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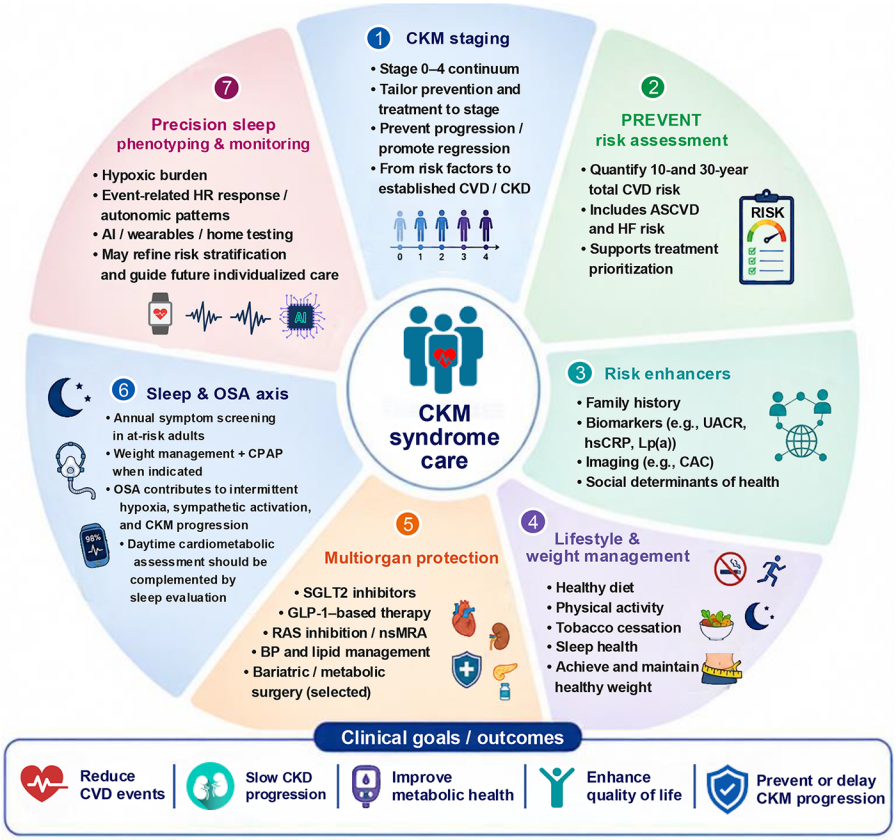
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Beyond organ silos

Integrated insights from the 2026 AHA/ACC/ADA/ASN cardiovascular–kidney–metabolic syndrome guideline

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Graphical abstract



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1. From concept to clinical practice: the 2026 CKM guideline

In 2026, the American Heart Association (AHA), American College of Cardiology (ACC), American Diabetes Association (ADA), and American Society of Nephrology (ASN) released the "Guideline for the Prevention, Detection, Evaluation, and Management of Cardiovascular-Kidney-Metabolic Syndrome."[1] Building on the 2023 AHA Presidential Advisory and companion scientific statement,[2,3] the guideline translates the cardiovascular–kidney–metabolic (CKM) framework into formal recommendations for prevention, staging, risk assessment, treatment selection, and longitudinal follow-up. Its principal advance is therefore not a new definition of CKM syndrome, but the operationalization of an interdisciplinary care pathway across the CKM continuum.

The guideline moves beyond isolated organ-based care. Obesity, hypertension, dysglycemia, albuminuria, heart failure, atrial fibrillation, coronary artery disease, and sleep-related breathing disorders frequently coexist and interact through inflammation, insulin resistance, neurohumoral activation, endothelial dysfunction, volume overload, and autonomic imbalance. The CKM framework therefore shifts attention from treating individual diagnoses to identifying a patient's position along a dynamic disease trajectory and addressing shared drivers of progression.

2. CKM staging, risk assessment, and multiorgan therapy

CKM staging provides an actionable framework for primordial and primary prevention at earlier stages and for the management of established cardiovascular, kidney, or advanced metabolic disease at later stages.[1] It reframes the clinical question from "Which disease should be treated first?" to "Which upstream driver should be targeted to prevent multiorgan deterioration?"

