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THE ROLE OF SLEEP QUALITY IN CARDIOMETABOLIC HEALTH: MECHANISMS AND CLINICAL EVIDENCE – A NARRATIVE REVIEW

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ABSTRACT

Background: Sleep quality is increasingly recognized as a fundamental pillar of health, recently emphasized in the American Heart Association's "Life's Essential 8". However, the multidimensional pathways linking sleep-such as duration, continuity, and regularity to metabolic and cardiovascular function remain complex.

Objective: This narrative review synthesizes clinical evidence and biological mechanisms connecting multidimensional sleep health with cardiometabolic outcomes, including metabolic syndrome, type 2 diabetes, coronary heart disease, and the newly defined Cardiovascular-Kidney-Metabolic (CKM) syndrome.

Methods: Peer-reviewed publications from 2018-2025 were analyzed, including prospective cohort studies, randomized controlled trials, meta-analyses, and scientific statements. Mechanisms involving inflammation, autonomic regulation, neuroendocrine activity, epigenetic modifications, and gut microbiota were evaluated.

Results: Poor sleep quality and irregular sleep patterns consistently correlate with increased metabolic dysregulation, obesity, and Major Adverse Cardiovascular Events (MACE). Recent findings link inadequate sleep with advanced CKM stages and accelerated epigenetic aging. Interventional studies show that extending sleep duration can reduce energy intake and support weight loss, although improvements in insulin sensitivity remain inconsistent.

Conclusions: Sleep quality is a modifiable and clinically relevant determinant of cardiometabolic health. A multidimensional assessment of sleep-not limited to duration-offers improved risk stratification and highlights potential avenues for preventive interventions.

Introduction

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality globally, imposing a substantial burden on public health systems and individual quality of life [You et al., 2024]. Traditionally, prevention strategies have focused on well-established modifiable risk factors such as diet, physical activity, and smoking cessation. However, accumulating evidence suggests that these factors alone do not fully account for the variation in cardiometabolic risk, pointing to the critical role of sleep as a biological imperative.

Historically often overlooked in clinical guidelines, sleep is now increasingly recognized as a foundational pillar of health. This paradigm shift was formalized in 2022 when the American Heart Association (AHA) updated its canonical cardiovascular health construct from "Life's Simple 7" to "Life's Essential 8", explicitly adding sleep duration as an essential metric for maintaining heart and brain health alongside traditional risk factors [Lloyd-Jones et al., 2022; St-Onge et al., 2025].

While sleep duration has historically been the most extensively studied metric, contemporary research emphasizes that sleep is a complex, multidimensional construct. The recent AHA scientific statement on multidimensional sleep health defines this construct as encompassing not only duration but also continuity, timing, regularity, satisfaction, and alertness [St-Onge et al., 2025]. This broader approach allows for more accurate characterization of sleep-related health risks. For instance, large-scale prospective cohort studies, such as those analyzing data from the UK Biobank (n>200,000), have demonstrated that a composite healthy sleep pattern-integrating adequate duration, early chronotype, and the absence of insomnia or snoring-is strongly associated with a reduced risk of Major Adverse Cardiovascular Events (MACE), independent of traditional cardiovascular risk factors [You et al., 2024].

Furthermore, findings from the Multi-Ethnic Study of Atherosclerosis (MESA) indicate that sleep irregularity is an independent predictor of cardiovascular events, suggesting that the stability of sleep–wake rhythms is as vital as total sleep duration [Huang et al., 2020].

The clinical relevance of sleep extends beyond isolated cardiovascular outcomes to complex systemic conditions. In 2023, the AHA defined the Cardiovascular-Kidney-Metabolic (CKM) syndrome, reflecting the interaction between obesity, diabetes, chronic kidney disease, and cardiovascular disease [Tu et al., 2025]. Recent NHANES data show that poor overall sleep quality is significantly associated with advanced CKM stages, suggesting that disturbed sleep may accelerate multimorbid disease progression [Tu et al., 2025].

