



Chrono nutrition and Cardiometabolic Health in Shift Workers: Exploring the Interplay between Chronotype, Dietary Intake, and the Timing of Food Intake

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Abstract: Circadian rhythms regulate various physiological and behavioral functions over a 24-hour period, are essential for maintaining metabolic health. Disruptions in these rhythms, particularly due to shift work, are increasingly associated with adverse cardiometabolic outcomes. This review explores the complex relationships between chronotype, shift work, meal timing, and their combined impact on cardiometabolic health. Shift work, especially involving night shifts, leads to circadian misalignment, which impairs insulin sensitivity, glucose metabolism, and overall metabolic efficiency. Chronotype, an individual's natural predisposition towards morning oriented or evening oriented, further influences the impact of shift work on health, with evening chronotypes often showing better adaptation to irregular work hours than morning chronotypes. The timing of food intake relative to circadian rhythms plays a critical role in metabolic health. Eating at times that are misaligned with an individual's circadian clock increases the risk of obesity, type 2 diabetes, and cardiovascular diseases. The evidence from multiple studies is consolidated in this review to show how shift work and irregular meal timings are linked to metabolic dysregulation. Shift workers often have extended eating durations and shorter fasting periods, leading to impaired metabolic outcomes. The review emphasizes the importance of consuming meals at biologically appropriate times to maintain metabolic homeostasis and mitigate the adverse effects of shift work. Understanding the relationships between circadian disruption, dietary habits, and cardiometabolic health is crucial for developing targeted interventions. This review calls for comprehensive research to further elucidate these complex interactions and advocates for implementing evidence-based guidelines and policies. Such measures are essential to improve the health and well-being of individuals engaged in shift work, ultimately reducing their risk of developing serious metabolic and cardiovascular conditions.

Index Terms: Cardiometabolic risk factors, chronobiology, chrono-nutrition, circadian misalignment

1 INTRODUCTION

Circadian rhythms play a crucial role in governing the physiological & behavioral functions of the human body. Numerous observational studies have established a connection between circadian disruption & the onset of cardiometabolic diseases. Circadian disruption can result from various lifestyle & environmental

factors. Multiple factors, including shift work, late chronotype, late sleep timing, sleep irregularity, and late meal timing, have been identified as disruptors of circadian rhythm alignment. These factors are associated with potential adverse effects on cardiometabolic health, such as increased BMI/obesity, higher blood pressure, greater dyslipidemia, inflammation, and diabetes. [1]. Shift work is a risk factor for conditions like overweight, obesity, Type 2 diabetes, increased blood pressure, and metabolic syndrome. It also influences eating behavior, food choices, energy intake, and macronutrient consumption [2]. Night-shift work, in particular, not only leads to a misalignment between the body's internal circadian system and the external light-dark cycle but also induces internal desynchronization among various levels of the circadian system and disrupts the expression of clock genes in various tissues. Metabolomics studies revealed shifts in metabolite timing during night work, further misaligning with the circadian system [3]. Chronotype has been shown to play a role in the effect of shift work on health [4]. To date, multiple studies have reported that morning types may be less able to adapt to shift work than evening types [5, 4, 6]. It was observed that individuals with an evening chronotype had elevated levels of proteins previously associated with cardiometabolic risk [7]. Chronotype is hypothesized to influence the relationship linking shift-induced circadian disruption to cardiometabolic outcomes [8, 9]. Limited research has explored this connection, and the findings are inconclusive. Some studies propose that both morning-oriented and evening-oriented chronotypes could contribute to the risk of cardiometabolic outcomes. [10, 11]. However, research into the role of chronotype in the effect of shift work on metabolic risk factors is still lacking [11].

Diet is a large contributor to both health [12] and performance [13, 14]. The timing of eating has become an important area of research given that food intake has been shown, largely in studies of rodents [15, 16], Circadian clocks regulate metabolic processes, glucose homeostasis, gastrointestinal motility and digestive processes [17]. It has been shown that eating food at times that contradict our circadian rhythms can therefore entrain rhythms in peripheral tissues, such as the liver [15]. This is particularly important to consider in shift workers, who are frequently distributing food intake across the 24 h period [18].

This altered meal timing includes eating during the night [19], which is problematic given that at night, the body is naturally primed for sleep" and we are eating at a time where we experience reduced glucose tolerance [20], reduced rates of gastric emptying and changes in body temperature [21]. Consequently, understanding and modifying the eating behaviors of shiftwork may play a key role in addressing the health risks associated with shiftwork [18].

The complex interplay among chronotype, shift work, circadian rhythms, and meal timing highlights the significant influence of each of these variables on cardiometabolic health. A growing body of evidence is consolidated in this review, which emphasizes how shift work disrupts internal biological clocks and metabolic processes, increasing the risk of cardiometabolic diseases. In order to establish focused interventions and policies aimed at reducing health risks among shift workers, it is imperative that the complexity of these interactions be acknowledged. This review aims to contribute to the field's expertise in order to guide future research paths and enable evidence-based initiatives that support the wellbeing of those managing non-traditional work schedules.

