Highlights of the Sleep and Breathing Conference 2025

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Shareable abstract (@ERSpublications)
The Sleep and Breathing Conference 2025 highlighted advances in precision diagnostics, personalised therapies beyond CPAP, and the use of novel markers and digital tools to improve the management of sleep disordered breathing. https://bit.ly/45UVfyz

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Abstract

The 2025 Sleep and Breathing Conference, co-hosted by the European Respiratory Society (ERS) and the European Sleep Research Society (ESRS), presented the latest advances in sleep disordered breathing and related fields. This comprehensive overview, written by Early Career Members of ERS Assembly 4, highlights the key scientific and clinical takeaways from the event. Symposia were dedicated to the pathophysiology of obstructive sleep apnoea (OSA), the role of intermittent hypoxia and autonomic dysregulation, diagnostic work-up, and treatment approaches for OSA, including the perspective of patients. Updates on central sleep apnoea, comorbid insomnia and sleep apnoea, obesity hypoventilation syndrome and sleep disordered breathing in neuromuscular disease were also presented. The event emphasised the importance of phenotyping, individualised treatment approaches and the integration of physiology into clinical decision-making in sleep disordered breathing.

Educational aims

- To provide an overview of current understanding of the pathophysiology of sleep disordered breathing.
- To explore emerging diagnostic tools and clinical assessment strategies in sleep medicine.
- To review established and novel treatment approaches for sleep-related breathing disorders.
- To highlight the importance of individualised and multidisciplinary approaches to patient care.
- To promote knowledge exchange and professional development among early career and experienced healthcare providers in respiratory and sleep medicine.

Introduction

Jointly organised by the European Respiratory Society (ERS) and the European Sleep Research Society (ESRS), the eighth Sleep and Breathing Conference took place in Antwerp (Belgium) in 2025. The Sleep and Breathing Conference is the largest European conference dedicated to this field and presents cutting-edge research and clinical advances in sleep disordered breathing. In 2025, the sessions offered new perspectives on sleep apnoea pathophysiology, management and treatment strategies, as well as an overview of other sleep disorders. Early career members had numerous opportunities to explore state-of-the-art treatment recommendations, the latest scientific findings and engage in valuable networking. This paper provides an overview of some of the most significant sessions and topics from the Sleep and Breathing Conference, written by early career members of ERS Assembly 4.

Symposium: intermittent hypoxia: from basic physiology to clinical practice

Silke Ryan (Dublin, Ireland) reviewed the pathophysiological responses to intermittent hypoxia (IH), emphasising the role of the hypoxia-inducible factor (HIF) in mediating transcriptional responses. HIF activation triggers an adaptive response to hypoxia, protecting cells from damage up to a certain threshold, which varies across different tissues. These adaptive responses are influenced primarily by individual and cellular or tissue susceptibility, as well as factors such as age and comorbidities. Inflammatory responses to IH are exacerbated by obesity, which transforms healthy adipose tissue into a dysfunctional state [1].

Sébastien Baillieul (Grenoble, France) presented animal models of IH that simulate various types of hypoxia (acute, chronic, with or without hypercapnia) by cyclically altering inspired gas composition, without involving respiratory effort. This approach closely mimics the hypoxic patterns seen in obstructive sleep apnoea (OSA). As early as 1992, IH exposure in rodents was shown to induce arterial hypertension and left ventricular hypertrophy, with the severity of IH correlating with the extent of cardiovascular remodelling [2]. Greater severity of the IH stimulus leads to dose-dependent adverse effects, whereas mild, brief IH may have beneficial effects on cardiac function [3]. However, results across IH models remain inconsistent due to varying experimental designs and confounding factors, such as sleep fragmentation, diet, weight changes and alterations in gut microbiota.

Frédéric Gagnadoux (Angers, France) addressed metrics of OSA severity and their relationship to clinical outcomes. He emphasised that the apnoea–hypopnoea index (AHI) correlates poorly with symptoms, cardiovascular events and mortality, limiting its utility in predicting outcomes and contributing to the inconclusive evidence regarding the cardiovascular benefits of continuous positive airway pressure (CPAP) therapy. However, there is considerable debate in the literature on this topic: emerging evidence highlights the importance of good long-term adherence to CPAP therapy, particularly in younger, sleepy patients with severe OSA and high hypoxaemic burden, as this group may gain the most cardiovascular benefit [4]. Notably, hypoxaemic burden, which captures both the depth and duration of oxygen desaturation following respiratory events, emerges as a more robust predictor. Hypoxaemic burden is independently associated with cardiovascular mortality, hypertension and the risk of major adverse cardiovascular events [5].

