these devices and in the management of HF. The TF also calls for further mechanistic research and urges funding agencies to support studies evaluating the safety and efficacy of ASV as well as other treatment modalities for CSA. The TF also strongly advises clinicians to engage in shared decision-making with patients, providing detailed discussions of the existing literature to inform treatment decisions.

A more recent hypothesis[35] suggests that Cheyne–Stokes respiration may be a compensatory or less harmful form of CSA or sleep-disordered breathing, potentially explaining the results of a trial evaluating ASV in CSA that did not show clinical benefit. However, this hypothesis needs to be tested and, if proven, can apply to all treatment modalities of CSA and not specifically ASV.

## Oxygen

Supplemental oxygen as treatment for CSA has been a subject of interest since the late 1980s. Several small RCTs and observational studies evaluated low-flow oxygen. Most of these studies had at least 8 weeks of follow-up allowing for evaluation of patient-reported outcome measures. Nevertheless, there were no reported benefits in sleepiness, insomnia, or exercise performance.

The individual response regarding breathing disturbances, symptoms, and consequences of the disease should be re-evaluated before prescribing oxygen over the long term.

Because oxygen treatment is available in many health care systems, this treatment option is clinically relevant. On the other hand, oxygen is currently not covered by all insurance companies, which limits patients' access to this option. Based on the reviewed evidence and these considerations, the TF provided a low certainty recommendation in favor of using low-flow oxygen for CSA in HF.

### Acetazolamide

Evidence to support the role of acetazolamide in CSA was limited for primary CSA, CSA due to HF, CSA due to medication or substance use, treatment-emergent CSA, CSA due to a medical condition or disorder, and CSA due to high altitude in adults, where it was found to reduce the AHI. There was an overall improvement in Epworth Sleepiness Scale scores. The change in left ventricular ejection fraction in the CSA due to HF group failed to meet the CMT. These results, however, are limited to a small number of studies, with small numbers of participants, and over a relatively short period of time (3–6 nights). Low-dose acetazolamide is generally well-tolerated but may cause side effects such as paresthesia, altered taste, hypokalemia, and, rarely, an increased risk of kidney stones. Overall, the TF felt these side effects were trivial. Although the TF felt the certainty of evidence for acetazolamide was low and outcomes focused mainly on central AHI, rather than objective cardiac markers or quality of sleep or life, they felt the balance of effects favored the use of acetazolamide. The TF felt the cost of acetazolamide to be negligible and the treatment to be acceptable and feasible. There were no studies of resource requirements or cost-effectiveness. Given that CSA due to HF or high altitude is characterized by hyperventilation, the TF raised concerns that acetazolamide, a respiratory stimulant, may disturb acid–base balance and electrolytes, which could lead to arrhythmias. Thus, if a 2- to 4-week trial of acetazolamide was to be considered as a replacement or additional diuretic, a follow-up assessment of electrolytes is recommended in addition to AHI, sleep quality, cardiac function, and side effects. The TF recommended that future research of acetazolamide should include assessment of ventilation during sleep, quality of sleep and life, plus objective markers of cardiac function, and electrolytes.

### Treatment of CSA due to high altitude

Low-flow oxygen (very low certainty) and acetazolamide (very low certainty) have been shown to acutely reduce the severity of CSA due to high altitude, as measured by the AHI or ODI.[36–39] It is notable that reduced AHI or ODI may not necessarily translate into improvements in subjective or objective sleep quality or daytime symptoms. Given the low risk, low cost, and feasibility of these interventions, however, the task force felt it was reasonable to pursue low-flow oxygen or acetazolamide as treatment options if individuals were concerned about developing CSA or were symptomatic with CSA at altitude. Because studies typically involved only 1 or 2 nights of therapy, the task force could not make recommendations about the duration of therapy, especially because some individuals may eventually acclimate over time.

Notably, CSA due to high altitude is a transient condition that does not always require intervention. CSA or periodic breathing, typically occurring during non-rapid eye movement sleep, develops commonly in those who ascend to high altitudes (> 2,500 m), including in healthy individuals.[40–48] Many will acclimate over time while at altitude with either resolution of CSA events or resolution of sleep-related symptoms.[49–52] The definitive treatment for high altitude–related CSA is descent. CSA is thought to develop as a function of alterations in acid–base status, chemo-responsiveness, and ventilatory control in response to high-altitude hypobaric hypoxemia.[53–55] The clinical significance of CSA at altitude is unknown, though it does not appear to be directly related to the risk of high-altitude pulmonary or cerebral edema.[56,57]

It is worth noting that OSA is a highly prevalent disease that may also worsen at altitude. There are theoretical risks whereby CPAP use at altitude when used to treat OSA may either induce, worsen, or improve CSA at altitude. This is an area that requires further study because OSA is a highly prevalent disorder, and individuals will require guidance about continuing CPAP for OSA at altitude (as it pertains to CSA risk).