2 CIRCADIEN RHYTHM

The internal circadian system is mainly regulated by an independent master clock situated in the suprachiasmatic nucleus (SCN) of the hypothalamus. This master clock is synchronized by ambient light

and aligns with secondary clocks in both the brain and various peripheral tissues throughout the body [22]. The primary function of the circadian system is believed to be the temporal organization of physiological processes, allowing anticipation of periods of activity and rest [23]. The central clock, in response, regulates peripheral clocks through various mechanisms, including the control of rhythms in body temperature, autonomic nervous system activity, and hormones like cortisol and melatonin [24, 25]. These processes' rhythms are governed by internal "clocks," with a central clock situated in the suprachiasmatic nucleus of the hypothalamus acting as the conductor for clocks present in nearly all body tissues. The widespread distribution of these clocks emphasizes their vital role in health. Optimal health requires maintaining synchrony, encompassing harmony between our internal clocks and the external environment, as well as coordination among all internal clocks. Light signals reaching the suprachiasmatic nucleus through retinal ganglion cells and originating from the eye are the primary means of synchronizing our internal rhythms with the external world [23].

The circadian clock, serving as an internal regulator within cells of organisms, orchestrates physiological and behavioral activities to align with daily environmental changes in 24-hour cycles. When there is dysfunction or misalignment of the circadian clock with environmental cues in humans, it disrupts the timing of the sleep-wake cycle, resulting in various circadian rhythm sleep disorders [26]. Notably, these secondary clocks are also influenced by external cues and behaviors, known as "zeitgebers," which include activities like eating and sleeping [27, 22]. Alternatively, peripheral clocks can also be synchronized through different signals, such as feeding and fasting [28]. The existence of 24-hour day and night cycles on Earth has driven the evolution of circadian rhythms within the body's cells. These rhythms help us determine when to rest, eat, or be alert to potential danger or predation. The roots of modern circadian biology trace back to the 1970s when geneticist Seymour Benzer and his student Ron Konopka delved into the study of genes responsible for biological timing in *Drosophila*, or fruit flies. Several counterparts of the core clock proteins found in *Drosophila*, such as CLK and PER, also play analogous roles in the circadian timekeeping of mammals [29].

In the hypothalamus, there is a region known as the Suprachiasmatic Nucleus (SCN) located above the optic chiasma. Research has shown that SCN controls circadian rhythms by receiving signals from photic cues that influence the biological clock [30]. Melatonin, a hormone produced by the Pineal Gland, serves as a significant signaling molecule employed by the master circadian oscillator to synchronize downstream circadian rhythms. Various factors, including age, light exposure, and environmental and physiological influences, impact its secretion [31]. Genetic disorders related to the melatonin receptor have been associated with disruptions in the glucose metabolism pathway, increasing the susceptibility to developing type 2 diabetes [32]. A reduction in melatonin secretion is linked to accelerated aging, tumor formation, visceral adiposity, and changes in cardiovascular function [33, 34]. Individuals vary in their response to work shifts, with the majority experiencing some degree of difficulty or challenges. Conversely, some find it particularly challenging to adjust to disruptions in their circadian rhythm, causing misalignment with their internal body's circadian rhythm compared to the external environment. This misalignment can lead to difficulties in daily activities. In the modern era, the advancement of technology has allowed social and work activities to become less dependent on the natural light/dark duration of the environment. The primary disorders associated with circadian rhythm are sleep disturbances and depression, both of which can be triggered by changes in work schedules. The physiological activities of the body, such as heart rate and the release of hormones like epinephrine and norepinephrine, synchronize with the circadian cycle [35].

Consequently, habits like long flights across continents (resulting in jet lag), shift work, and night work have become common in modern lifestyles, impacting circadian rhythm function [36, 37]. This has prompted investigations into the connection between circadian disturbance and cardiovascular risk factors and health outcomes. Shift work, which is associated with both circadian disruption and sleep loss, is prevalent, with estimates indicating under 20% in the industrial world [38].