Symposium: markers of autonomic dysregulation and other non-hypoxaemia-related markers in OSA

Winfried Randerath (Solingen, Germany) emphasised the role of arousal threshold and loop gain in OSA. Low loop gain indicates reduced ventilatory response, but often predicts a better response to CPAP. Conversely, oscillatory ventilatory patterns during exercise suggest a high loop gain and worse prognosis [6]. Apnoeas may terminate through an arousal, particularly in low arousal threshold individuals, or *via* chemical drive at the recruitment threshold. Low arousal threshold is associated with stronger muscle activation, shorter apnoeas and shallower desaturations, but also with sympathetic activation, breathing instability and hypocapnia [7]. Polysomnographic traces can help infer endotypes, which has implications for treatment. Some pharmacological approaches, such as carbonic anhydrase inhibitors or combinations like zolpidem with atomoxetine–oxybutynin, can modify loop gain and arousal threshold [8].

Raphael Heinzer (Lausanne, Switzerland) discussed autonomic markers. Pulse transit time (PTT) – the delay between the ECG R wave and the peripheral pulse – may drop in response to apnoeas, sympathetic surges, periodic limb movements or arousals [9]. Pulse wave amplitude (PWA), which is derived from oximetry, reflects sympathetic activity. PWA drop indices, measuring frequency and duration, have been linked to increased cardiovascular risk. In large cohort studies, frequent PWA drops predicted adverse cardiovascular outcomes, while CPAP therapy mitigated this risk [10].

Carolina Lombardi (Milan, Italy) highlighted the significance of heart rate variability (HRV) and heart rate response (ΔHR) in OSA. HRV reflects autonomic balance and is influenced by sleep stage, posture and individual characteristics. Short-term HRV indicates acute responses to apnoeas, while long-term variability relates to prognosis. Typically, OSA causes bradycardia during events followed by tachycardia at event termination; the ΔHR is a strong predictor of mortality and CPAP efficacy [11]. β-blockers reduce these fluctuations, and reduced HRV has been linked to daytime sleepiness and cardiovascular risk.

Symposium: hypercapnia from bench to bedside

Francesco Fanfulla (Pavia, Italy) opened the symposium by exploring the complexity of central respiratory chemosensors, focusing particularly on carbon dioxide (CO_2)-sensitive regions like the retrotrapezoid nucleus (RTN). He described the RTN's distinctive vasodynamic properties, which limit rapid CO_2 washout and help sustain ventilatory drive. He also emphasised how large CO_2 fluctuations can trigger arousal-related stress and lead to dyspnoea. In this context, hypercapnic hypoxia has been shown to elicit a

more pronounced and rapid increase in blood pressure, heart rate and sympathetic activity than hypocapnic hypoxia, while also contributing to impaired renal function [12].

Winfried Randerath (Solingen, Germany) provided an overview of the pathophysiology of hypercapnia caused by hypoventilation. Sleep-related hypoventilation is typically assessed through arterial carbon dioxide tension (P_{aCO_2}) or its surrogates, such as end-tidal carbon dioxide tension (P_{ETCO_2}) or transcutaneous carbon dioxide tension (P_{tcCO_2}). Long-term capnometry is recommended for patients who appear normocapnic while awake but exhibit symptoms or risk factors for sleep-related or latent hypoventilation, as well as for those with sleep apnoea who may be at risk of concurrent nocturnal hypoventilation [13]. Both P_{tcCO_2} and P_{ETCO_2} measurement are affected by potential errors when estimating real P_{aCO_2}. However, SCHWARZ *et al.* [14] demonstrated that P_{ETCO_2} severely underestimates P_{aCO_2}, while transcutaneous P_{tcCO_2} showed a much smaller bias.

Jean-Louis Pépin (Grenoble, France) addressed key challenges in managing obesity hypoventilation syndrome (OHS), emphasising its increasing prevalence with higher obesity classes and the associated elevated risk of adverse outcomes. PÉPIN *et al.* [15] found that OHS patients requiring noninvasive ventilation (NIV) after acute intensive care unit hospitalisation had a significantly higher mortality risk, with the worst prognosis regardless of gender, age or comorbidities. In OHS, hypercapnia results from increased work of breathing, impaired central respiratory drive, and sleep-related breathing disturbances [15]. Moreover, a mismatch between CO_2 build-up during prolonged apnoeic events and insufficient ventilatory compensation afterwards further contributes to the development of daytime hypoventilation [16].

Symposium: sleep disorders in women

J. Theorell-Haglöw (Uppsala, Sweden) opened the session on sleep disorders in women, highlighting how these conditions evolve and vary across a woman's lifespan. Notably, the prevalence of OSA increases by >50% in the postmenopausal period in women. During menopause and the years following, the incidence of insomnia, general sleep disturbances and sleep disordered breathing all increase, while both sleep duration and sleep quality tend to decline. HAUFE *et al.* [17] suggest that this may be linked to decreased levels of oestrogen and progesterone during this transitional phase.