### TPNS

The evidence supporting the use of TPNS primarily comes from 1 RCT that enrolled 151 participants, 64% of whom had CSA due to HF, and 11% had primary CSA.[13] Patients with opioid-related CSA were excluded from the study. Because TPNS targets central apneas specifically, the ideal candidate for this treatment is a patient with few obstructive events. The RCT evaluated TPNS over a 6-month period, with extended follow-up reported for smaller cohorts lasting up to 5 years.[58–60] The study found improvements in central event indices, oxygen desaturation index, quality of life, and several sleep architecture measures.

The cost and availability of TPNS therapy may be prohibitive for many patients. Establishing a successful TPNS program requires substantial infrastructure and training for both cardiologists (electrophysiologists) and sleep specialists to manage these patients. The cost, invasive nature of the procedure, and the resources needed—combined with the relatively small sample size of published studies and the lack of comprehensive long-term follow-up—tempered the positive trial results in the task force's assessment. Consequently, the task force issued a conditional recommendation for TPNS as an option for patients with primary CSA and CSA due to HF.

## CONCLUSIONS

Studies regarding the treatment of CSA have received substantially less attention than obstructive sleep apnea. PAP, in all its modalities, has received the lion's share of research on treatment modalities of CSA. However, whether long-term, clinically important outcomes are improved remains an open question. The introduction of TPNS provides a promising option that awaits long-term outcome data. The guidelines are based on relatively small studies and do not address real-world barriers to CSA care, including variability in the diagnosis of

CSA, device access, and insurance hurdles. Overall, limitations in existing studies precluded strong recommendations for any intervention and highlight the need for mechanistic studies to identify and test optimal interventions for CSA treatment.

## ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
ASV, adaptive servo-ventilation
BPAP, bilevel positive airway pressure
CAHI, central apnea-hypopnea index
CAI, central apnea index
CMT, clinically meaningful threshold
CPAP, continuous positive airway pressure
CPG, clinical practice guideline
CSA, central sleep apnea
GRADE, Grading of Recommendations Assessment, Development and Evaluation
HF, heart failure
HFrEF, heart failure with reduced ejection fraction
ODI, oxygen desaturation index
OSA, obstructive sleep apnea
PAP, positive airway pressure
RCT, randomized controlled trial
TF, task force
TPNS, transvenous phrenic nerve stimulation

