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Sleep and Circadian Disturbance in Cardiovascular Risk

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Abstract

Purpose of review: We discuss the relationship between sleep and circadian factors with cardiovascular disease (CVD) risk, including physiologic, behavioral, and psychological mechanisms along this pathway.

Recent findings: The relationship between short- and long sleep duration, as well as insomnia, with CVD risk is well-established. Recent work has highlighted how other sleep factors, such as sleep regularity (i.e., consistency of sleep timing), multidimensional sleep health, and circadian factors like chronotype and social jetlag, relate to CVD risk. Sleep-focused interventions (e.g., cognitive behavioral therapy for insomnia and sleep extension) may be effective to reduce CVD risk and disease burden.

Summary: Sleep is increasingly recognized as an integral component of cardiovascular health. This was underscored by the recent inclusion of sleep duration as a health behavior in the American Heart Association's Life's Essential 8 for defining optimal cardiovascular health.

Keywords

sleep; circadian rhythms; cardiovascular health; cardiovascular disease prevention; psychological; health behaviors

Introduction

Sleep is an essential biological state, influencing nearly all major organ systems, physiologic processes, and functions within the body. Sleep is also a crucial modifiable behavior and

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Conflict of Interest

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is considered one of the three pillars of a healthy lifestyle, along with diet and exercise, to promote optimal health and well-being [1]. More than simply a turning off or an “idling” of the brain that occurs when the body is quiescent, sleep is an actively produced and dynamic brain state that directly influences cognition, memory, and emotion [2]. However, sleep is as much *for the body as it is for the brain* [3]. Sleep is associated with metabolism, immune function, neurohormone secretion, and appetite regulation, as well as the development and progression of obesity, diabetes, and cardiovascular disease (CVD) [4].

The sections below will focus on behavioral aspects of sleep, as well as insomnia, a sleep disorder with a large psychological component, in relation to cardiovascular risk. We also discuss recent findings on how circadian disruption relates to CVD-related outcomes, and sleep-focused therapeutic interventions that may be helpful to reduce CVD risk and burden.

Sleep duration

Both short and long sleep duration are associated with CVD risk. In a meta-analysis of 153 prospective cohort studies (n=5,172,710 participants) [5], short sleep duration (typically defined as <6 or <7 hours) was significantly associated with hypertension (risk ratio [RR]: 1.17), coronary heart disease (RR: 1.26), CVD events (RR: 1.16), and mortality (RR: 1.12). In another meta-analysis of 137 prospective studies (n=5,134,036 participants) [6], long sleep duration (typically defined as >9 or >10 hours) was significantly associated with coronary heart disease (RR: 1.24), CVD events (RR: 1.25), stroke (RR: 1.46), and mortality (RR: 1.39).

Several potential physiologic pathways may link short sleep duration to CVD. Shorter sleep duration has been observationally and experimentally associated with increases in blood pressure [7–10]. Additional mechanistic evidence comes from a randomized crossover study in healthy young adults, which found that prolonged sleep restriction (4 hours/night for 9 nights) resulted in increased 24-hour and sleep-time blood pressure, attenuated endothelial function, and increased sympathetic activation [11••]. In observational findings from the Multi-Ethnic Study of Atherosclerosis (MESA), short sleep duration (<6 hours) was associated with lower levels of cardiac parasympathetic tone and higher sympathetic tone (e.g., higher heart rate, greater heart rate orthostatic reactivity, and lower high-frequency heart rate variability) [12]. Short sleep duration may also contribute to CVD risk via increasing adiposity and metabolic dysfunction [13].

The pathways linking long sleep and adverse cardiovascular outcomes are currently less clear. Long sleep duration, similar to short sleep, has been associated with increased systemic inflammation [14], and higher blood pressure [15]. However, it has been proposed that long sleep duration per se may not confer CVD risk, and that as opposed to being a causal risk factor, long sleep could be a marker of underlying illness [16]. Perhaps related to this, daytime napping appears to have a complex relationship with CVD risk. Daytime napping was associated with increased risk of CVD events and deaths in those with >6 hours of nighttime sleep, but not in those sleeping ≤6 hours/night [17]. Therefore, daytime napping may be beneficial as a means of mitigating risks associated with habitual short sleep duration, but not for individuals with sleep of sufficient or long duration.