Despite substantial epidemiological evidence linking poor sleep to metabolic syndrome, type 2 diabetes, and hypertension [Hu et al., 2022; Kim & Yeom, 2020], the underlying biological mechanisms remain under active investigation. Current research highlights a complex network of pathways including autonomic dysregulation, systemic inflammation mediated by TLR4 and NF-κB signaling [Hong et al., 2025], neuroendocrine disturbances [Sukor et al., 2025; Duraccio et al., 2024], and emerging evidence involving gut microbiota and epigenetic aging [Pala et al., 2024; Lee et al., 2024].

This narrative review aims to synthesize the latest clinical evidence and mechanistic insights regarding the role of sleep quality in cardiometabolic health. By integrating findings from large observational cohorts, interventional trials on sleep extension [Tasali et al., 2022], mechanistic and experimental evidence linking sleep loss to behavioral regulation of energy balance [Duraccio et al., 2024], and emerging biological data, this review seeks to provide a comprehensive overview of how multidimensional sleep health shapes cardiometabolic risk and to highlight opportunities for targeted therapeutic interventions in clinical practice.

Methodology

Study Design and Search Strategy

This narrative review synthesizes peer-reviewed scientific evidence published primarily between 2018 and 2025, examining the complex interplay between multidimensional sleep health and cardiometabolic outcomes. The methodological approach was designed to integrate findings across a hierarchy of evidence-ranging from molecular mechanisms to large-scale epidemiological associations and clinical guidelines. A targeted literature search was conducted to identify high-quality sources, resulting in the final selection of 27 key publications representing four primary evidence categories: large-scale prospective cohort studies (e.g., UK Biobank, NHANES, SWAN, MESA), randomized controlled trials (RCTs) and interventional studies, systematic reviews and meta-analyses, and authoritative scientific statements from major medical organizations such as the American Heart Association.

Eligibility Criteria

Studies were selected based on the following inclusion criteria: (1) peer-reviewed original research, systematic reviews, and scientific statements published in English; (2) evaluation of sleep health using multidimensional constructs, including sleep duration, quality (e.g., PSQI scores), timing, and regularity, as well as the presence of sleep disorders like obstructive sleep apnea; (3) assessment of specific cardiometabolic endpoints, namely metabolic syndrome, type 2 diabetes, coronary heart disease (CHD), Major Adverse Cardiovascular Events (MACE), and the novel Cardiovascular-Kidney-Metabolic (CKM) syndrome; and (4) investigation of mechanistic pathways linking sleep to disease, such as autonomic regulation, inflammatory pathways including NF-κB signaling and inflammasome-related mechanisms, gut microbiota dysbiosis, and epigenetic age acceleration (e.g., GrimAge, DunedinPACE). Editorials without data, non-peer-reviewed preprints, and studies lacking methodological rigor regarding sleep or metabolic assessment were excluded.

Data Extraction and Categorization

Data extraction focused on capturing the complexity of sleep-health relationships across different study designs. For observational studies, priority was given to large cohorts (e.g., n>200,000 in UK Biobank analyses) to ensure statistical power, extracting hazard ratios (HR) and odds ratios (OR) for hard clinical endpoints like MACE and advanced CKM stages. Regarding mechanistic studies, data were extracted on specific biological mediators, including inflammatory cytokines, gut bacterial taxa, and DNA methylation markers. For interventional studies, the efficacy of strategies such as sleep extension and CPAP therapy on metabolic parameters, including energy intake and insulin sensitivity, was evaluated. Additionally, definitions and frameworks from recent guidelines, specifically "Life's Essential 8" and "Multidimensional Sleep Health," were extracted to contextualize clinical relevance.

Analytic Approach

Given the substantial heterogeneity in study designs (ranging from molecular analyses to population-based surveys) and outcome definitions, a formal meta-analysis was not conducted. Instead, a thematic narrative synthesis was employed to organize the evidence into three primary domains: pathophysiological mechanisms (integrating findings on inflammation, neuroendocrine regulation, gut dysbiosis, and epigenetics), clinical epidemiology (summarizing associations between sleep characteristics and specific cardiometabolic conditions such as obesity, T2D, CVD, and CKM Syndrome), and interventional implications (evaluation of sleep modification strategies within cardiometabolic prevention). Across domains, findings were contextualized using contemporary frameworks of multidimensional sleep health and cardiometabolic risk.