## REFERENCES


1. Aurora RN, Bista SR, Casey KR, et al. Updated adaptive servo-ventilation recommendations for the 2012 AASM guideline: "the treatment of central sleep apnea syndromes in adults: practice parameters with an evidence-based literature review and meta-analyses". *J Clin Sleep Med.* 2016;12(5):757–761.
2. Aurora RN, Chowdhuri S, Ramar K, et al. The treatment of central sleep apnea syndromes in adults: practice parameters with an evidence-based literature review and meta-analyses. *Sleep.* 2012;35(1):17–40.
3. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64(4):383–394.
4. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd edition, text revision. Darien, IL: American Academy of Sleep Medicine; 2023.
5. Badr MS. Central sleep breathing disorders: a critical evaluation of classification and diagnosis. *Curr Sleep Med Rep.* 2024;10(3):314–319.
6. Randerath WJ, Treml M, Priegnitz C, Stieglitz S, Hagmeyer L, Morgenstern C. Evaluation of a noninvasive algorithm for differentiation of obstructive and central hypopneas. *Sleep.* 2013;36(3):363–368.
7. Khayat R, Jarjoura D, Porter K, et al. Sleep disordered breathing and post-discharge mortality in patients with acute heart failure. *Eur Heart J.* 2015;36(23):1463–1469.
8. Brack T, Randerath W, Bloch KE. Cheyne-Stokes respiration in patients with heart failure: prevalence, causes, consequences and treatments. *Respiration.* 2012;83(2):165–176.
9. Agrawal R, Sharafkhaneh A, Gottlieb DJ, Nowakowski S, Razjouyan J. Mortality patterns associated with central sleep apnea among veterans: a large, retrospective, longitudinal report. *Ann Am Thorac Soc.* 2023;20(3):450–455.
10. Badr MS, Khayat RN, Allam JS, et al. Treatment of central sleep apnea in adults: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med.* 2025;21(12):2213–2236.
11. Dempsey JA. Central sleep apnea: misunderstood and mistreated! *F1000Res.* 2019;8:F1000 Faculty Rev-981.
12. Bradley TD, Logan AG, Lorenzi Filho G, et al. Adaptive servo-ventilation for sleep-disordered breathing in patients with heart failure with reduced ejection fraction (ADVENT-HF): a multicentre, multinational, parallel-group, open-label, phase 3 randomised controlled trial. *Lancet Respir Med.* 2024;12(2):153–166.
13. Costanzo MR, Ponikowski P, Javaheri S, et al. Transvenous neurostimulation for central sleep apnoea: a randomised controlled trial. *Lancet.* 2016;388(10048):974–982.
14. Morgenthaler TI, Deriy L, Heald JL, Thomas SM. The evolution of the AASM clinical practice guidelines: another step forward. *J Clin Sleep Med.* 2016;12(1):129–135.
15. Meza S, Mendez M, Ostrowski M, Younes M. Susceptibility to periodic breathing with assisted ventilation during sleep in normal subjects. *J Appl Physiol (1985).* 1998;85(5):1929–1940.
16. Johnson KG, Johnson DC. Bilevel positive airway pressure worsens central apneas during sleep. *Chest.* 2005;128(4):2141–2150.
17. Xie A, Skatrud JB, Puleo DS, Rahko PS, Dempsey JA. Apnea-hypopnea threshold for $CO_2$ in patients with congestive heart failure. *Am J Respir Crit Care Med.* 2002;165(9):1245–1250.
18. Kundel V, Ahn A, Arzt M, et al. Insights, recommendations, and research priorities for central sleep apnea: report from an expert panel. *J Clin Sleep Med.* 2025;21(2):405–416.
19. Troester MM, Quan SF, Berry RB, et al; for the American Academy of Sleep Medicine. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications.* Version 3. Darien, IL: American Academy of Sleep Medicine; 2023.
20. Bradley TD, Logan AG, Kimoff RJ, et al. Continuous positive airway pressure for central sleep apnea and heart failure. *N Engl J Med.* 2005;353(19):2025–2033.
21. Granton JT, Naughton MT, Benard DC, Liu PP, Goldstein RS, Bradley TD. CPAP improves inspiratory muscle strength in patients with heart failure and central sleep apnea. *Am J Respir Crit Care Med.* 1996;153(1):277–282.
22. Naughton MT, Benard DC, Liu PP, Rutherford R, Rankin F, Bradley TD. Effects of nasal CPAP on sympathetic activity in patients with heart failure and central sleep apnea. *Am J Respir Crit Care Med.* 1995;152(2):473–479.
23. Naughton MT, Benard DC, Rutherford R, Bradley TD. Effect of continuous positive airway pressure on central sleep apnea and nocturnal PCO2 in heart failure. *Am J Respir Crit Care Med.* 1994;150(6 Pt 1):1598–1604.
24. Naughton MT, Liu PP, Bernard DC, Goldstein RS, Bradley TD. Treatment of congestive heart failure and Cheyne-Stokes respiration during sleep by continuous positive airway pressure. *Am J Respir Crit Care Med.* 1995;151(1):92–97.
25. Teschler H, Döhring J, Wang YM, Berthon-Jones M. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure. *Am J Respir Crit Care Med.* 2001;164(4):614–619.
26. Cowie MR, Woehrle H, Wegscheider K, et al. Adaptive servo-ventilation for central sleep apnea in systolic heart failure. *N Engl J Med.* 2015;373(12):1095–1105.
27. American Academy of Sleep Medicine. Special safety notice: ASV therapy for central sleep apnea patients with heart failure. https://aasm.org/special-safety-notice-asv-therapy-for-central-sleep-apnea-patients-with-heart-failure/. Accessed November 10, 2024.
28. Randerath WJ, Nothofer G, Priegnitz C, et al. Long-term auto-servoventilation or constant positive pressure in heart failure and coexisting central with obstructive sleep apnea. *Chest.* 2012;142(2):440–447.
29. Philippe C, Stoïca-Herman M, Drouot X, et al. Compliance with and effectiveness of adaptive servoventilation versus continuous positive airway pressure in the treatment of Cheyne-Stokes respiration in heart failure over a six month period. *Heart.* 2006;92(3):337–342.
30. Arzt M, Munt O, Pépin JL, et al. Effects of adaptive servo-ventilation on quality of life: the READ-ASV Registry. *Ann Am Thorac Soc.* 2024;21(4):651–657.
31. Oldenburg O, Wellmann B, Bitter T, et al. Adaptive servo-ventilation to treat central sleep apnea in heart failure with reduced ejection fraction: the Bad Oeynhausen Prospective ASV Registry. *Clin Res Cardiol.* 2018;107(8):719–728.
32. Sun P, Porter K, Randerath W, Jarjoura D, Khayat R. Adaptive servo-ventilation and mortality in patients with systolic heart failure and Central sleep apnea: a single-center experience. *Sleep Breath.* 2023;27(5):1909–1915.

