

Revising OSA Care Standards: Aligning Treatment with Phenotype

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Obstructive sleep apnea (OSA) is biologically heterogeneous, and distinct phenotypes show different treatment responses and adherence patterns. The current uniform, AHI-driven care is misaligned with how the disease actually presents in many patients.

Obstructive sleep apnea (OSA) is typically diagnosed and treated as a single, uniform disease. In reality, it is heterogeneous. Distinct phenotypes and endotypes can present similarly on a sleep study but respond very differently to treatment.

OSA reflects multiple underlying biological drivers and clinical presentations. While these may produce similar Apnea-Hypopnea Index (AHI) scores, real-world treatment response and long-term adherence vary widely. A meaningful proportion of this variability is predictable, not random.

Why “one-size-fits-all” OSA care falls short

AHI is the most widely used measure of OSA severity, but it correlates poorly with symptom burden and treatment needs across patient groups.¹ Despite these limitations, AHI remains the primary determinant of diagnosis, treatment eligibility and reimbursement across most health systems. It’s essentially a simplified view of a complex disease that’s effectively codified into policy.

It captures event frequency, but not the underlying mechanisms, timing or the influence of comorbidities on patient experience. When AHI-defined OSA is treated as a singular disease, it assumes treatment response will be similar across mild, moderate and severe patients.

As a result, non-adherence is often misclassified as a patient failure rather than a predictable consequence of the mismatch between therapy or care delivery and underlying phenotype. This has system-level consequences. It shapes reimbursement eligibility, limits access to alternative therapies, reinforces short-term compliance metrics, and ultimately undermines long-term disease control.

Phenotyping studies consistently show that patients with similar AHI values cluster into distinct groups based on symptoms and cardiovascular comorbidities.^{2,3} At the same time, therapeutic homogeneity reinforces this issue. Positive airway pressure (PAP) remains the default first-line therapy, and appropriately so, but long-term adherence is far from universal.

Nearly one in four patients in Japan discontinue PAP therapy within the first year, and about one-third

discontinue by year three. Comparable one-year discontinuation rates have been reported in the United States (18.9%) and France (23.1%).⁴

Adherence patterns also stabilize early, often within the first few months, highlighting the importance of getting treatment fit right from the outset.⁵

Evidence that phenotypes predict treatment response

A growing body of research shows that certain pathophysiologic traits can predict treatment response. These include upper airway anatomy, ventilatory control stability, arousal threshold and airway muscle responsiveness.

Patients with favorable anatomical traits and muscle responsiveness, for example, are more likely to respond to mandibular advancement devices (MADs).⁶ Similarly, patients with positional OSA have higher response rates to MADs than those with non-positional disease.⁷

Comorbid insomnia and sleep apnea (COMISA) is another clinically meaningful phenotype. Compared to OSA-only patients, COMISA patients tend to have less upper airway collapsibility and lower loop gain, alongside insomnia-related hyperarousal.⁸ This can lower arousal thresholds, alter disease presentation and make standard treatments harder to sustain.

Taken together, these findings reinforce that variability in treatment success is not purely behavioral. When phenotypes are considered, response patterns will become more predictable.

Early models of phenotype-informed stratification at the guideline level are already emerging. In Europe, the modified Baveno classification has begun to move beyond AHI by incorporating symptom burden and cardiovascular risk into treatment decisions.

How phenotyping can meaningfully shape OSA care

A phenotype-informed approach helps identify when treatments are likely to succeed as monotherapy, who may need additional support and where combination strategies should be introduced earlier.

Phenotypes should inform decision-making at three key points:

- **At diagnosis**

Phenotypes should be characterized at the point of diagnosis, not after PAP failure. AHI can be complemented with symptom clusters, hypoxic burden and positional or REM dominance to guide initial treatment and follow-up intensity. This requires guideline-level expansion of diagnostic frameworks beyond AHI alone.

- **At therapy selection and initiation**

Risk stratification should incorporate phenotypes associated with higher cardiovascular or mortality risk, to enable earlier treatment initiation and closer monitoring.

Treatment selection algorithms should be formalized within guidelines and payer policies, enabling access to combination or progressive therapies.

For instance, non-anatomical traits, such as heightened arousability in COMISA, should prompt the early inclusion of complementary therapies like CBT-I. And for positional OSA, positional therapy, oral appliances or combination strategies should be early considerations.

- **At early follow-up**

Declining adherence should be treated as clinical data. Early reassessment should be standardized as part of care pathways and reimbursed as a clinical decision point, not treated as optional follow-up.

Phenotypic heterogeneity must be a first-order care design principle

Real-world adherence to OSA therapies declines substantially early on, so durability must now be treated as a design criterion, not a downstream expectation.

Health systems do not require complex, research-level endotyping to act. They need updated and pragmatic frameworks, pathway redesign and reimbursement models that recognize heterogeneity as clinically actionable.

In practice, this means complementing AHI use with symptom and risk-based stratification, formalizing phenotype-informed treatment pathways and standardizing longitudinal follow up.

Without these changes, variability in outcomes will continue to be misattributed and adherence will remain a poor proxy for effectiveness rather than a signal of system design failure.

References

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