The labs of Hall, Rosbash, and Young ushered in the molecular era of circadian biology by focusing on a specific gene. This gene, known as PER, encodes a protein discovered by Jeffrey Hall and Michael Rosbash. The protein exhibits an increase during the night and a decrease during the day, and its levels are thought to play a crucial role in informing the cell about the current time. The mechanism resembles a negative feedback system, akin to how a thermostat regulates the temperature of a space. When the temperature falls below the set point, the thermostat activates the heater, and conversely, when the space becomes too warm, the thermostat deactivates the furnace. In this context, Hall and Rosbash propose that the PER protein may block the activity of the period gene by turning itself off each day. Throughout the night, levels of PER gradually rise, and as the protein levels decline, the process initiates again, constituting a negative feedback loop. This intricate biological balance mirrors the regulatory mechanisms that maintain stability in various aspects, from blood sugar levels to circadian rhythms, throughout the body [39]. "Lifestyle encompasses a collection of goals, plans, values, attitudes, behaviors, and beliefs that manifest in an individual's personal and family life, as well as in their social and cultural interactions. It represents an interdisciplinary concept that incorporates a health-oriented perspective on the physical, psychological, social, and spiritual dimensions of life" [40]. Lifestyle is inherently interconnected with social and cultural structures and contexts. In practical terms, it involves the routine activities of an individual on a daily basis, including aspects like sleep and waking time.

With the surge in chronic diseases over the past decade in developing countries, resulting in heightened health challenges, particularly obesity, [41], cardiovascular diseases, and diabetes, it becomes imperative to modify various aspects of lifestyle across all segments of society. The metabolism of cardiomyocytes is subject to circadian control [33], and circadian and diurnal rhythms are observed in key cardiovascular indicators like blood pressure, heart rate, platelet aggregation, and the incidence of various cardiovascular diseases [42]. Approximately 25% of the global population is affected by metabolic syndrome. Individuals with this syndrome face a five-fold higher risk of developing type 2 diabetes and are exposed to a threefold higher risk of heart attacks or strokes [43]. A disturbance in circadian rhythm, attributed to lighting conditions and lifestyle, has been associated with a variety of mood disorders, including impulsivity, mania, and depression, particularly in individuals exposed to such conditions [44]. Exposure to artificial light, even for brief periods during the night, induces a significant shift in circadian rhythms, leading to symptoms such as irritability, anxiety, and depressive behaviors. Additionally, it can decrease learning and memory efficiency in animal models [45, 46].

When environmental and behavioral factors consistently deviate from the SCN-driven internal circadian cycle, such as when food is consumed during the night, the integration of mistimed signals can disrupt the precisely regulated peripheral system, leading to a loss of homeostasis, commonly referred to as circadian misalignment [22]. Certain aspects of urban living have direct and impactful connections to health. One of the foremost factors is diet, with the consumption of fast foods and junk foods contributing to nutritional issues such as obesity and cardiovascular diseases [47]. Geological cycles, such as the length of daylight

and darkness in different seasons resulting from the Earth's movements, including rotation and transition, are crucial factors affecting circadian rhythms. These geophysical events play a role in the adaptation processes of all organisms, requiring them to adjust their physiology to environmental changes. In winter, when the days become shorter and nights lengthen compared to spring and summer, there is an increase in depression due to reduced sunlight exposure. This transient mood disorder is known as seasonal affective disorder (SAD). Individuals living in regions where seasonal changes are more pronounced, characterized by shorter days and diminished sunlight during winter, are more susceptible to experiencing depression [30].

The circadian rhythm, regulated by the suprachiasmatic nucleus (SCN), influences various physiological processes. Dysregulation, linked to lighting conditions and lifestyle, can lead to circadian misalignment. This misalignment is associated with mood disorders and disruptions in cardiovascular indicators, contributing to chronic diseases like obesity, cardiovascular diseases, and diabetes. Metabolic syndrome affects approximately 25% of the global population, posing increased risks of type 2 diabetes, heart attacks, and strokes. Disturbances in circadian rhythm have been linked to mood disorders, including depression. Artificial light exposure during the night can induce shifts in circadian rhythms, impacting behavior and memory efficiency. Urban living factors, such as diet and exposure to artificial light, contribute to health issues. The length of daylight and darkness in different seasons influences circadian rhythms, with reduced sunlight in winter contributing to seasonal affective disorder. Modifying lifestyle aspects, including sleep-wake cycles and diet, becomes crucial in mitigating the risks associated with circadian disruptions and improving overall health outcomes in the context of the surge in chronic diseases.

3 CIRCADIEN DESYNCHRONIZATION

The most substantial evidence regarding the influence of circadian misalignment on human health comes from clinical interventions that replicate conditions similar to shift work in healthy individuals who do not typically work shifts. These interventions induce acute circadian misalignment through simulated night shifts or forced desynchrony protocols, altering active and rest phases or artificially extending/shortening the day. This effectively disrupts the normal behavioral patterns of sleep and eating, putting them out of sync with the inherent rhythm of the SCN master clock and significantly impacting the input received by peripheral clocks that regulate metabolism [48]. Several clinical interventions have shown that acute circadian misalignment disrupts glucose-insulin metabolism. Misaligned mealtimes lead to elevated postprandial glucose levels and reduced insulin sensitivity, which could potentially increase the risk of type 2 diabetes [49, 50, 51].