33. Tamisier R, Damy T, Bailly S, et al. FACE study: 2-year follow-up of adaptive servo-ventilation for sleep-disordered breathing in a chronic heart failure cohort. *Sleep Med.* 2024;113:412–421.
34. Knitter J, Bailey OF, Poongkunran C, et al. Comparison of physiological performance of four adaptive servo ventilation devices in patients with complex sleep apnea. *Am J Respir Crit Care Med.* 2019;199(7):925–928.
35. Naughton MT. PRO: persistent central sleep apnea/Hunter-Cheyne-Stokes breathing, despite best guideline-based therapy of heart failure with reduced ejection fraction, is a compensatory mechanism and should not be suppressed. *J Clin Sleep Med.* 2018;14(6):909–914.
36. Fischer R, Lang SM, Leitl M, Thiere M, Steiner U, Huber RM. Theophylline and acetazolamide reduce sleep-disordered breathing at high altitude. *Eur Respir J.* 2004;23(1):47–52.
37. Hackett PH, Roach RC, Harrison GL, Schoene RB, Mills WJ Jr. Respiratory stimulants and sleep periodic breathing at high altitude. Almitrine versus acetazolamide. *Am Rev Respir Dis.* 1987;135(4):896–898.
38. Orr JE, Heinrich EC, Djokic M, et al. Adaptive servoventilation as treatment for central sleep apnea due to high-altitude periodic breathing in nonacclimatized healthy individuals. *High Alt Med Biol.* 2018;19(2):178–184.
39. Heinrich EC, Djokic MA, Gilbertson D, et al. Cognitive function and mood at high altitude following acclimatization and use of supplemental oxygen and adaptive servoventilation sleep treatments. *PLoS One.* 2019;14(6):e0217089.
40. Johnson PL, Edwards N, Burgess KR, Sullivan CE. Sleep architecture changes during a trek from 1400 to 5000 m in the Nepal Himalaya. *J Sleep Res.* 2010;19(1 Pt 2):148–156.
41. Kohler M, Kriemler S, Wilhelm EM, Brunner-LaRocca H, Zehnder M, Bloch KE. Children at high altitude have less nocturnal periodic breathing than adults. *Eur Respir J.* 2008;32(1):189–197.
42. Lombardi C, Meriggi P, Agostoni P, et al. High-altitude hypoxia and periodic breathing during sleep: gender-related differences. *J Sleep Res.* 2013;22(3):322–330.
43. Shogilev DJ, Tanner JB, Chang Y, Harris NS. Periodic breathing and behavioral awakenings at high altitude. *Sleep Disord.* 2015;2015:279263.
44. Salvaggio A, Insalaco G, Marrone O, et al. Effects of high-altitude periodic breathing on sleep and arterial oxyhaemoglobin saturation. *Eur Respir J.* 1998;12(2):408–413.
45. Zieliński J, Koziej M, Mańkowski M, et al. The quality of sleep and periodic breathing in healthy subjects at an altitude of 3,200 m. *High Alt Med Biol.* 2000;1(4):331–336.
46. Coote JH, Tsang G, Baker A, Stone B. Respiratory changes and structure of sleep in young high-altitude dwellers in the Andes of Peru. *Eur J Appl Physiol Occup Physiol.* 1993;66(3):249–253.
47. West JB, Peters RM Jr, Aksnes G, Maret KH, Milledge JS, Schoene RB. Nocturnal periodic breathing at altitudes of 6,300 and 8,050 m. *J Appl Physiol (1985).* 1986;61(1):280–287.
48. Latshang TD, Lo Cascio CM, Stöwhas AC, et al. Are nocturnal breathing, sleep, and cognitive performance impaired at moderate altitude (1,630-2,590 m)? *Sleep.* 2013;36(12):1969–1976.
49. Bloch KE, Latshang TD, Turk AJ, et al. Nocturnal periodic breathing during acclimatization at very high altitude at Mount Muztagh Ata (7,546 m). *Am J Respir Crit Care Med.* 2010;182(4):562–568.
50. Furian M, Bitos K, Hartmann SE, et al. Acute high altitude exposure, acclimatization and re-exposure on nocturnal breathing. *Front Physiol.* 2022;13:965021.
51. Moraga FA, Jiménez D, Richalet JP, Vargas M, Osorio J. Periodic breathing and oxygen supplementation in Chilean miners at high altitude (4200m). *Respir Physiol Neurobiol.* 2014;203:109–115.
52. Nussbaumer-Ochsner Y, Ursprung J, Siebenmann C, Maggiorini M, Bloch KE. Effect of short-term acclimatization to high altitude on sleep and nocturnal breathing. *Sleep.* 2012;35(3):419–423.
53. Shi XF, Carlson PJ, Kim TS, et al. Effect of altitude on brain intracellular pH and inorganic phosphate levels. *Psychiatry Res.* 2014;222(3):149–156.
54. Ainslie PN, Lucas SJ, Burgess KR. Breathing and sleep at high altitude. *Respir Physiol Neurobiol.* 2013;188(3):233–256.
55. Robbins PA. Role of the peripheral chemoreflex in the early stages of ventilatory acclimatization to altitude. *Respir Physiol Neurobiol.* 2007;158(2–3):237–242.
56. Bian SZ, Zhang C, Rao RS, Ding XH, Huang L. Systemic blood predictors of elevated pulmonary artery pressure assessed by non-invasive echocardiography after acute exposure to high altitude: a prospective cohort study. *Front Cardiovasc Med.* 2022;9:866093.
57. Van Osta A, Moraine JJ, Mélot C, Mairbäurl H, Maggiorini M, Naeije R. Effects of high altitude exposure on cerebral hemodynamics in normal subjects. *Stroke.* 2005;36(3):557–560.
58. Costanzo MR, Javaheri S, Ponikowski P, et al. Transvenous phrenic nerve stimulation for treatment of central sleep apnea: five-year safety and efficacy outcomes. *Nat Sci Sleep.* 2021;13:515–526.
59. Fox H, Oldenburg O, Javaheri S, et al. Long-term efficacy and safety of phrenic nerve stimulation for the treatment of central sleep apnea. *Sleep.* 2019;42(11):zsz158.
60. Costanzo MR, Ponikowski P, Coats A, et al. Phrenic nerve stimulation to treat patients with central sleep apnoea and heart failure. *Eur J Heart Fail.* 2018;20(12):1746–1754.