The PREVENT equations complement staging by estimating the 10-year and 30-year risk of total cardiovascular disease, including atherosclerotic cardiovascular disease and heart failure, among adults without established cardiovascular disease.[4] Compared with older risk tools, PREVENT includes variables that are more relevant to CKM health, such as body mass index and estimated glomerular filtration rate, with optional consideration of urine albumin-to-creatinine ratio, hemoglobin A1c, and social deprivation index.[4] Traditional atherosclerotic risk alone may not capture heart failure, kidney disease progression, or metabolic deterioration; PREVENT may therefore support patient-clinician discussions, treatment prioritization, and resource allocation.

The guideline also harmonizes cardioprotective, kidney-protective, and metabolic therapies. Lifestyle modification and weight management remain foundational, while sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide-1-based therapy, renin–angiotensin system inhibition, nonsteroidal mineralocorticoid receptor antagonists, and metabolic or bariatric surgery offer multiorgan benefits where appropriate.[1] Recent outcome trials reinforce this concept: the SELECT trial showed that semaglutide reduced major adverse cardiovascular events in adults with overweight or obesity and established cardiovascular disease without diabetes,[5] whereas FLOW demonstrated kidney and cardiovascular benefits in patients with type 2 diabetes and chronic kidney disease.[6] Obesity and metabolic dysfunction should therefore be treated as modifiable cardiovascular targets rather than background conditions.

3. Sleep and obstructive sleep apnea in the CKM continuum

The guideline's attention to sleep and obstructive sleep apnea (OSA) is particularly relevant to cardiovascular practice. Sleep health has already been incorporated into the AHA's Life's Essential 8 framework,[7] and OSA represents an important entry point for CKM care because it is prevalent, mechanistically linked to cardiovascular, kidney, and metabolic dysfunction, and amenable to structured evaluation. The 2026 CKM guideline considers annual assessment for sleep apnea symptoms, including validated screening tools, reasonable in adults with CKM syndrome and obesity. It also recommends that treatment strategies for OSA include weight management where indicated, alongside continuous positive airway pressure (CPAP) and other therapies, to improve symptoms and reduce the risk of CKM stage progression.[1]

OSA is common in obesity, resistant hypertension, atrial fibrillation, heart failure, coronary artery disease, stroke, pulmonary hypertension, and type 2 diabetes,[8–10] yet remains underdetected in cardiology practice. Many patients with CKM syndrome may undergo repeated evaluation for blood pressure, lipids, glucose, kidney function, natriuretic peptides, and cardiac imaging, but still have no structured assessment of sleep quality, snoring, witnessed apnea, nocturnal hypoxemia, or excessive daytime sleepiness. The guideline provides an opportunity to address this blind spot: asking "How does the patient sleep?" should become part of comprehensive cardiovascular risk assessment.

However, OSA should not be viewed merely as another comorbidity but as a potential nocturnal manifestation and amplifier of CKM pathophysiology. Recurrent upper airway obstruction causes intermittent hypoxemia, sleep fragmentation, and negative intrathoracic pressure swings, promoting carotid-body chemoreflex sensitization, sympathetic activation, blood-pressure and heart-rate surges, endothelial dysfunction, oxidative stress, inflammation, and renin–angiotensin-aldosterone system activation.[8] These effects increase ventricular afterload and may contribute to renal vasoconstriction, glomerular hypertension, albuminuria, and kidney-function decline.[8,11] Conversely, obesity, fluid redistribution, metabolic dysfunction, adipokine dysregulation, and heart failure may worsen OSA, creating a bidirectional cycle that

could accelerate CKM progression. These mechanisms support hypoxic and autonomic phenotyping, although the treatment-guiding value of such phenotyping remains unproven.