Shift work, especially involving night shifts, disrupts the regular circadian sleep-wake cycle due to frequent changes in daily light profiles, leading to impaired health. Among rotational shift workers and night workers, sleep disturbances and sleep deprivation are particularly prevalent issues [52, 53]. Long-term shift work is linked to metabolic disruption and a positive energy balance, leading to an elevated risk of obesity, type 2 diabetes, heart disease, and metabolic syndrome [54]. Therefore, night shift workers tend to sleep fewer hours, exhibit higher weight and body mass index, and have an almost three times higher rate of abdominal obesity compared to day shift workers [55]. Furthermore, the changed phase misalignment between the internal circadian clock and the external environment results in reduced metabolic efficiency and disrupted cardiac function. [56]. In humans, research has demonstrated phase

shifts in peripheral clock activity when sleep and food intake occur at inappropriate times. However, the phase of the SCN master clock remains unchanged [48, 57].

One study in humans has assessed the metabolic effects of meal timing using an experimental design [58]. Energy intake and expenditure, along with sleep deprivation and fat intake, play crucial roles in the development of obesity, metabolic syndrome, and diabetes [59]. Despite an increased risk of obesity and chronic disorders in these shift work groups, studies have not consistently reported significant differences in energy intake among shift workers based on objective measures [60] or self-report [61, 62, 63]. A suggested factor contributing to the heightened risk of obesity in shift workers is increased energy intake, possibly influenced by changes in hunger and satiety hormones ghrelin and leptin due to circadian misalignment. Various simulated shiftwork studies have noted reduced leptin levels [64, 50, 51, 65] and elevated ghrelin levels [65, 64] during circadian misalignment compared to aligned conditions. According to a recent study [65], these effects may vary based on sex. Earlier sleep and mealtimes were linked to higher ghrelin concentrations and had no impact on leptin concentrations. Conversely, the combination of normal sleep and mealtimes had a reducing effect on food intakes [66]. Heightened hunger and reduced satiety resulting from circadian misalignment, especially in relation to meal timing, may contribute to weight gain in both shift workers [54] and individuals who eat later [67]. However, it's important to consider that these findings could be influenced by inherent biases in food intake measurement methods [68].

"Social jet lag" is proposed as another cause of circadian misalignment in the general population [69]. It is characterized by the shift in schedule between workdays and free days, where individuals typically use an alarm clock to wake up earlier on workdays or school days and sleep later on weekends or days off. Essentially, social jet lag measures the misalignment between an individual's work schedule and their internal schedule. Epidemiological research has shown that most individuals experience shifts in their sleep patterns between workdays and free days. [70] [71]. In a study involving a population with obesity-related chronic diseases, greater social jetlag was linked to higher calorie, saturated fat, and cholesterol intake during dinner, as well as increased protein, total fat, saturated fat, and cholesterol consumption during lunch. Additionally, more total fat and saturated fat were consumed during the morning snack. Social jetlag was also associated with delayed mealtimes for breakfast, early afternoon snack, and dinner due to later waking times [72]. Certain studies have indicated that short sleep duration is associated with an increase in food intake [66, 73]. No significant relationship was observed among normal weight individuals concerning social jet lag. Additionally, social jet lag has been linked to smoking, alcohol consumption, and caffeine consumption [74].

Epidemiological studies reveal that individuals with greater social jetlag, indicated by differences in the midpoint of sleep periods between work and free days, exhibit higher BMI, adiposity, and increased odds of obesity, metabolic syndrome, and type 2 diabetes [75] [76]. Circadian misalignment is gaining recognition as a risk factor for obesity and cardiometabolic disease. Although shift workers are particularly affected, there is an emerging awareness that even mild shifts in eating and sleeping patterns, such as social jetlag and eating jetlag, can lead to adverse health consequences. Both social and eating jetlag's contribute to later meal consumption patterns, potentially causing individuals to eat at biologically unfavorable times for energy and macronutrient metabolism [77]. An observational study indicated that individuals with a later midpoint of sleep, though not necessarily experiencing social jetlag, demonstrated higher energy intakes

during dinner and after 8 PM. These behaviors were associated with a higher BMI, along with increased consumption of fast food, sugar-sweetened beverages, and reduced intake of fruits and vegetables [77]. Another study demonstrated that sleep restriction for two nights, followed by two nights of sleep recovery, and an additional two nights of sleep restriction, effectively shifting the midpoint of sleep by 2.5 hours between sleep restriction and sleep recovery, led to an increase in food intake relative to baseline/pre-study sleep [78].

Multiple studies have shown the existence of a circadian rhythm in mood. Investigations conducted in forced desynchrony settings have revealed that these daily mood variations follow a significant circadian pattern. Additionally, there is an interaction with prior wakefulness, where the trough of mood is lowest around the time of the core body temperature minimum and tends to deteriorate over the wake period [79, 80]. This relationship holds true for both healthy controls and individuals with seasonal affective disorder. [81]. Studies in mice indicate that consuming food during the biological night that similar to human night shift work leads to a 12-hour shift in peripheral clock activity, leaving the central clock unaffected [82]. A separate study highlighted potential adverse effects of eating during the sleep period. Mice fed during the biological night (light period) consumed an equivalent number of calories but gained twice as much weight compared to mice fed during the dark period [83].