## ACKNOWLEDGMENTS

The authors thank GRADE methodologist Rebecca Morgan, PhD, MPH. The task force appreciates the insightful feedback provided by the external reviewers Najib Ayas, MD (University of British Columbia, Vancouver, Canada), Susmita Chowdhuri, MD (Wayne State University, Detroit, Michigan), and Esther Irene Schwarz, MD (University Hospital Zurich, Zurich, Switzerland). Additionally, the task force acknowledges the contributions of Uzma Kazmi, MPH and Kelly Keeler, MS, who provided staff support during the early phase of this project. The American Academy of Otolaryngology-Head and Neck Surgery and its Foundation affirmed the value of this guideline. This guideline was endorsed by the Alliance of Sleep Apnea Partners, the American Association for Respiratory Care, American Association of Sleep Technologists, the Australasian Sleep Association, the European Respiratory Society, the European Sleep Research Society, the Heart Failure Society of America, the Society of Anesthesia and Sleep Medicine, and the Society of Behavioral Sleep Medicine.

## SUBMISSION & CORRESPONDENCE INFORMATION

**Submitted for publication August 14, 2025**
**Accepted for publication August 14, 2025**
Address correspondence to: M. Safwan Badr, MD, MBA, Department of Internal Medicine, Wayne State University School of Medicine, 540 E. Canfield St., Detroit, MI 48201; Email: sbadr@med.wayne.edu

## DISCLOSURE STATEMENT

The development of this paper was funded by the American Academy of Sleep Medicine (AASM). Dr. Hyer is employed by the AASM. Dr. Mustafa is a paid consultant for the AASM and an affiliated member of the U.S. Grading of Recommendations Assessment, Development and Evaluation Network and the Evidence Foundation. Dr. Patil serves on the AASM Board of Directors and the Guideline Advisory Panel. Dr. Patil is a consultant for Primasun, Inc. Dr. Randerath received support for a speaking engagement from Philips Respironics (2023) and therefore did not participate in voting for the adaptive servo-ventilation recommendation. Dr. Won served on the Society of Anesthesia and Sleep Medicine Board of Directors (2018–2023) and is the immediate past president (2024–2026). No other task force members have relevant conflicts of interests to disclose.