Results
1. Epidemiological Associations with Cardiometabolic Outcomes
1.1. Metabolic Syndrome (MetS) and Type 2 Diabetes

A substantial body of epidemiological evidence consistently identifies poor sleep as a robust and independent predictor of metabolic dysregulation. Meta-analyses of observational studies involving large adult populations indicate that the relationship between sleep duration and metabolic syndrome follows a U-shaped curve, where both short and long sleep durations are associated with elevated risk [Hu et al., 2022]. This pattern highlights that either insufficient or excessive sleep may undermine metabolic health. The use of sleep medication was associated with a 32% increased risk of developing metabolic syndrome (OR = 1.32; 95% CI: 1.14–1.52) [Hu et al., 2022]. Furthermore, individual sleep disturbances-including difficulty falling asleep (+12% risk), difficulty maintaining sleep (+20%), and sleep-related breathing disorders (+62%)-emerged as independent risk factors. Beyond duration, subjective sleep quality is a critical determinant. Research from the Korean Genome and Epidemiology Study shows that even with ≥6 hours of sleep, poor perceived sleep quality significantly increases MetS risk (OR = 1.24) [Kim & Yeom, 2020]. Additionally, difficulty initiating sleep and frequent nocturnal awakenings have been prospectively linked to higher HbA1c and increased incidence of type 2 diabetes [Hong et al., 2025].

1.2. Cardiovascular Disease (CVD) and Major Adverse Cardiovascular Events (MACE)

Large-scale prospective cohorts provide compelling evidence regarding the impact of multidimensional sleep health on hard cardiovascular endpoints. In the UK Biobank study, which followed over 200,000 participants, researchers utilized a comprehensive multidimensional sleep score encompassing five key dimensions: chronotype, sleep duration, insomnia complaints, snoring, and excessive daytime sleepiness. The findings established a clear gradient of risk: compared to individuals with a "healthy sleep pattern," those with intermediate and poor sleep patterns faced progressively higher risks of Major Adverse Cardiovascular Events (MACE). This adverse association extended beyond the composite MACE outcome to its individual components, specifically increasing the risk of myocardial infarction, stroke, and cardiovascular mortality.

Crucially, this study highlighted a synergistic interaction between sleep patterns and traditional cardiovascular health (CVH) metrics (assessed via "Life's Simple 7"). The combination of a poor sleep pattern and poor CVH generated the highest clinical risk. While improving either sleep quality or CVH status independently lowered cardiovascular risk, the most profound protective effect was observed in participants possessing both a healthy sleep pattern and ideal CVH (HR = 0.306). This demonstrates that sleep acts as a critical risk modifier; even among individuals with optimal metabolic profiles, poor sleep quality can attenuate the protective benefits of traditional health factors.[You et al., 2024]. Additionally, sleep regularity has been identified as a novel and potent risk factor. Data from the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrated that high day-to-day variability in sleep duration is associated with a significantly increased risk of incident cardiovascular disease events, independent of average sleep duration. This underscores the importance of maintaining a consistent sleep-wake schedule [Huang et al., 2020]. Regarding mortality, a comprehensive dose-response meta-analysis of 74 cohorts identified a J-shaped relationship between sleep duration and all-cause mortality. While short sleep was associated with a moderate risk increase, the risk escalated more sharply for durations exceeding the recommended 7-8 hours. Specifically, the relative risk rose to 1.14 for 9 hours, 1.30 for 10 hours, and reached 1.47 for 11 hours, highlighting the substantial hazard of prolonged sleep compared to sleep deprivation [Kwok et al., 2018].

1.3. Cardiovascular-Kidney-Metabolic (CKM) Syndrome

Recent investigations utilize the American Heart Association's novel CKM framework, which stratifies cardiovascular-kidney-metabolic multimorbidity into stages ranging from excess adiposity (Stage 1) to clinical cardiovascular disease (Stage 4). A cross-sectional analysis of NHANES 2015-2020 data (n=12,245) examined the impact of multidimensional sleep health within this continuum. Overall sleep quality was assessed using a composite score encompassing five behaviors: sleep duration, trouble sleeping, excessive daytime sleepiness, snoring, and nocturia [Tu et al., 2025].