Insomnia

Insomnia is the most common sleep disorder in the U.S. and is associated with cardiometabolic and psychiatric morbidity [18]. A meta-analysis of 13 prospective studies (n=311,260 participants) demonstrated that insomnia is associated with a 45% increased risk of developing or dying from CVD [19]. Some specific insomnia symptoms, namely difficulty falling asleep and non-restorative sleep, were particularly associated with all-cause and CVD-related mortality [20•]. A prospective cohort study (n=44,080 participants with a 10-year follow-up) also demonstrated that insomnia is an antecedent risk factor for acute myocardial infarction (hazard ratio: 1.68) [21].

The conditioned hyperarousal and psycho-physiologic stress that occurs in insomnia [22, 23] likely contribute to the development of sleep-wake disturbances and CVD risk linked to the disorder. Insomnia is associated with dysregulated autonomic and hypothalamic-pituitary-adrenal (HPA) axis function (e.g., increased heart rate, norepinephrine, and evening cortisol; decreased parasympathetic tone), and potentially, increased systemic inflammation [24, 25]. Compared to good sleeping controls, individuals with chronic insomnia had higher nighttime systolic blood pressure and blunted daytime-to-nighttime reductions in blood pressure (i.e., blood pressure *dipping*; discussed further below) [26]. Moreover, compared to those without insomnia, individuals with insomnia were nearly 10 times more likely to have clinically significant depression and over 17 times more likely to have clinically significant anxiety [27]. This is critical because psychological factors, including depression, stress, and anxiety, have been implicated in the development and progression of CVD (discussed further below) [28].

Sleep regularity

The regularity of sleep duration and timing across days is increasingly recognized as an important modifiable sleep-related risk factor for CVD. In a landmark analysis within the MESA Study, the standard deviation (SD) of sleep duration and sleep onset timing was utilized as a measure of day-to-day variability in these metrics; having sleep duration and onset timing SD >120 vs. ≤60 minutes and >90 vs. ≤30 minutes, respectively, was related to >2-fold higher CVD risk in older U.S. adults [29••]. Two reviews of the epidemiologic evidence published between 2014-2020 highlighted that more variable sleep patterns, characterized by higher sleep duration and timing SDs or a lower sleep regularity index (another computed measure of sleep variability), are associated with higher risk for hypertension, type 2 diabetes, excess adiposity, and clusters of metabolic abnormalities, thereby elucidating some of the mechanisms through which variable sleep patterns may predispose to CVD [30, 31]. Other work from the MESA Sleep cohort has linked irregular sleep duration and timing to metabolic dysfunction and central adiposity [32–34]. A study of 50 college students (mean age: 20 years) showed that greater sleep irregularity (i.e., sleep duration SD), is related to poorer microvascular function, measured via passive leg movement, providing evidence for an additional mechanism through which sleep regularity could influence future CVD risk [35].

Multidimensional sleep health

Sleep is multifaceted and not wholly defined by a single dimension. In considering its relationship to health outcomes, efforts have been made to move beyond focusing on discrete sleep domains. For example, both insomnia and short sleep duration are associated with psycho-physiologic changes along the pathway to CVD, and are predictive of CVD risk [4]. Yet, these conditions often co-occur, and the combination represents a phenotype associated with severe cardiometabolic risk [36, 37]. Seminal work from the Penn State Cohort first established that insomnia with objectively measured short sleep duration is association with risk for hypertension [38]. This finding was later confirmed in a ~7.5-year longitudinal study of the same cohort. Individuals with chronic insomnia combined with short sleep duration had nearly 4 times the risk of incident hypertension vs. participants without insomnia who slept ≥6 hours [39]. In an ~11-year prospective analysis from the Sleep Heart Health Study, individuals with combined insomnia/poor sleep and short sleep duration had 29% higher risk of incident CVD vs. the non-insomnia/non-short sleep group [40••]. Autonomic dysfunction may explain this risk, as insomnia combined with short sleep duration is associated with lower parasympathetic and higher sympathetic activity [12, 41, 42].