Sophia Schiza (Heraklion, Greece) emphasised that women often present with different and more atypical symptoms of OSA when compared to men, which contributes to frequent underdiagnosis or misdiagnosis of OSA in women. Instead of the classic symptoms, like loud snoring or observed apnoeas, women are more likely to report bad sleep quality, fatigue, morning headaches and depressive symptoms. One review noted that women typically have a lower AHI than men, but are more likely to experience rapid eye movement (REM)-related OSA, which is characterised by apnoeas occurring predominantly during REM sleep [18]. From a pathophysiological perspective women with OSA also exhibit unique characteristics. Premenopausal women tend to have a less collapsible upper airway when compared to men, although airway length can increase with age particularly during and after menopause. Women usually begin at a lower baseline level of ventilatory response to hypoxia and sustain a more stable response during sleep. Additionally, women typically have a lower metabolic rate, reduced respiratory drive instability (lower loop gain), and are influenced by progesterone, which can stimulate ventilation and enhance the contractility of upper airway muscles. Premenopausal women have lower arousal thresholds and display a predominantly subcutaneous and peripheral fat distribution, which may influence OSA presentation.

When discussing hypoventilation syndromes, in particular OHS, Esther I. Schwarz (Zurich, Switzerland) highlighted that women are often diagnosed with OHS around 10 years later than men. As a result, women tend to be older and present with more advanced stages of OHS at the time of diagnosis. Despite experiencing more severe hypoxaemia and hypercapnia, women are less likely to be prescribed positive airway pressure therapy (NIV or CPAP) when discharged from the hospital. Once adjusted for age, gender was found to not be independently associated with more severe clinical outcomes [19]. All these differences between men and women underscore the need to improve screening, diagnostic approaches and treatment strategies for sleep disorders tailored to women.

Symposium: comorbid insomnia and sleep apnoea

Alexander Sweetman (Bridgewater, Australia), who introduced the acronym COMISA (comorbid insomnia and sleep apnoea), Dirk Pevernagie (Gent, Belgium) and Johan Verbraecken (Edegem, Belgium) highlighted the difficulties in diagnosing and treating insomnia and OSA as comorbidities. In the general population ~10% have one of the two diseases. However, their combined incidence (COMISA) is much higher, as 30–50% of OSA patients fulfil the criteria for insomnia and 30–40% of patients with insomnia fulfil the criteria for OSA [20]. OSA and insomnia share some of their typical symptoms like daytime

impairments and frequent awakenings from sleep, but together they have more severe adverse effects than either condition on its own. OSA and insomnia can exacerbate each other, resulting in a positive feedback loop. Insomnia comprises difficulty with sleep initiation, sleep maintenance or early awakening despite adequate sleep circumstances and is not solely due to another sleep disorder. Sleep maintenance insomnia, which is the most prevalent type of insomnia in COMISA, may indicate OSA; while sleep-onset or early awakening insomnia may indicate comorbid insomnia in OSA, but can lead to misdiagnosing OSA as insomnia. The speakers emphasised that this difficulty raises the important question of whether insomnia in patients with OSA is a secondary symptom or a comorbid condition (COMISA). Obvious patterns of secondary insomnia may include brief awakenings, easy return to sleep or improvement after CPAP therapy. The identification, assessment and diagnosis of COMISA directly impacts treatment approaches and outcomes. Assessing patients' medical history, polysomnography data, questionnaires like the Epworth Sleepiness Scale (ESS) or Insomnia Severity Index, sleep diaries, and CPAP device data aid in diagnosing COMISA, but there is still a need for a working definition. Last but not least, there is difficulty with treatment options for COMISA and the question which of the components should be treated first. Generally, CPAP therapy is the recommended treatment option for OSA, while cognitive behavioural therapy (CBTi) is intended for insomnia, which in the long-term is often maintained by underlying psychological and behavioural factors. However, CPAP therapy itself can provoke night-time awakenings. In addition, there is concern that insomnia may affect CPAP adherence as COMISA patients often have a low arousal threshold. CBTi may aggravate sleepiness through sleep deprivation and hypnotics may aggravate OSA. The speakers have shown that the combination of CPAP and CBTi has a greater effect on sleep maintenance insomnia compared with CPAP therapy alone [21]. In COMISA patients with predominant insomnia, starting CBTi first is recommended. If OSA is predominant, starting CPAP first is the advised therapy initiation. It was noted that non-CPAP therapies for OSA have rarely been studied in the context of COMISA.