The analysis demonstrated a clear graded inverse association, whereby individuals with moderate or high sleep quality exhibited significantly lower odds of being classified in advanced CKM stages, defined as Stage 3 (subclinical cardiovascular disease) and Stage 4 (clinical cardiovascular disease), with odds ratios of 0.68 and 0.55, respectively [Tu et al., 2025]. Examination of individual sleep components indicated that qualitative disturbances, particularly trouble sleeping, excessive daytime sleepiness, and nocturia, were independently associated with more advanced CKM stages, whereas sleep duration alone showed weaker and less consistent associations after multivariable adjustment. Subgroup analyses further indicated that the protective association of higher sleep quality was generally robust across demographic groups, with particularly strong associations observed among Non-Hispanic Black and Asian participants [Tu et al., 2025].

1.4. Population-Specific Findings

The influence of sleep on cardiometabolic health exhibits distinct variations across the lifespan. In midlife, the chronicity of sleep disturbance appears to be a critical determinant of risk. Longitudinal data from the Study of Women's Health Across the Nation (SWAN), which tracked sleep trajectories over 22 years, demonstrated that women with persistently high insomnia symptoms faced a significantly elevated risk of incident cardiovascular disease events compared to those maintaining low symptom levels [Thurston et al., 2024]. This underscores that long-term cumulative exposure to sleep fragmentation drives cardiovascular vulnerability in this demographic. Conversely, research in the "oldest old" (≥90 years) revealed a paradoxical pattern: metabolic syndrome was correlated with *better* subjective sleep quality, with higher sleep quality reported as the number of MetS components increased [Laudisio et al., 2020]. The authors propose survival bias or altered physiological resilience as potential explanations. These contrasting findings caution against universal assumptions about sleep health across demographic groups and emphasize the need for age-contextualized interpretation.

2. Pathophysiological Mechanisms
2.1. Inflammation and Oxidative Stress

Sleep disturbances activate multiple components of the innate immune system, leading to a pro-inflammatory state that contributes to cardiometabolic dysfunction. Experimental and clinical evidence shows that insufficient or fragmented sleep elevates circulating inflammatory cytokines, including IL-6 and TNF-α, and enhances activation of transcriptional pathways such as TLR4-mediated NF-κB signaling, which promotes the expression of downstream inflammatory mediators [Hong et al., 2025]. These processes create a chronic low-grade inflammatory environment that contributes to insulin resistance, endothelial dysfunction, and heightened cardiometabolic vulnerability. Although inflammasome pathways (e.g., NLRP3) are discussed in mechanistic frameworks as potential amplifiers of inflammatory signaling, current human studies do not establish sleep fragmentation as a confirmed trigger of inflammasome activation. Sleep-disordered breathing further intensifies inflammatory and oxidative stress mechanisms. Intermittent hypoxia associated with obstructive sleep apnea induces bursts of reactive oxygen species, endothelial injury, and upregulation of adhesion molecules, promoting atherosclerotic plaque formation and vascular dysfunction [Yeghiazarians et al., 2021]. Collectively, these findings support a model in which sleep disruption contributes indirectly to cardiometabolic disease through inflammatory and oxidative pathways, with the strongest evidence centered on NF-κB-driven signaling rather than specific inflammasome activation.

2.2. Gut Microbiota Dysbiosis

Growing evidence suggests that insufficient or irregular sleep is associated with alterations in gut microbiota composition that may contribute to cardiometabolic vulnerability. Studies indicate that sleep disruption can shift the relative abundance of key microbial taxa-including changes in the Firmicutes/Bacteroidetes ratio and reductions in short-chain-fatty-acid-producing bacteria, a pattern associated with low-grade inflammation and metabolic dysregulation [Pala et al., 2024]. Sleep loss may also impair

intestinal barrier integrity, increasing circulating endotoxins and stimulating inflammatory responses [Hong et al., 2025]. These findings indicate that sleep-related microbiota changes may act as intermediaries rather than a distinct "sleep-gut-cardiovascular axis," and current evidence remains associative rather than causal. Collectively, gut dysbiosis appears to be an emerging, though still developing, mechanistic pathway linking sleep disturbances to cardiometabolic outcomes.