Building off this, there has been a shift to frame overall *sleep health* as an aggregate measure of multiple sleep domains [43–45]. The term multidimensional sleep health (MDSH), as initially proposed by Buysse, encompasses the dimensions sleep regularity, satisfaction, alertness, timing, efficiency, and duration [43]. Several studies have modified this initial framework based on cohort sleep data availability or data-driven approaches in order to select the most relevant sleep health dimensions in relation to other health outcomes. In a study of >8,000 older U.S. adults (age: 65+ years), the multidimensional sleep metric characterized using a machine-learning algorithm from self-reported measures aggregated across three epidemiological cohorts was predictive of cardiovascular mortality [46]. In an analysis of >400,000 adults from the UK Biobank, a healthy sleep score, comprising self-reported measures of chronotype, sleep duration, insomnia, snoring, and excessive daytime sleepiness, was inversely related to incidence of heart failure, with 15% lower risk observed per 1 unit increase in the sleep score [47]. One analysis from a nationally representative cohort of ~4500 U.S. adults from 2017-2018 National Health and Nutrition Examination Survey (NHANES) data evaluated a MDSH score based on self-reported sleep duration, sleep regularity, difficulty falling asleep, symptoms of sleep disorders, and daytime sleepiness in relation to prevalent CVD and cardiometabolic disease. In that study, having ideal vs. moderate/poor MDSH was associated with 32% lower odds of prevalent CVD, with stronger associations reported among women [48]. Importantly, while the MDSH score was associated with CVD, significant relations were not necessarily observed for all score components, suggesting that utilizing a MDSH framework may better predict future CVD risk, but this warrants confirmation in longitudinal studies.

Differential associations have been reported for MDSH in relation to CVD risk factors. For instance, in the NHANES analysis, having ideal or moderate vs. poor MDSH were associated with having up to 73% lower odds of hypertension, obesity, and central adiposity, with evidence of a dose-response relationship; having ideal vs. moderate/poor MDSH was

related to 40% lower odds of prevalent type 2 diabetes [48]. Consistent with these findings, favorable overall sleep health, operationalized using both self-report and actigraphy-based sleep dimensions, was related to ~10% lower odds of cardiometabolic morbidity (including heart disease, hypertension, stroke, and diabetes) in 268 adults from the Midlife in the United States Study [49•].

Circadian rhythms

C*ircadian rhythms* refer to ~24-hour variations in physiologic and mental processes that are generated by an endogenous biological clock but are responsive to external signals, such as light. The human circadian system has evolved to match, or synchronize, with the light-dark cycle on earth. A result is that certain physiologic functions and behaviors typically occur during the daytime hours (e.g., waking, feeding, physical activity), while others typically occur during the nighttime hours (e.g., sleeping, fasting). Circadian variations in cardiovascular function may help explain the longstanding clinical observation of heightened risk for adverse cardiovascular events in the morning hours [50–52]. Disruptions in proper circadian function may also confer risk for CVD (described further below).

A *diurnal* or day-night variation of blood pressure is well established [53]. This pattern varies as a function of the sleep-wake cycle, such that blood pressure is typically highest during the wake period and lowest during sleep. An absence of this pattern of sleep-dependent decreases in blood pressure (i.e., a lack of nocturnal blood pressure *dipping*) is predictive of cardiovascular events and mortality [54]. In contrast to these *diurnal* effects, studies conducted under highly controlled conditions or using specialized experimental paradigms can be employed to isolate the effects of the circadian clock on physiologic processes while minimizing the confounding effects of behavioral or environmental factors [55, 56]. Using such procedures, an endogenous *circadian* (as opposed to sleep-dependent) variation of blood pressure was observed, with a peak occurring in the evening and trough in the morning [57, 58]. A circadian-regulated blood pressure trough in the morning may be a protective factor to help counteract behaviorally-induced surges in blood pressure during this time that are related to awakening from sleep, sudden changes in posture, and increases in physical activity [59].