Symposium: hypoventilation and other respiratory disorders

Renaud Tamisier (Grenoble, France) opened the session by emphasising the growing impact of obesity, with rates rising across Europe and globally. Obesity is well known to increase all-cause mortality risk. In affected individuals, impaired lung mechanics and leptin resistance often coexist, contributing synergistically to the development and worsening of hypercapnia. Four stages of hypoventilation in obese patients have been described, ranging from intermittent nocturnal hypercapnia with daytime recovery (stage I) to sustained daytime hypercapnia with comorbidities, defining OHS (stage IV) [22]. Compared to individuals with OSA, patients with OHS engage in lower levels of physical activity; however, structured exercise interventions have been shown to lower blood pressure and improve cardiovascular outcomes in this population [23]. Pressure-supported ventilation remains a key component in the management of sleep-related hypoventilation, helping to improve both sleep efficiency and quality, as reflected by better Pittsburgh Sleep Quality Index scores, and reducing daytime sleepiness, as measured by the ESS. Renaud Tamisier concluded his talk by outlining future directions, highlighting promising new therapies targeting leptin and orexin receptors as potential strategies to restore ventilatory drive.

Mafalda Van Zeller (Porto, Portugal), presenting on the topic of COPD–OSA overlap (OVS), began by addressing the prevalence of OVS within both the OSA and COPD populations. She went on to explain that the combination of COPD-related chronic hypoventilation and OSA-induced intermittent desaturation markedly increases nocturnal hypoxaemic burden and exacerbates cardiovascular strain. This synergistic hypoxia is reflected in heightened systemic inflammation: patients with OVS exhibit elevated levels of interleukin-6, high sensitivity C-reactive protein and granulocyte colony-stimulating factor compared to healthy controls and those with isolated OSA. Additionally, leukocyte and neutrophil counts are significantly higher [24]. Clinically, OVS tends to present with more frequent and severe exacerbations, higher rates of hospitalisation and greater mortality than either COPD or OSA alone. CPAP therapy has been shown to help reduce these risks and improve overall outcomes [25]. Future perspectives include nocturnal high-flow oxygen therapy as a potentially effective alternative, showing promising results in reducing respiratory events during sleep.

Anita Simonds (London, UK) provided an overview of neuromuscular disorders and sleep in adults, with a particular focus on the role of NIV. She emphasised that nocturnal hypoventilation can sometimes develop silently, without daytime abnormalities or symptoms, making early detection through sleep studies essential. In this context, current evidence indicates that in patients with amyotrophic lateral sclerosis (ALS), early initiation of NIV yields outcomes comparable to later initiation [26] Furthermore, initiating NIV in uncomplicated stable patients with ALS at home results in similar adherence to inpatient initiation, with the added benefit of faster treatment onset and no loss of efficacy [27]. Nevertheless, we know that persistent obstructive apnoeas during NIV significantly reduce survival benefit in ALS.

Symposium: central sleep apnoea

Renaud Tamisier (Grenoble, France) focused on the phenotypes of central sleep apnoea (CSA), emphasising the heterogeneity among CSA patients in terms of ventilation patterns, aetiologies, sociocultural backgrounds and clinical presentations. Different ventilation patterns have been identified, including high loop gain with an excessive ventilatory response, for example, Cheyne–Stokes respiration seen in heart failure, and a limited ventilatory response to CO_2. With the aim of better exploring CSA phenotypes, real-world European registries have sought to categorise CSA patients into subgroups such as treatment-emergent CSA, cardiovascular disease-related CSA, neurological disease-related CSA, idiopathic CSA and drug-induced CSA [28]. Within the cardiovascular group, distinct CSA phenotypes may correspond to specific subtypes of heart failure patients who, through precise identification and characterisation, could respond differently to personalised therapeutic approaches. Thus, cluster analyses have been conducted to characterise patient features and prognosis, aiming to tailor treatment options for individual patients [29].

Moving on to treatment options, Sébastien Baillieul (Grenoble, France) highlighted that therapeutic decisions should be guided primarily by patient symptoms, particularly in heart failure patients, in whom the presence of CSA and Cheyne–Stokes respiration is associated with a poor prognosis. When evaluating the impact of treatment on patient outcomes, it is essential to carefully assess each individual's condition, as CSA patients exhibit diverse clinical histories and pathophysiological profiles. Both the ADVENT-HF trial and the real-world FACIL-VAA study demonstrated that adaptive servo-ventilation (ASV) can effectively improve symptoms in patients with CSA. Overall, CSA treatment has the potential to positively influence health trajectories, relieve symptoms and enhance quality of life [30].

Winfried Randerath (Solingen, Germany) reviewed the recent evidence on ASV in CSA, that built the background for new recommendations and statements by the ERS and the American Academy of Sleep Medicine (AASM). Following the SERVE-HF trial, ASV was contraindicated in patients with CSA and heart failure with reduced ejection fraction. However, more recent randomised controlled trials and observational studies using current devices and optimised settings provide new evidence that needs to be considered. By stratifying patients according to phenotypes, it may be possible to identify clusters who would benefit most from ASV therapy [31]. Although the ADVENT-HF trial was statistically underpowered to conclude on the effect of ASV on mortality in CSA [32], it reported no safety concerns alongside improvements in sleep architecture, symptoms and quality of life. Notably, the ASV algorithms and pressure settings used in ADVENT-HF differed from those in SERVE-HF. Updated statements and recommendations from the ERS task force and AASM on CSA treatment are expected in the near future.