Additional research has indicated that both light exposure and feeding period contribute to these effects. mice exposed to constant bright light gained more weight than those in constant dim light or a standard 12-hour light-dark cycle. However, the detrimental effects of bright light were mitigated when food was restricted to the dark phase (typical feeding time). Another study demonstrated that feeding mice high-fat diets exclusively during the dark phase prevented the development of metabolic syndrome. [84, 85].

Considering meal timing in relation to chronotype, which measures an individual's innate preference for morning or evening, and has been shown to modulate the risk associated with late eating [86], might be a strategy to alleviate the burden in those at high risk. Individuals with evening chronotypes are more susceptible to experiencing larger social jet lag, primarily because they have to adhere to a conventional work schedule. In an analysis of a substantial database comprising 65,000 participants, it was observed that social jet lag was linked to higher BMI, and this association persisted even after accounting for sleep duration and chronotype. Notably, the association was particularly evident among overweight individuals [87].

Circadian desynchronization, stemming from factors like shift work and social jet lag, profoundly affects human health. Clinical interventions simulating shift work reveal disruptions in glucose-insulin metabolism, elevating the risk of type 2 diabetes. Shift work, particularly night shifts, is linked to metabolic disruption, obesity, and cardiovascular risks. Social jet lag, characterized by shifts in sleep patterns between workdays and free days, contributes to misalignments in eating and sleeping patterns, impacting calorie intake and increasing the odds of obesity-related chronic diseases. Even mild shifts, such as social and eating jet lag, have adverse health consequences, influencing meal consumption patterns. Meal timing in relation to chronotype is crucial, with evening chronotypes more susceptible to social jet lag, linking to higher BMI. Studies also highlight the circadian rhythm's impact on mood and the potential adverse effects of eating during the biological night. Considering meal timing in the context of chronotype emerges as a strategic approach for mitigating health risks associated with circadian disruptions, emphasizing the holistic

importance of circadian rhythms in overall well-being.

The intricate network of circadian rhythms, orchestrated by the suprachiasmatic nucleus and synchronized by environmental cues like light exposure, governs essential physiological processes throughout the body. Disruptions in these rhythms, whether due to shift work, irregular meal timing, or artificial light exposure, can lead to circadian misalignment. This misalignment is associated with a spectrum of health consequences, including mood disorders, cardiovascular disturbances, and metabolic dysregulation. As urban lifestyles increasingly challenge natural circadian patterns, understanding and mitigating these disruptions become imperative for promoting overall health and well-being. Future research and interventions targeting lifestyle modifications, such as sleep hygiene and dietary habits, hold promises in addressing the pervasive impact of circadian disturbances on global health.

4 CHRONOTYPE

The assessment of circadian phase is a key task in circadian biology. It involves tracking day-to-day changes in phase to calculate the period and revealing internal phase relationships among individual rhythms like sleep, melatonin, and core body temperature (CBT). This comparison helps understand the circadian machinery, determining whether various rhythms are governed by a single oscillator or a network of oscillators [88]. The phenomenon of "internal desynchronization" has been observed not only in complex organisms but also in simple single-cell organisms [89]. While experiments in constant conditions provide valuable insights into the circadian system, understanding its operation under entrainment poses the ultimate challenge. Analyzing entrainment experiments requires reliable methods to quantify the phase of entrainment. In humans, melatonin or core body temperature (CBT) is often used to determine phase, but these methods are laborious and costly, limiting their applicability for large-scale studies. To address this, researchers have employed questionnaires based on sleep-wake preferences to assess χ , primarily focusing on individual differences in sleep timing known as chronotype. The morningness-eveningness questionnaire (MEQ) was the first instrument developed for assessing sleep timing, producing scores indicative of morning or evening types [90]. Analyzing potentially circadian variables, such as biomarkers or performance, can lead to misinterpretations, especially when differences may be attributed to varying chronotypes, even if measurements are conducted at the same local time. To address this, results should be plotted against internal time, a correction that score-based instruments like the Morningness-Eveningness Questionnaire (MEQ) do not allow. In response, an alternative instrument, the Munich Chronotype Questionnaire (MCTQ), was developed. Unlike the MEQ, the MCTQ assesses chronotype based on subjective reports of actual sleep times on both work and free days. The aim is to calculate the midpoint of sleep on work-free days (MSF) as a phase marker, allowing analysis of circadian measurements based on internal time, accounting for potential oversleep on free days due to sleep loss during the work week (MSFsc) [71].