Several other cardiovascular factors show circadian and/or diurnal variations in their expression. Sympathetic nervous system activity (e.g., circulating catecholamines) peaks at midday with lowest levels during the biological night, in a pattern roughly opposite to that of vagal tone [58]. Platelet aggregability and plasminogen activator inhibitor-1 levels, favoring increased ability to clot blood, peak during the morning hours [60–63]. While this may be an evolutionary adaptation to anticipate laceration risk after awakening, it may contribute to the increased risk for cardiovascular events in the morning in vulnerable individuals [59].

Disturbances to circadian rhythms can result in *circadian misalignment*, or a perturbation of the temporal harmony that usually exists between the endogenous circadian system and the timing of behaviors, such as sleeping/waking and feeding/fasting. Circadian misalignment can contribute to a variety of mental and physical disorders, including CVD risk [64]. Conditions representative of circadian misalignment and their relationship to CVD factors are described below.

Chronotype

Chronotype is a construct that describes an individual's temporal organization or diurnal preference, and is influenced by genetic, demographic (e.g., age, sex), and environmental (e.g., light exposure) factors. Chronotype can be assessed with questionnaires about one's preferred sleep-wake times and subjective times of peak performance and alertness, or quantified via the timing of sleep, as a behavioral manifestation of the internal circadian timekeeping system [65]. Having a relatively later chronotype (i.e., an evening vs. morning preference) is associated with several potential contributors to CVD risk, including mood disorders [66], metabolic dysfunction [67], and poor health behaviors like smoking [68], unhealthy diets [69–71], low physical activity [71], and high alcohol consumption [72]. In a sample of over 500 women, being an evening (vs. morning or intermediate) type was associated with >2-fold higher odds of having overall poor cardiovascular health (assessed with the American Heart Association's [AHA] Life's Simple 7 score) [73]. Having an evening (vs. morning) chronotype was also associated with higher odds of having hypertension [74].

More work, including prospective longitudinal studies, are needed to better determine if chronotype is associated with the development and progression of CVD. External light exposure is the strongest cue that synchronizes an individual's biological timing to the solar 24-hour day, and by extension, is a modifiable determinant of chronotype [75]. It would therefore be interesting to determine if chronotype represents a preventive or therapeutic target in individuals with or at risk for CVD.

Social jetlag

Social jetlag is related to chronotype, and describes the discrepancy between an individual's biological timing and the timing imposed by social obligations (e.g., work or school schedule) [65]. Based on one's chronotype (and also an accumulation of sleep loss during the work week), an individual's bed- and wake timing will typically delay and sleep episode duration will lengthen on work-free (e.g., weekend) compared to work (e.g., week) days when the circadian system is not constrained by social timing [65]. Thus, social jetlag (as quantified as the difference between the midpoint of sleep on work-free and workdays) is a measure of circadian misalignment. Weekday vs. weekend differences in sleep patterns, expressed as social jetlag, is also a form of sleep irregularity described above. Social jetlag is common, with ~70% of individuals experiencing a difference in biological and social clocks of >1 hour [76]. Greater social jetlag has been linked with various adverse behavioral and health outcomes, including mood/psychiatric disorders, obesity, metabolic dysfunction, poor diet, smoking, and lower physical activity [77]. Several studies examined the potential link between social jetlag and blood pressure or hypertension but failed to find significant relationships [78–82]. However, greater social jetlag was associated with other CVD-related factors, including higher levels of triglycerides [79, 82], total cholesterol [79], and cortisol [80], lower HDL cholesterol [82], and higher resting heart rate [80].

Shift work

Shift work (i.e., working non-standard hours outside of the typical 9-to-5 day) can lead to recurrent circadian misalignment and subsequent sleep impairments [83]. Accordingly, some

of the main consequences of shift work are chronic short sleep duration [84] and shift-work related insomnia [85]. Independent of sleep, however, circadian misalignment is associated with a range of adverse health outcomes and can increase risk for CVD, diabetes, obesity, and depression [64]. Shift work has been significantly associated with risk of myocardial infarction, stroke, and coronary events [86]. A meta-analysis of prospective cohort studies reported a dose-response relationship in which increased years of shift work are associated with increased risk of CVD morbidity and mortality [87].