Symposium: pharmacotherapy in sleep apnoea: from endophenotypic traits to personalised treatments

Elisa Perger (Milan, Italy) opened the session by presenting promising treatment strategies for OSA that target muscle responsiveness, upper airway collapsibility and loop gain. In terms of muscle reactivation during sleep, nasal administration of a non-selective potassium (K[?]) channel antagonist has been shown to enhance upper airway muscle activity and reduce pharyngeal collapsibility in both animal models and humans [33]. Additionally, the combination of a noradrenergic agent with an antimuscarinic drug effectively reactivates dilator muscle activity during sleep, with the atomoxetine and aroxybutynin combination being the most extensively studied [34]. Regarding CSA, beyond acetazolamide, which is known to reduce plant gain, agents such as buspirone and purinergic antagonists are emerging as potential treatments targeting the controller gain [35].

Jan Hedner (Gothenburg, Sweden) focused on the role of carbonic anhydrase inhibitors in modulating loop gain. Drugs like acetazolamide and sulthiame improve OSA by inducing bicarbonaturia and mild hyperchloraemic acidosis, which shifts the hypercapnic ventilatory response curve to the left, thereby dampening loop gain. This effect may also be mediated through a HIF-1α-related pathway [36].

Turning to wake-promoting agents for residual sleepiness, Jean-Louis Pépin (Grenoble, France) highlighted that while CPAP improves sleepiness and attention in most patients, 10–15% continue to experience residual sleepiness. Before prescribing stimulants, it is crucial to optimise CPAP therapy, perform polysomnography under treatment, assess lifestyle factors and exclude other causes. Solriamfetol has been shown to improve sleepiness and reaction time but may elevate blood pressure [37], whereas pitolisant offers a modest (three-point) reduction in the ESS score without cardiovascular side-effects [38].

Symposium: targeting the upper airway in OSA

Emily Schoustra (Amsterdam, the Netherlands) opened her presentation by introducing the VOTE classifications and illustrating the main indications for drug-induced sleep endoscopy (DISE), highlighting

upper airway surgery and hypoglossal nerve stimulation (HGNS) as primary uses, with oral appliance therapy and positional therapy also considered appropriate options. Under DISE, various oropharyngeal collapse patterns can be observed. Among them, complete concentric collapse of the palate (CCCp) is a negative predictor for the success of surgery (pharyngoplasty), mandibular advancement device and HGNS. While CCCp correlates with body mass index (BMI), no specific BMI cut-off reliably predicts its presence. AHI, tonsil size and neck circumference improve prediction of upper airway collapse type, but due to its multifactorial nature, DISE remains the only definitive diagnostic tool [39]. Additionally, pharyngeal opening pressure (PhOP), the minimum pressure needed to restore non-flow-limited breathing, has been shown to correlate with higher BMI, younger age, elevated AHI and lower oxygen saturation nadir [40].

Alan R. Schwartz (Pennsylvania, USA) introduced his session by illustrating hypoglossus stimulation systems. HGNS is more effective in patients with obstructive hypopnoeas rather than full apnoeas, aligning with evidence linking higher PhOP to poorer HGNS outcomes. Additionally, a higher arousal threshold significantly predicts better treatment response [41]. Pharyngeal shape also offers predictive value: a lower anteroposterior-to-lateral diameter ratio indicates higher critical closing pressure, which correlates with elevated PhOP and reduced HGNS efficacy [42]. Alan R. Schwartz concluded by presenting a promising new target: the ansa cervicalis (AC), whose stimulation reduces lateral wall collapse without tongue advancement, as seen with hypoglossal stimulation, significantly lowering collapsibility under DISE [43].

Johan Verbraecken (Antwerp, Belgium) opened his talk by discussing pharmacological approaches targeting upper airway muscle responsiveness. Among these, the combination of noradrenergic and antimuscarinic agents, particularly atomoxetine and oxybutynin, has shown the most promise, achieving up to a 60% reduction in AHI and significantly increasing genioglossus activity. While monotherapy yields minimal benefit, combined use has led to clinically meaningful improvements in a substantial subset of patients, with off-label use currently feasible given both drugs are already marketed [44]. The final part of