Under entrained conditions, mid-sleep-in humans is typically centered around the core body temperature (CBT) minimum. However, in temporal isolation, sleep generally begins at the CBT minimum. Depending on conditions, different chronotypes may exhibit varying internal phase relationships between melatonin and sleep [91, 92]. While chronotype has a genetic component, it is not a fixed trait. Consistent with circadian theory, chronotype depends on light exposure [70]. Observational studies have established a connection between evening chronotypes and a heightened prevalence of various cardiovascular and

metabolic diseases. This association includes an increased prevalence of conditions such as diabetes, metabolic syndrome, and cardiovascular disease (CVD) [93, 94]. A meta-analysis of cross-sectional studies revealed that individuals with evening chronotypes were more likely to have diabetes (odds ratio [OR] 1.30; 95% confidence interval [CI]: 1.20–1.41; $n = 7$ studies) compared to morning types. However, no significant association was observed for hypertension (OR 0.99; 95% CI: 0.77–1.27; $n = 5$ studies) [95]. Yet, in a prospective analysis involving 319 participants with a follow-up period of more than 2 years, chronotype did not show an association with incident diabetes in fully adjusted models [11].

Analysis of the UK Biobank, involving almost 400,000 participants, revealed that an early chronotype was associated with a reduced risk of incident cardiovascular disease (hazard ratio 0.93; 95% CI: 0.89–0.97) and a reduced risk of incident coronary heart disease (hazard ratio 0.92; 0.87–0.98) over a median follow-up period of 8.5 years [94]. Risk factors and subclinical predictors of cardiometabolic disease have shown associations with chronotype. A meta-analysis of cross-sectional studies, evening chronotypes, compared with morning types, exhibited significantly higher fasting blood glucose (mean difference [MD] 7.82; 95% CI: 3.18–12.45; $n = 8$ studies), higher hemoglobin A1c (MD 7.6; 95% CI: 3.1–12.2; $n = 8$ studies), higher low-density lipoprotein cholesterol (MD 13.69; 95% CI: 6.8–20.5; $n = 6$ studies), and higher triglycerides (MD 12.62; 95% CI: 0.90–24.4; $n = 8$ studies). However, no significant differences were observed for BMI ($n = 33$ studies), energy intake ($n = 16$ studies), or blood pressure ($n = 9$ studies) [96].

The phase of entrainment of the sleep-wake cycle is influenced by the sun rather than local time. Additionally, chronotype is influenced by age and sex [97]. Chronotype influences both sleep timing and meal timing [98], and these factors have been associated with cardiometabolic health, as discussed subsequently. In a study involving middle- to older-aged individuals ($n = 872$), those with a later chronotype exhibited later sleep timing and a later mealtime compared to individuals with an earlier chronotype [99]. In another study involving 596 health care workers, no significant differences in cardiometabolic risk factors were observed among shift workers with different chronotypes [100]. The link between evening chronotypes and the risk of cardiometabolic diseases may be attributed to environmental and behavioral factors. Individuals with an evening chronotype, for instance, might exhibit poorer-quality diets and higher dietary energy density compared to those with morning or intermediate chronotype [94, 98]. Evening chronotypes are also exposed to light at inopportune times, potentially leading to circadian disruption [101].

Comparisons between chronotypes pose challenges due to various factors, such as age, sex, and geographical location. MSFsc, expressed in local time, reveals a distribution in central Europe centered around 4:00. Chronotype distributions vary globally, with India having an earlier center around 3:00, causing intermediate chronotypes in central Europe to be considered late types in India based on local time [87].

Chronotype, defined by individual preferences in sleep timing, plays a significant role in shaping circadian rhythms and influencing health outcomes. Evening chronotypes, characterized by later sleep and meal timings, are associated with increased risks of metabolic and cardiovascular diseases. While genetic predispositions contribute to chronotype, environmental factors such as light exposure and lifestyle behaviors further modulate these preferences. Research underscores the complexity of chronotype's impact

on health, highlighting associations with metabolic syndrome markers and cardiovascular risk factors. Understanding these relationships is crucial for developing personalized health strategies tailored to individual circadian profiles. Future studies should continue to explore the interaction between chronotype, lifestyle interventions, and health outcomes to mitigate the adverse effects of circadian misalignment on global health.

5 DIETARY INTAKE

Nutrition plays a significant role in both health [12] and performance [14, 13]. Numerous studies have delved into the relationship between sleep and eating habits. For the majority of investigations and meta-analyses focusing on healthy adults, a consistent finding is that shorter sleep duration correlates with an overall increase in total energy intake [102, 103]. However, the outcomes tend to vary and are somewhat limited concerning the consumption of specific macronutrients. A prevalent observation is the heightened fat intake and diminished protein intake among individuals with shorter sleep durations (≤ 6 h) [102, 104]. Both research papers underscore a connection between inadequate sleep duration, nutritional quality, and erratic eating patterns.