4. Precision sleep phenotyping and treatment implications

Epidemiological associations and biological plausibility do not establish that treating OSA reduces CKM-related cardiovascular or kidney events. CPAP improves sleepiness, quality of life, and blood pressure in many patients with OSA, but randomized trials have not consistently shown reductions in major cardiovascular events in broad secondary prevention populations.[12,13] Adherence is central to interpreting these trials: an individual participant data meta-analysis found no significant benefit in intention-to-treat analyses, whereas CPAP use for at least 4 h per day was associated with fewer recurrent major adverse cardiac or cerebrovascular events.[14] Because this was an on-treatment analysis, residual healthy-adherer bias cannot be excluded.

The apnea–hypopnea index alone may inadequately capture cardiovascular risk. Patients with similar values can have markedly different hypoxic burden, arousal intensity, autonomic response, heart-rate dynamics, blood pressure dipping patterns, and inflammatory profiles. Hypoxic burden may predict cardiovascular mortality better than event frequency alone.[15] A post hoc ISAACC analysis further suggested that baseline hypoxic burden may identify heterogeneity in cardiovascular response to CPAP, with potential benefit among patients with higher hypoxic burden.[16] This hypothesis-generating finding requires prospective validation before hypoxic burden can guide treatment allocation. The future of OSA management may therefore depend less on counting respiratory events and more on identifying harmful and modifiable physiological signatures.

This issue is especially relevant in the era of artificial intelligence, home sleep testing, wearable sensors, and continuous physiological monitoring. Overnight oxygen saturation trajectories, heart-rate variability, event-related heart-rate surges, nocturnal arrhythmia burden, sleep fragmentation, and circadian rhythm patterns may provide clinically meaningful information. These signals may help identify patients with disproportionate autonomic activation, severe intermittent hypoxia, impaired recovery after respiratory events, or vulnerable right-heart and pulmonary vascular phenotypes. These investigational approaches align with the CKM guideline's emphasis on longitudinal risk assessment and individualized prevention.

The treatment landscape is also changing. Weight loss is central to both CKM and OSA care. In the SURMOUNT-OSA trials, tirzepatide reduced apnea–hypopnea index, body weight, hypoxic burden, high-sensitivity C-reactive protein, and systolic blood pressure, and improved sleep-related patient-reported outcomes in adults with moderate-to-severe OSA and obesity.[17] These findings support the guideline's view that OSA management in CKM syndrome should include weight management where indicated. Nevertheless, several cautions are needed. Long-term cardiovascular and kidney outcome data in OSA populations are still needed, while cost, access, adherence, gastrointestinal adverse effects, muscle preservation, and weight regain require consideration. Treatment should also be individualized according to obesity severity, symptoms, cardiometabolic risk, patient preference, and local resources.

5. Implementation challenges and the China context

Implementation challenges include fragmented clinical ownership and referral pathways, limited access to sleep diagnostics and multidisciplinary obesity care, affordability and reimbursement constraints, and the need to validate risk tools across populations. Locally adapted shared-care pathways should define referral triggers and standardize assessment of body mass index, waist circumference, blood pressure, lipids, glucose, estimated glomerular filtration rate, urine albumin-to-creatinine ratio, cardiovascular history, social determinants, and sleep apnea symptoms. Multidisciplinary coordination is essential because patients often move across specialties without a single point of clinical ownership.

Questionnaires and overnight oximetry may support initial risk stratification but do not establish an OSA diagnosis. Home sleep apnea testing is reasonable in uncomplicated adults with a high pretest probability of moderate-to-severe OSA. Attended polysomnography should be preferred in patients with significant cardiorespiratory disease, suspected central sleep apnea or sleep-related hypoventilation, or a negative or inconclusive home test.[18] This distinction is particularly relevant in cardiovascular centers, where complex comorbidities and nonobstructive sleep-disordered breathing are common.