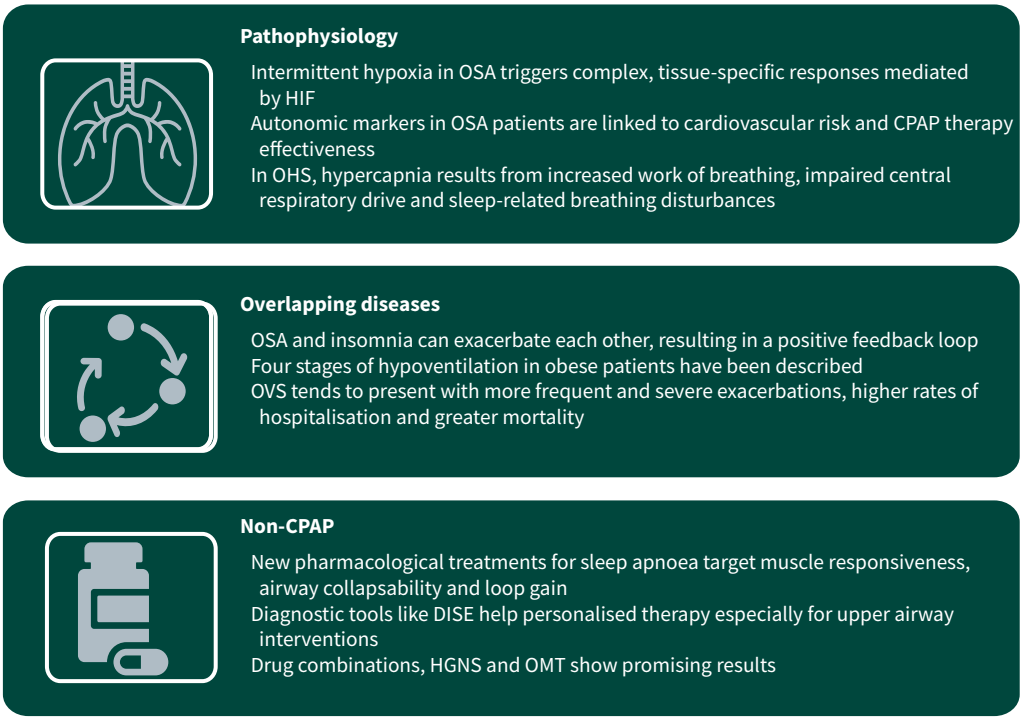

FIGURE 1 Summary of key themes from the Sleep and Breathing Conference 2025. OSA: obstructive sleep apnoea; HIF: hypoxia-inducible factor; CPAP: continuous positive airway pressure; OHS: obesity hypoventilation syndrome; OVS: overlap syndrome; DISE: drug-induced sleep endoscopy; HGNS: hypoglossal nerve stimulation; OMT: orofacial myofunctional therapy.

the presentation focused on highlighting the role of orofacial myofunctional therapy (OMT). Although not yet widely accessible, OMT has shown promising results in some studies, with reductions in AHI of up to 50% [45]. The ERS guidelines recognise OMT as a non-CPAP therapeutic option, which is particularly recommended when other treatments are not feasible or have failed [46].

Take home message

The Sleep and Breathing Conference 2025 showcased the dynamic and evolving landscape of sleep medicine with a focus on sleep disordered breathing, emphasising the growing importance of precision diagnostics, individualised treatment and interdisciplinary collaboration. Advances in understanding the pathophysiology of sleep disordered breathing, ranging from intermittent hypoxia to autonomic and metabolic consequences, are reshaping how we assess and manage these conditions. The conference highlighted the limitations of traditional metrics like the AHI and the relevance of other sleep study markers, such as hypoxaemic burden and surrogate markers of autonomic disturbance. Novel therapies, both pharmacological and device-based, are expanding the toolbox beyond CPAP, offering new hope for patients with complex phenotypes, including those with CSA, COMISA and OHS (figure 1). Further research is needed to refine phenotyping tools, validate novel biomarkers and assess long-term outcomes of emerging therapies. Integration of real-world data, digital health technologies and personalised approaches will be essential to advance sleep medicine and improve patient care.

Key points

- Intermittent hypoxia and hypercapnia drive systemic inflammation and cardiovascular risk in OSA.
- CSA has a wide range of causes and requires phenotype-based treatment recommendations.
- OHS is associated with OSA, hypoventilation due to a high load on the upper airway, respiratory muscle pump and decreased respiratory drive, and hypoxaemia due to ventilation–perfusion mismatch, which must be considered in the treatment of sleep disordered breathing.
- Tailored therapies beyond CPAP improve outcomes in sleep disorders.

Self-evaluation questions

1. Which parameter has shown better prognostic value than AHI in predicting cardiovascular outcomes in OSA?
   a) Sleep latency
   b) Hypoxic burden
   c) Respiratory rate
   d) REM sleep duration
   e) Total sleep time
2. In COMISA (comorbid insomnia and sleep apnoea), what is the most evidence-based combined treatment approach?
   a) CPAP and antidepressants
   b) Sleep restriction alone
   c) CBTi and CPAP
   d) Melatonin and positional therapy
   e) Oxygen therapy and benzodiazepines
3. Which of the following traits is not typically associated with CSA phenotypes?
   a) Cheyne–Stokes respiration
   b) High loop gain
   c) Structural upper airway collapse
   d) Reduced CO sensitivity
   e) Post-heart failure status

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References

1 Ryan S. Adipose tissue inflammation by intermittent hypoxia: mechanistic link between obstructive sleep apnoea and metabolic dysfunction. *J Physiol* 2017; 595: 2423–2430.
2 Fletcher EC, Lesske J, Qian W, *et al.* Repetitive, episodic hypoxia causes diurnal elevation of blood pressure in rats. *Hypertension* 1992; 19: 555–561.
3 Lim DC, Brady DC, Soans R, *et al.* Different cyclical intermittent hypoxia severities have different effects on hippocampal microvasculature. *J Appl Physiol* 2016; 121: 78–88.