Shift work is a prospective risk factor for future increases in blood pressure [88]. Compared to day workers, shift workers had significantly higher odds of experiencing increases in systolic or diastolic blood pressure of 10% to 25% from baseline over a 14-year follow-up period (odds ratios ranging from 1.15-1.24) [88]. Compared to day workers, nurses working night shifts were more likely to show a non-dipping blood pressure pattern, and also had heightened cardiovascular reactivity in response to a laboratory-based psychological stressor [89]. The detrimental effects of social jetlag on CVD outcomes (described above) may be exacerbated in shift workers. Social jetlag is common among shift workers and was found to be a factor contributing to a higher cardiovascular risk score [90•].

Laboratory-based studies help define some of the mechanistic pathways by which shift work can lead to CVD. In healthy non-shift working participants, the induction of an acute circadian misalignment simulating a night shift work schedule significantly increased 24-hour blood pressure vs. a day-schedule condition [91]. A mediation analysis found that these increases were partially due to a circadian misalignment-related decrease in sleep duration, and partially independent of changes in sleep duration [91]. In a similarly designed study, chronic shift workers had significantly increased 24-hour systolic blood pressure and C-reactive protein (CRP) under night- vs. day shift conditions [92]. In a laboratory-based model particularly relevant for shift work, experimentally-induced circadian misalignment combined with sleep restriction was found to adversely impact autonomic function; short sleep duration combined with circadian misalignment (but not circadian alignment) increased urinary norepinephrine and decreased nocturnal heart rate variability vs. baseline [93].

24-hour rest-activity rhythm

In community dwelling individuals, the estimation of rest-activity rhythms (RARs) from accelerometer data, reflecting physical activity patterns, sleep-wake cycles, and circadian influences, enables the investigation of the most evident manifestation of the circadian rhythm in relation to cardiovascular risk [94–96]. Two approaches that are typically employed to estimate RARs in the scientific literature are extended cosinor model analysis and non-parametric methods [97, 98]. In cosinor model analysis, the observed data are fit to a cosine curve and relevant parameters describing the rhythm are extracted from the fitted curve. Some of the relevant parameters obtained from cosinor analysis include amplitude, mesor, acrophase, and period (Table). However, this method may be limited because the rest-activity rhythm may not be ideally modelled as a sinusoid waveform. Thus, non-parametric methods may also be used to describe rest-activity rhythms and are a suitable alternative to cosinor analysis, as they do not make assumptions about the shape of

the 24-hour rest-activity rhythm. The non-parametric rest-activity rhythm variables include intradaily variability, interdaily stability, and relative amplitude of daily activity, computed from the timing and activity counts of the most active ten-hour period (M10) and the least active five-hour period (L5) of the day (Table).

There are limited data on associations of RARs with cardiovascular risk, and the existing data are derived primarily from studies of older adults [99, 100]. In a cohort of ~3000 older U.S. men (age: 67+ years), a RAR indicative of decreased circadian activity rhythm robustness (i.e., reduced amplitude and greater minimum, estimated using cosine model analysis) was associated with up to 39% increased risk of CVD events, primarily through increased risk of coronary heart disease or stroke [99]. Reduced F-value and a later occurring acrophase, also indicating reduced circadian activity rhythm robustness, were related to up to ~3-fold higher risk of peripheral vascular disease.