Circadian clocks intricately regulate metabolic processes, glucose homeostasis, gastrointestinal motility, and digestive functions [59]. Consuming meals at times that conflict with our circadian rhythms can synchronize rhythms in peripheral tissues, such as the liver [15], leading to weight gain and obesity [105]. This holds particular significance for shift workers who often distribute their food intake throughout the 24-hour period [106, 18]. The altered meal timing, including nighttime eating, poses challenges as the body is naturally geared for sleep during the night [52], and eating during this period coincides with reduced glucose tolerance [20], slower rates of gastric emptying [107], and changes in body temperature [21]. Consequently, understanding and modifying the eating behaviors associated with shift work may be pivotal in addressing the health risks linked to shift work [18]. There is a scarcity of comprehensive evidence specifically addressing the effects of shift work on eating patterns.

Additionally, individuals with shorter sleep durations tend to consume irregular, highly palatable (energy-dense) meals and snacks [102]. In a controlled laboratory study where sleep was restricted to 5 h for 5 consecutive nights, sleep deprivation resulted in a 5% increase in total energy expenditure. However, the more significant rise in total food intake led to a positive energy balance and a modest weight gain [108]. In a comprehensive meta-analysis of 11 studies, it outlined the link between sleep deprivation and a positive energy balance [73]. Although there was no discernible effect on energy expenditure, the impact on weight was not explicitly detailed. Notably, a study that restricted calorie intake to 10% of energy requirements for 48 h revealed that deep sleep duration increased, returning to baseline levels after normal energy intake was reinstated [109]. This study suggests a potential bidirectional relationship between sleep duration and energy intake, warranting further investigation.

Shift workers commonly consume full meals during the day, while nighttime is characterized by more prevalent snacking [36, 110]. This eating pattern has been observed in various professions, including nurses [111, 112], transport workers [113], airline crew [114], slaughterhouse workers [115], and oil refinery workers [116]. Notably, nurses working night shifts have reported a lower kilojoule intake at dinner compared to other shift types [110]. Shift workers consume a variety of foods, with common choices including sandwiches, fruit, cake, potato chips, and biscuits, all of which tend to be high in carbohydrates

and fat content [116, 117]. Nurses, in particular, have reported significantly higher carbohydrate consumption compared to non-shift workers [118]. A study involving 340 Korean nurses found that 30% reported daily consumption of carbohydrate-heavy snacks [111]. Moreover, a study of Brazilian nurses revealed that longer work hours were associated with increased consumption of fried foods [119]. The majority of studies indicate no significant difference in energy intake when comparing shift workers to day workers, and this holds true for various shift schedules (early morning, day, afternoon/evening, or night shifts) [60, 63, 61]. However, there are exceptions to this trend. Notably, some observed no disparity in total energy intake between shift workers during night shifts and non-night shifts, but there was a redistribution of energy intake during the night shift [120]. Conversely, a minority of studies reported an increased energy intake among shift workers [60]. However, there are exceptions to this trend. Notably, some observed no disparity in total energy intake between shift workers during night shifts and non-night shifts, but there was a redistribution of energy intake during the night shift [120]. Conversely, a minority of studies reported an increased energy intake among shift workers [121, 122, 123]. For example, some studies found that rotating shift workers had an adjusted mean energy intake of 2005 kcal (95%CI 1928–2084), while day shift workers had 1850 kcal (95%CI 1782–1921) ($p = 0.007$) [122].

Limited research has focused on macronutrient intake among shift workers, and the existing studies often present conflicting findings [124]. The systematic review found no discernible difference in macronutrient intake between night shift workers and non-shift workers [61]. Conversely, in a study comparing various shifts among American healthcare workers, some identified an association between shift work and calorie intake, indicating higher fat and carbohydrate consumption [121]. A similar trend was observed among Polish healthcare professionals, where daily fat and carbohydrate intake showed a significant increase during rotating night shifts in comparison to day shifts (adjusted mean 78 g/day, 95%CI 74–82, vs. 70 g/day, 95%CI 67–74 for fat; 266 g/day, 95%CI 254–278 vs. 244 g/day, 95%CI 233–254 for carbohydrates) [122]. Shift work appears to affect fruit and vegetable intake across various occupations. Garbage collectors reported consuming less fruit during night shifts compared to morning and afternoon shifts [125]. Nurses, in general, reported consuming fewer servings of fruit and vegetables compared to government guidelines [126]]. Night-shift bus drivers also reported eating fewer vegetables than their day-shift counterparts [127]. Notably, in a study involving nurses, overweight participants consumed fewer servings of fruits and vegetables than those who perceived themselves as being normal or underweight [126]. Nurses in India reported a lower number of meals and more snacks per 24 hours, with significantly reduced carbohydrate, protein, and fat intake during night shifts compared to other shift type [110]. For industrial workers, while shift work did not impact on the 24-hour nutrient intake, there was a notable decrease in protein, total carbohydrates, sucrose, total fat, and calcium consumption during night shifts compared to afternoon shifts [116, 128]. A cross-sectional study covering various industries, including postal, printing, nursing, oil, and gas, reported differences in nutrient content. Night shift workers across industries consumed the highest percentage of saturated fat, and 12-hour shift workers consumed fewer carbohydrates than morning workers [129]. In a study involving male oil refinery operators, more milk and milk products, non-alcoholic beverages, yellow and green vegetables were consumed during the night shift compared to day or afternoon shifts [117]. Interestingly, milk consumption also varied between female in-flight workers (flight attendants and pilots) and shift workers (aircraft service and customer service), with in-flight workers consuming more high-fat milk products [130]. In a cross-sectional study, a comparison was made between night and day healthcare shift workers following a series of two to three consecutive work shifts [60]. The study revealed a lower proportion of protein consumption during meals in the night shift group, although no