4 Bradicich M, Pengo MF, Steier J, *et al.* Cardiovascular effects of obstructive sleep apnoea and effects of continuous positive airway pressure therapy: evidence from different study models. *ERJ Open Res* 2025; 11: 00718-2024.
5 Trzepizur W, Blanchard M, Ganem T, *et al.* Sleep apnea–specific hypoxic burden, symptom subtypes, and risk of cardiovascular events and all-cause mortality. *Am J Respir Crit Care Med* 2022; 205: 108–117.
6 Kazimierczak A, Krzyżanowski K, Wierzbowski R, *et al.* Resolution of exercise oscillatory ventilation with adaptive servoventilation in patients with chronic heart failure and Cheyne–Stokes respiration: preliminary study. *Kardiol Pol* 2011; 69: 1266–1271.
7 Eckert DJ, Younes MK. Arousal from sleep: implications for obstructive sleep apnea pathogenesis and treatment. *J Appl Physiol* 2014; 116: 302–313.
8 Messineo L, Sands SA, Labarca G. Hypnotics on obstructive sleep apnea severity and endotypes: a systematic review and meta-analysis. *Am J Respir Crit Care Med* 2024; 210: 1461–1474.
9 Kwon Y, Wiles C, Parker BE, *et al.* Pulse arrival time, a novel sleep cardiovascular marker: the multi-ethnic study of atherosclerosis. *Thorax* 2021; 76: 1124–1130.
10 Solelhac G, Sánchez-de-la-Torre M, Blanchard M, *et al.* Pulse wave amplitude drops index: a biomarker of cardiovascular risk in obstructive sleep apnea. *Am J Respir Crit Care Med* 2023; 207: 1620–1632.
11 Messineo L, Sands SA, Schmickl C, *et al.* Treatment of sleep apnea and reduction in blood pressure: the role of heart rate response and hypoxic burden. *Hypertension* 2024; 81: 1106–1114.
12 Tamisier R, Nieto L, Anand A, *et al.* Sustained muscle sympathetic activity after hypercapnic but not hypocapnic hypoxia in normal humans. *Respir Physiol Neurobiol* 2004; 141: 145–155.
13 Ragette R. Patterns and predictors of sleep disordered breathing in primary myopathies. *Thorax* 2002; 57: 724–728.
14 Schwarz SB, Windisch W, Magnet FS, *et al.* Continuous non-invasive PCO_2 monitoring in weaning patients: Transcutaneous is advantageous over end-tidal PCO_2. *Respirology* 2017; 22: 1579–1584.
15 Pépin JL, Timsit JF, Tamisier R, *et al.* Prevention and care of respiratory failure in obese patients. *Lancet Respir Med* 2016; 4: 407–418.
16 Ayappa I, Berger KI, Norman RG, *et al.* Hypercapnia and ventilatory periodicity in obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2002; 166: 1112–1115.
17 Haufe A, Leeners B. Sleep disturbances across a woman's lifespan: what is the role of reproductive hormones? *J Endocr Soc* 2023; 7: bvad036.
18 Schiza SE, Bouloukaki I. Does gender matter: sex-specific aspects of symptoms, outcome, and therapy of obstructive sleep apnea. *Curr Opin Pulm Med* 2020; 26: 642–649.
19 Nowalk NC, Mokhlesi B, Neborak JM, *et al.* Gender differences in outcomes of ambulatory and hospitalized patients with obesity hypoventilation syndrome. *Chest* 2025; 167: 245–258.
20 Sweetman A, Lack L, McEvoy RD, *et al.* Bi-directional relationships between co-morbid insomnia and sleep apnea (COMISA). *Sleep Med Rev* 2021; 60: 101519.
21 Sweetman A, Lack L, Catcheside P, *et al.* Changes in initial, middle and late insomnia subtypes during CBT-i and CPAP therapy in co-morbid insomnia and sleep apnea (COMISA). *Sleep Medicine* 2019; 64: S370–S371.
22 Randerath W, Verbraecken J, Andreas S, *et al.* Definition, discrimination, diagnosis and treatment of central breathing disturbances during sleep. *Eur Respir J* 2017; 49: 1600959.
23 Karkala A, Baxevanidis A, Chasiotou A, *et al.* Comparison of physical activity and quality of life between obese individuals with obstructive sleep apnea syndrome and individuals with obesity hypoventilation syndrome. *Sleep Breath* 2024; 28: 2683–2691.
24 Sanchez-Azofra A, Gu W, Masso-Silva JA, *et al.* Inflammation biomarkers in OSA, chronic obstructive pulmonary disease, and chronic obstructive pulmonary disease/OSA overlap syndrome. *J Clin Sleep Med* 2023; 19: 1447–1456.
25 Marin JM, Soriano JB, Marin-Oto M, *et al.* Sleep-disordered breathing in patients with chronic obstructive pulmonary disease: prevalence and outcomes. *Ann Am Thorac Soc* 2025; 22: 1227–1235.
26 Vitacca M, Banfi P, Montini A, *et al*. Does timing of initiation influence acceptance and adherence to NIV in patients with ALS? *Pulmonology* 2020; 26: 45–48.
27 Réginault T, Bouteleux B, Wibart P, *et al.* At-home noninvasive ventilation initiation with telemonitoring in amyotrophic lateral sclerosis patients: a retrospective study. *ERJ Open Res* 2023; 9: 00438-2022.
28 Arzt M, Munt O, Pépin JL, *et al.* Registry on the treatment of central and complex sleep-disordered breathing with adaptive servo-ventilation (READ-ASV): protocol and cohort profile. *ERJ Open Res* 2023; 9: 00618-2022.
29 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.
30 Randerath W, Baillieul S, Tamisier R. Central sleep apnoea: not just one phenotype. *Eur Respir Rev* 2024; 33: 230141.
31 Tamisier R, Damy T, Bailly S, *et al.* Adaptive servo ventilation for sleep apnoea in heart failure: the FACE study 3-month data. *Thorax* 2022; 77: 178–185.