Studies of RARs and hypertension have focused on the interdaily stability metric from non-parametric analysis, as a measure of invariability in sleep-wake and rest-activity cycles across days, and have demonstrated associations with higher blood pressure and greater hypertension odds, particularly among non-shift workers (reviewed in [30]). This interdaily stability metric has additionally been linked to lower odds of having obesity or dyslipidemia in a cohort of >1,000 older adults [100]; similar associations have been reported in a modest sample of emerging adults (n=52) with both higher interdaily stability and lower intradaily variability being related to lower total and non-HDL cholesterol and CRP [101]. In a community-based sample of >500 predominantly female U.S. adults, lower relative amplitude, indicating a less robust RAR and lower rhythmicity, was consistently associated with higher BMI, but associations were not significant for other RAR characteristics [94]. Overall, additional epidemiologic studies are warranted to investigate RARs in relation to hard CVD outcomes and aspects of cardiometabolic health. This is particularly relevant for RARs estimated using the non-parametric approach, which does not make assumptions regarding the data distribution, and thus, may be superior to other approaches.

Does mental health mediate the relationship between sleep/circadian factors and CVD?

Sleep is closely linked to mental health, which itself can influence CVD risk [28]. Disturbances to sleep and mental health may contribute as independent risk factors along a common pathway towards CVD, or they may interact to confer unique risk. Based on recent work showing benefits of sleep-focused therapeutic interventions on psychological outcomes, sleep disturbance likely has a causal influence on the development of depression and anxiety [102, 103]. A theoretical extension is that psychosocial factors may be mediators of the relationship between sleep and CVD [104]. One example in support of this comes from a longitudinal study reporting that the positive relationship between short sleep duration and CVD was mediated by emotional distress [105]. However, based on the bidirectional relationship of sleep with anxiety and depression, it is also possible that sleep disturbances act as the intermediate between mental health and CVD [106]. In a 10-year prospective study, short sleep duration and insomnia were found to mediate the relationship

between depression and hypertension incidence [107]. Thus, the relationship between sleep, mental health, and CVD is complex, and more work should be done to clarify the interplay among these factors.

Sleep-focused interventions for CVD

The likely causal relationship between sleep disturbance and cardiovascular outcomes suggests that sleep-focused therapeutic interventions may be helpful to reduce CVD risk and disease burden.

Interventions for insomnia

Cognitive behavioral therapy for insomnia (CBT-I) is considered the first-line treatment for insomnia, with clinically meaningful effects that can be more durable than pharmacologic approaches [108]. This multi-component intervention is traditionally administered in-person but, promisingly, can also be effectively delivered remotely via digital platforms (e.g., smartphone applications) [109]. Administering CBT-I is feasible and efficacious in a variety of chronic conditions, including in patients with coronary artery disease. This specific approach, therefore, can be effective in improving sleep despite the presence of medical conditions and associated sequelae [110]. In the HeartSleep Study, Redeker and colleagues conducted a randomized clinical trial (RCT) testing the effects of CBT-I (n=91) vs. attention control (n=84) in patients with heart failure and insomnia of at-least mild severity [111•]. The CBT-I group had sustained, and comparatively larger, improvements in insomnia severity, self-reported sleep quality, daytime sleepiness, and functional performance (6-minute walk test) vs. control [111]. While future work is needed, CBT-I can potentially improve CVD outcomes by influencing biological stress markers (e.g., inflammatory, autonomic, and/or HPA pathways). For instance, CBT-I was found to reduce CRP levels and monocyte production of proinflammatory cytokines [112], and CBT-I related improvements in sleep were associated with increases in the ratio of daytime to nighttime urinary cortisol and epinephrine in patients with heart failure [113]. Reductions in blood pressure were seen after CBT-I in patients with comorbid hypertension and insomnia [114]. On the other hand, negative trials have been reported. An 8-week RCT of digital CBT-I (n=54) vs. control (n=67) in participants with mild sleep impairment and elevated blood pressure found that the intervention had no effect on 24-hour blood pressure despite significant improvements in insomnia symptoms [115]. Another 8-week RCT of clinician provided CBT-I (n=23) vs. control (n=23) in healthy participants with insomnia found that while insomnia was significantly improved, there were no effects on daily ambulatory blood pressure, heart rate, heart rate variability, CRP, n-terminal pro-brain natriuretic peptide, or cystatin C [116]. These negative trials, however, included participants without CVD.