For China and other rapidly aging societies, CKM implementation requires local adaptation. The burden of obesity, diabetes, hypertension, chronic kidney disease, heart failure, and atrial fibrillation continues to rise, while sleep-disordered breathing remains underdiagnosed.[19] In a prospective Chinese cohort of 1,925 patients with acute coronary syndrome, 52.6% had OSA, illustrating its substantial burden in cardiovascular practice.[20] Integration of sleep assessment into CKM care remains constrained by limited sleep-laboratory capacity, uneven availability of portable diagnostic devices and trained personnel, fragmented referral pathways, and variable reimbursement for diagnostic testing and long-term treatment. PREVENT should therefore be externally validated and recalibrated in Asian populations, considering differences in body composition, visceral adiposity, dietary patterns, health insurance systems, drug availability, and sleep medicine infrastructure. Large cardiovascular centers may provide an appropriate setting for integrated CKM pathways because they

concentrate high-risk patients and can coordinate expertise in cardiology, nephrology, endocrinology, obesity medicine, and sleep medicine.

Vulnerable groups also require individualized judgment. Frailty, sarcopenia, polypharmacy, and competing risks should inform treatment intensity in older adults. Advanced CKD requires attention to kidney function, electrolyte status, and medication eligibility. Because most contemporary therapeutic evidence concerns type 2 diabetes, patients with type 1 diabetes need disease-specific cardiovascular and kidney risk assessment. Affordability and access to CPAP, anti-obesity therapies, and specialist care should inform shared decision-making in low-income populations.

6. Evidence gaps and future directions

Several evidence gaps deserve attention. First, future studies should clarify how OSA and other sleep phenotypes influence CKM stage progression. Second, randomized trials should determine whether treating OSA according to physiological risk markers, such as hypoxic burden or autonomic response, improves cardiovascular and kidney outcomes. Third, pragmatic implementation studies should evaluate whether CKM clinics that integrate sleep screening improve detection, adherence, symptoms, and long-term outcomes. Fourth, artificial intelligence models based on sleep signals should be developed with transparent methodology, external validation, fairness assessment, and clinical interpretability. Finally, clinical pathways should avoid both underdiagnosis and indiscriminate testing. Screening should be targeted, efficient, and linked to actionable management.

7. Conclusions

In summary, the 2026 AHA/ACC/ADA/ASN CKM guideline is a landmark document because it changes the unit of cardiovascular prevention from a single organ to an interconnected biological system. It recognizes that cardiovascular risk is shaped by metabolic, kidney, social, behavioral, and now nocturnal factors. For cardiovascular clinicians, the guideline provides a timely reminder that CKM health does not stop during the night. Sleep, nocturnal hypoxia, and autonomic instability may represent clinically relevant and potentially modifiable dimensions of cardiovascular risk, although the effects of phenotype-guided treatment on hard cardiovascular and kidney outcomes remain to be established. The next step is to translate this framework into practical, equitable, and evidence-based care models that can detect CKM progression earlier, treat shared drivers more effectively, and improve outcomes across the full 24-h cycle of human physiology.

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Ethical statements

Not applicable.

Conflicts of interest

ZH, QL, and ZL have no conflicts of interest to disclose. RJT is a co-inventor and patent holder of the ECG-derived sleep spectrogram, which may be used to phenotype sleep quality and central/complex sleep apnea. The technology is licensed by Beth Israel Deaconess Medical Center to MyCardio, LLC. He is also co-inventor and patent holder of the Positive Airway Pressure Gas Modulator, being developed as treatment of central/complex sleep apnea. He consults for Guidepoint Global and GLG Councils. He is a co-inventor of a licensed auto-CPAP software to DeVilbiss-Drive. RJT, Westover, Oppersma and Nassi are co-inventors of a respiratory self-similarity algorithm, licensed to Sleepcare Asia. Enhanced Expiratory Rebreathing Space, a treatment for high loop gain apnea, has a patent submitted and licesed to Sleepcare Asia.

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Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Author contributions

Zhihua Huang conceptualized the comment, drafted the manuscript, prepared the graphical abstract, and revised the paper.

Robert Joseph Thomas provided expert review and important intellectual input.

Qin Luo and Zhihong Liu provided critical review, clinical interpretation, and important intellectual input.

All authors reviewed and approved the final manuscript.

AI statement

During the preparation of this work, the author used AI tools for language and grammar polishing. After using the tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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