2.3. Neuroendocrine and Autonomic Regulation

Sleep disturbances induce broad neuroendocrine and autonomic changes that contribute to cardiometabolic dysfunction. In circadian misalignment, such as in shift workers, the hypothalamic–pituitary–adrenal (HPA) axis often displays altered cortisol rhythms, including elevated evening cortisol and blunted morning cortisol, patterns associated with increased visceral adiposity and impaired metabolic regulation [Sukor et al., 2025]. These neuroendocrine disruptions may also worsen sleep architecture, creating a reinforcing cycle of stress and poor sleep. Insufficient or fragmented sleep additionally influences appetite regulation. Experimental studies report increased caloric intake following sleep restriction, along with greater preference for energy-dense foods and reward-driven eating, although hormonal changes in leptin and ghrelin remain inconsistent across studies [Duraccio et al., 2024]. Autonomic imbalance represents another well-established pathway. Repeated arousals and intermittent hypoxia in obstructive sleep apnea trigger persistent sympathetic overactivation, reducing nocturnal blood pressure dipping and increasing vascular shear stress [Yeghiazarians et al., 2021]. Sustained sympathetic activation contributes to hypertension, endothelial dysfunction, and elevated cardiometabolic risk.

2.4. Epigenetic Modifications

Emerging evidence suggests that sleep quality may influence biological aging through epigenetic mechanisms. Individuals with poor or irregular sleep exhibit accelerated epigenetic aging, as measured by DNA-methylation-based biomarkers such as GrimAge and DunedinPACE [Lee et al., 2024]. These markers are thought to reflect cumulative physiological stress and have been associated with cardiometabolic vulnerability. The relationship between sleep disturbances and epigenetic aging appears to involve multiple pathways, including inflammation, oxidative stress, and neuroendocrine dysregulation. However, current evidence is largely associative, and the extent to which epigenetic aging mediates cardiometabolic outcomes remains unclear. Most available studies are cross-sectional and rely on heterogeneous sleep assessments. Despite these limitations, epigenetic aging is an important emerging biomarker that may capture the long-term physiological burden imposed by chronic sleep disruption.

3. Interventional Evidence
3.1. Sleep Extension and Metabolic Outcomes

Interventional studies provide proof-of-concept evidence that optimizing sleep duration can modify behavioral drivers of energy balance. A landmark single-center randomized clinical trial demonstrated that a 2-week individualized sleep hygiene intervention in adults with overweight and habitual short sleep (<6.5 hours) increased sleep duration by approximately 1.2 hours per night. This extension resulted in a clinically significant reduction in objectively assessed daily energy intake of approximately 270 kcal per day compared with controls, without compensatory changes in total energy expenditure, leading to a weight reduction of 0.87 kg over the intervention period. Furthermore, each additional hour of sleep was associated with a decrease in energy intake of about 162 kcal per day, indicating a dose–response relationship [Tasali et al., 2022]. Broader evidence suggests that the effects of sleep extension depend on both the magnitude of sleep increase and baseline cardiometabolic risk. Modest sleep extensions (e.g., ~21 minutes) have been associated with improvements in diet quality, including reduced free sugar intake, whereas evidence for consistent improvements in insulin sensitivity remains limited. Data on blood pressure are preliminary, with pilot studies suggesting potential reductions among individuals with prehypertension or stage 1 hypertension, underscoring the need for larger, adequately powered trials [Duraccio et al., 2024].

3.2. Management of Sleep Disorders (OSA)

Obstructive Sleep Apnea (OSA) represents a major, treatable driver of cardiovascular risk. Treatment with Continuous Positive Airway Pressure (CPAP) has been shown to reliably mitigate intermittent hypoxia and sympathetic overactivation, which are key drivers of resistant hypertension and arrhythmia [Yeghiazarians et al., 2021]. While evidence regarding the reduction of major adverse cardiovascular events remains mixed, CPAP therapy consistently improves blood pressure control and may enhance glycemic stability in patients with type 2 diabetes, underscoring its role in comprehensive cardiometabolic risk management [Yeghiazarians et al., 2021].