32 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: 153–166.

33 Osman AM, Mukherjee S, Altree TJ, *et al.* Topical potassium channel blockage improves pharyngeal collapsibility. *Chest* 2023; 163: 953–965.

34 Schweitzer PK, Taranto-Montemurro L, Ojile JM, *et al.* The combination of aroxybutynin and atomoxetine in the treatment of obstructive sleep apnea (MARIPOSA): a randomized controlled trial. *Am J Respir Crit Care Med* 2023; 208: 1316–1327.

35 Giannoni A, Borrelli C, Mirizzi G, *et al.* Benefit of buspirone on chemoreflex and central apnoeas in heart failure: a randomized controlled crossover trial. *Eur J Heart Fail* 2021; 23: 312–320.

36 Kumar S, Rulhania S, Jaswal S, *et al.* Recent advances in the medicinal chemistry of carbonic anhydrase inhibitors. *Eur J Med Chem* 2021; 209: 112923.

37 Schweitzer PK, Rosenberg R, Zammit GK, *et al.* Solriamfetol for excessive sleepiness in obstructive sleep apnea (TONES 3). A randomized controlled trial. *Am J Respir Crit Care Med* 2019; 199: 1421–1431.

38 Pépin J-L, Attali V, Caussé C, *et al.* Long-term efficacy and safety of pitolisant for residual sleepiness due to OSA. *Chest* 2024; 165: 692–703.

39 Schoustra E, Leentjens M, Van Maanen JP, *et al.* Predicting complete concentric collapse at the palatal level during drug-induced sleep endoscopy: an analysis of 1761 cases. *Sleep Breath* 2025; 29: 22.

40 Parekh M, Triantafillou V, Keenan BT, *et al.* Airway collapsibility during drug-induced sleep endoscopy relates with clinical features of obstructive sleep apnea. *Laryngoscope* 2024; 134: 1978–1985.

41 Op De Beeck S, Wellman A, Dieltjens M, *et al.* Endotypic mechanisms of successful hypoglossal nerve stimulation for obstructive sleep apnea. *Am J Respir Crit Care Med* 2021; 203: 746–755.

42 Dotan Y, Golibroda T, Oliven R, *et al.* Parameters affecting pharyngeal response to genioglossus stimulation in sleep apnoea. *Eur Respir J* 2011; 38: 338–347.

43 Li Y, Richard KE, Schwartz AR, *et al.* Quantitative effects of ansa cervicalis stimulation in obstructive sleep apnea. *Am J Respir Crit Care Med* 2023; 207: 1097–1099.

44 Perger E, Taranto-Montemurro L. Upper airway muscles: influence on obstructive sleep apnoea pathophysiology and pharmacological and technical treatment options. *Curr Opin Pulm Med* 2021; 27: 505–513.

45 De Felicio CM, Dias FV, Trawitzki LV. Obstructive sleep apnea: focus on myofunctional therapy. *Nat Sci Sleep* 2018; 10: 271–286.

46 Randerath W, Verbraecken J, de Raaff CAL, *et al.* European respiratory society guideline on non-CPAP therapies for obstructive sleep apnoea. *Eur Respir Rev* 2021; 30: 210200.

Suggested answers

1. b.
2. c.
3. c.