Sleep extension

Behavioral interventions are effective in extending sleep duration, with a meta-analysis showing an overall pooled effect size of about 45 minutes from various approaches [117]. Accordingly, several sleep extension trials have been initiated to determine if alleviating habitual short sleep duration can improve cardiometabolic outcomes. In the earliest study, a 6-week intervention in participants with short sleep duration and prehypertension or

stage 1 hypertension increased sleep duration by ~35 minutes [118]. This was associated with a statistically significant decrease in 24-hour beat-to-beat systolic (−14 ± 3 mmHg) and diastolic (−8 ± 3 mmHg) blood pressure from pre-to-post intervention. Levels of inflammatory markers and urinary norepinephrine were not affected by the intervention, though these should be interpreted with caution due to the small sample size and exploratory nature of the study [118]. Another small RCT in participants with habitual short sleep duration and prehypertension/stage 1 hypertension found that a 6-week intervention that increased sleep duration by ~30 minutes resulted in greater reductions in 24-hour systolic (−9 mmHg vs. 0 mmHg) and diastolic (−5 mmHg vs. −2 mmHg) blood pressure vs. control [119•]. In a single-arm pre-post sleep extension study in healthy college students, the intervention was found to increase sleep duration by ~43 minutes and was associated with significantly reduced systolic blood pressure (7.0 ± 3.0 mmHg) [120].

Conclusion: Sleep, An Integral Component of Cardiovascular Health

Overall, accumulating evidence points to a strong link between sleep and circadian factors with CVD-related outcomes. The key role of sleep for CVD prevention has been formally acknowledged by its recent inclusion as a factor used by the AHA to define optimal cardiovascular health (along with diet, physical activity, smoking, obesity, cholesterol, blood glucose and blood pressure, dubbed “Life’s Essential 8”) [121••]. Healthy sleep characteristics, including sufficient sleep duration, good sleep quality, not having insomnia or snoring, and being low risk for obstructive sleep apnea, have been previously linked to more favorable cardiovascular health profiles, as measured by the AHA’s original Life’s Simple 7 [122]. In a 2022 analysis within MESA, the addition of an 8th, sleep-focused, metric to the seven health factors and behaviors already included in the AHA’s Life’s Simple 7, was shown to predict CVD risk over and beyond the original metrics [123•]. In that study, cardiovascular health scores that encompass the AHA’s Life’s Simple 7 plus a sleep health metric were associated with up to 47% lower CVD risk. Notably, cardiovascular health scores that included sleep duration only or a measure of MDSH as the 8th sleep metric were both predictive of CVD incidence, suggesting that screening for sleep duration may represent a feasible, efficient approach for assessing sleep health in settings where comprehensive evaluation of sleep behaviors, problems, and disorders is not possible. These findings are in line with the AHA’s recommendation to operationalize a sleep duration greater than or equal to 7 hours but less than 9 hours as representative of ideal sleep health in the new Essential 8 guidelines [121••]. Nevertheless, as described here, sleep is a multidimensional construct and future work is needed to determine the optimal approach to define, measure, and monitor sleep (and circadian) health for CVD prevention and treatment in clinical and public health settings.

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Table:

24-hour rest-activity rhythm metrics

Variable	Description
Cosinor analysis	
Amplitude	The difference between the peak and mean value (mesor) of a fitted waveform
Mesor	Mean value of the fitted waveform
Acrophase	The time at which the peak of a rhythm occurs
Period	Time elapsed for one cycle of the rhythm, i.e., time elapsed from peak to successive peak (or trough) of the waveform
Non-parametric analysis	
Interdaily stability	Quantifies the consistency of rest-activity rhythm across days, reflecting degree of synchronization of rest-activity rhythms to the external light-dark cycle
Intradaily variability	Quantifies the amount of fragmentation in the rest-activity rhythm, reflecting disturbance of the rest-activity rhythm
Most active ten-hour period (M10)	Mean activity during the most active ten hours of the day, typically reflecting daytime activity
Least active five-hour period (L5)	Mean activity during the least active five hours of the day, typically reflecting nighttime activity
Relative amplitude	Computed from the timing and activity counts of M10 and L5, reflecting robustness of the rest-activity rhythm