Discussion

Integration of Sleep into the Cardiometabolic Paradigm

This narrative review synthesizes evidence indicating that poor multidimensional sleep health contributes to cardiometabolic dysfunction through converging biological pathways, including systemic inflammation, neuroendocrine dysregulation, and behavioral drivers of energy balance. Accelerated epigenetic aging has been associated with poor sleep quality and metabolic syndrome, particularly in older adults, suggesting a potential molecular correlate of cumulative physiological stress rather than a confirmed mediating mechanism [Lee et al., 2024]. In parallel, broader sleep disturbances are consistently associated with more advanced stages of cardiovascular, kidney, and metabolic syndrome (CKM) [Tu et al., 2025]. Interventional studies further demonstrate that targeted sleep optimization can favorably modify energy intake and related behaviors, supporting sleep as a practical and modifiable therapeutic target. The inclusion of sleep duration in the American Heart Association's Life's Essential 8 framework underscores its importance in cardiovascular health promotion [Lloyd-Jones et al., 2022]. However, evidence reviewed here indicates that sleep duration alone is insufficient for comprehensive risk assessment. Data from the UK Biobank show strong associations between multidimensional sleep patterns, including regularity, timing, and subjective sleep quality, and Major Adverse Cardiovascular Events (MACE), independent of traditional risk factors [You et al., 2024]. Similarly, findings from the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrate that sleep irregularity independently predicts cardiovascular events, challenging the traditional clinical focus on average sleep duration and highlighting circadian stability as a novel and potentially modifiable target for prevention [Huang et al., 2020].

The CKM Syndrome and Systemic Multimorbidity

A major recent development in cardiometabolic research is the positioning of sleep within the Cardiovascular-Kidney-Metabolic (CKM) syndrome framework. The inverse association between sleep quality and advanced CKM stages indicates that individuals with poorer sleep tend to exhibit greater multimorbidity rather than isolated metabolic or cardiovascular conditions [Tu et al., 2025]. Moreover, specific symptoms such as trouble sleeping, nocturia, and excessive daytime sleepiness were more strongly linked to advanced disease. These findings suggest that qualitative sleep symptoms may reflect more advanced underlying cardiometabolic impairment. The stronger associations observed in Non-Hispanic Black and Asian adults highlight important demographic differences in vulnerability. However, it remains unclear whether improvements in sleep quality directly translate into reductions in cardiometabolic disparities, as current evidence is primarily observational.

Mechanistic Convergence: Inflammation, Microbiota, and Epigenetics

Multiple complementary mechanistic pathways support the observed epidemiological associations between sleep disturbances and cardiometabolic outcomes. Sleep disruption has been associated with activation of TLR4-dependent inflammatory signaling and downstream NF-κB pathways, promoting increased levels of pro-inflammatory cytokines such as IL-6 and TNF-α [Hong et al., 2025]. Inflammasome activity, including NLRP3, has been proposed as a potential amplifier of inflammatory responses, although its precise role in human sleep disturbances remains uncertain. In parallel, sleep-disordered breathing provides an additional inflammatory and oxidative burden. Intermittent hypoxia in obstructive sleep apnea induces endothelial activation and upregulation of vascular adhesion molecules, contributing to atherosclerotic progression [Yeghiazarians et al., 2021]. Neuroendocrine dysregulation also contributes to metabolic vulnerability, with circadian misalignment in shift workers associated with altered cortisol rhythmicity and impaired metabolic regulation [Sukor et al., 2025]. Gut microbiome alterations, including shifts in the Firmicutes to Bacteroidetes ratio and increased intestinal permeability, represent another complementary pathway linking sleep disruption to metabolic inflammation [Pala et al., 2024]. Finally, associations between poor sleep quality and accelerated epigenetic aging, as assessed by GrimAge and DunedinPACE, suggest longer-term molecular consequences of chronic sleep disruption and may reflect cumulative physiological stress [Lee et al., 2024].

Therapeutic Implications: Sleep as a Modifiable Risk Factor

From a clinical perspective, the interventional evidence reviewed here underscores the value of incorporating sleep health into cardiometabolic risk reduction strategies. A simple, individualized sleep-extension intervention was shown to reduce daily energy intake by approximately 270 kcal and produce a modest but statistically significant weight loss of 0.87 kg over two weeks, without any dietary prescription, indicating that addressing insufficient sleep can favorably influence short-term energy balance [Tasali et al., 2022]. These effects appear to be driven primarily by changes in eating behavior, consistent with evidence that

sleep loss increases reward-driven food preferences and hedonic eating, rather than by consistent alterations in appetite-regulating hormones [Duraccio et al., 2024]. In the context of obstructive sleep apnea, continuous positive airway pressure (CPAP) therapy remains a cornerstone of clinical management. Although randomized controlled trials have not consistently demonstrated reductions in major adverse cardiovascular events in intention-to-treat analyses, CPAP exerts well-established benefits on intermediate pathophysiological mechanisms, including reductions in sympathetic overactivation, mitigation of intermittent hypoxia, and improvements in endothelial function and blood pressure regulation [Yeghiazarians et al., 2021]. In individuals with obstructive sleep apnea and type 2 diabetes, CPAP has also been shown to improve glycemic control and reduce physiological stressors linked to cardiometabolic risk, even when long-term cardiovascular outcome trials yield neutral results [Yeghiazarians et al., 2021]. Collectively, these findings support the integration of sleep-focused interventions as adjunctive components of comprehensive cardiometabolic care. Their clinical impact is likely to depend on patient adherence, baseline risk profiles, and alignment with established lifestyle and pharmacological strategies, underscoring the importance of individualized implementation rather than universal application.

Population-Specific Nuances and "Reverse Epidemiology"

Evidence indicates that the relationship between sleep and cardiometabolic health varies across the lifespan. Data from the SWAN cohort show that women with persistently high insomnia symptoms during midlife face an elevated risk of incident cardiovascular events, underscoring the importance of chronic sleep disturbance rather than transient symptoms in shaping long-term risk [Thurston et al., 2024]. This suggests that midlife may represent a particularly sensitive window for the cardiometabolic consequences of poor sleep. In contrast, findings from the Mugello Study of adults aged 90 years and older reveal a paradoxical pattern in which metabolic syndrome is associated with better subjective sleep quality, with the likelihood of reporting good sleep increasing alongside the number of metabolic syndrome components [Laudisio et al., 2020]. This "reverse epidemiology" likely reflects selective survival or distinct physiological adaptations in extreme aging rather than a protective effect of metabolic syndrome. Together, these observations highlight the need to interpret sleep–health associations within specific demographic and life-course contexts.

Conclusions

This narrative review synthesizes multidisciplinary evidence demonstrating that sleep quality is a fundamental, yet often underrecognized, determinant of cardiometabolic health. Across large epidemiological cohorts, poor multidimensional sleep health, including insufficient duration, irregularity, insomnia symptoms, and excessive daytime sleepiness, was consistently associated with increased risk of metabolic dysfunction, cardiovascular events, and higher stages of Cardiovascular-Kidney-Metabolic (CKM) syndrome. These associations persisted after adjusting for traditional risk factors, emphasizing sleep as an independent contributor to cardiometabolic risk.

Mechanistic research supports these findings by showing that sleep disruption promotes inflammatory activation, neuroendocrine dysregulation, autonomic imbalance, gut microbiota alterations, and accelerated epigenetic aging. Together, these pathways provide biologically plausible explanations for how poor sleep influences metabolic homeostasis and vascular health.

Interventional studies suggest that targeted improvements in sleep, such as sleep extension or treatment of sleep-disordered breathing, can yield measurable metabolic benefits, including reduced energy intake, better blood pressure control, and improved glycemic stability. While long-term effects on hard cardiovascular endpoints remain incompletely characterized, current evidence indicates that sleep represents a promising modifiable target in cardiometabolic prevention.

Population-specific analyses reveal important nuances. Chronic insomnia symptoms in midlife women are linked to higher cardiovascular risk, while in the oldest old, metabolic syndrome correlates with better subjective sleep. These contrasting patterns highlight the need for age-sensitive interpretation of sleep and cardiometabolic outcomes.

Despite substantial progress, important gaps remain. Most studies rely on self-reported sleep measures, cross-sectional designs, and short-term interventions. Future research should prioritize longitudinal studies that incorporate objective sleep assessments, mechanistic biomarkers, and diverse populations to clarify causal pathways. Evaluating long-term effectiveness and scalability of sleep-focused interventions will be essential for integrating sleep into cardiometabolic prevention strategies.

Taken together, the available evidence positions sleep quality as a meaningful and modifiable determinant of cardiometabolic health. Strengthening scientific understanding of sleep's biological mechanisms and translational potential may open new opportunities to reduce the burden of cardiovascular and metabolic disease.

Disclosures
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