significant difference was observed in overall energy and macronutrient intake between the two groups. Another laboratory study involving non-shift workers found no variance in total calorie, protein, or carbohydrate consumption after a simulated night shift. However, an increased preference for foods with high-fat content was demonstrated [131].

Among firefighters, there was no disparity in overall energy intake between day and night shifts. However, it was observed that a significantly higher percentage of energy was derived from sugar during 24-hour periods with a night shift compared to those with a day shift [132]. It is noteworthy that night-shift workers often report the consumption of drinks high in sugar, including soft drinks and energy drinks, as well as hot beverages such as tea and coffee to which sugar may be added. This pattern of consumption may contribute to the increased sugar intake reported by night-shift workers [132, 112]. Healthcare workers frequently cited their schedule as the predominant factor influencing their decision to eat, while the availability of time was identified as the primary determinant for the type of food chosen. Similar patterns were observed among firefighters [132] and truck drivers [113], where schedule considerations played a key role in motivating food intake.

In their comprehensive review, a study discovered a higher consumption of unhealthy foods, including saturated fat and soft drinks, among shift workers [133]. An observational study involving Swiss industry workers revealed that even a single night shift was linked to the consumption of unhealthy food across various shift schedules, as assessed by adherence to the French Programmed National Nutrition Santé Guideline Score [134]. [134]. In a cross-sectional study focused on Polish rotating shift healthcare workers, specifically identified increased consumption of energy, fat, carbohydrates, and saccharose, along with decreased consumption of fruits and vegetables [122]. Using a device recording the timestamp of hand movements to the mouth, a study demonstrated that night shift workers indulged in more snacks compared to both day and rotating shift healthcare workers [121]. Similarly, in a cross-sectional study involving Canadian nurses, reported elevated consumption of snacks in terms of quantity, frequency, and quality [135]. Contrarily, in a Dutch cohort study reported contrasting results, with no discernible difference in meal and snack frequency or snack quality between shift workers and day workers [10].

Dietary intake among shift workers is influenced by complex interactions between circadian rhythms, sleep duration, and work schedules. Shift work often disrupts meal timing, leading to irregular eating patterns and altered food choices characterized by higher intake of energy-dense foods, saturated fats, and sugars. This dietary behavior is compounded by factors such as convenience, availability, and time constraints during night shifts. Despite some variability in findings across studies, there is consistent evidence indicating shifts towards less healthy dietary patterns among shift workers, potentially contributing to increased risks of obesity and chronic diseases. Strategies aimed at promoting healthier eating habits in shift work environments are crucial for mitigating these health risks and improving overall well-being.

6 THE TIMING OF FOOD INTAKE

Shift workers, engaged in irregular working hours, encounter challenges in maintaining consistent eating patterns [136, 124]. Research indicates that engaging in shift work is linked to an extended eating duration, referring to the time span between the initial and final consumption within a 24-hour period [62, 63, 135]. A review of factors influencing the eating behavior of shift workers, emphasizing that, in addition to food

content (what is consumed), the timing of eating (when), the environment and source of food (where), and the reasons for eating during the shift (why) are integral components of the eating behavior of shift workers [137].

Irregular work schedules and time constraints can influence the timing of food consumption during shifts [138]. Shift work not only disrupts the distribution of energy throughout the 24-hour period but also contributes to irregular meal patterns [135, 122]. Nurses on rotating shifts exhibit more atypical temporal eating patterns and imbalanced diets compared to those on day shifts [139]. A study involving healthcare professionals found that those working night shifts reported a lengthier eating duration compared to their counterparts on day shifts (mean 14.2 hours \pm SD 3.8 hours vs. 12.0 hours \pm 1.5 hours, respectively, $p = 0.02$) [63]. Consequently, the fasting period for shift workers was shorter (11.8 hours \pm 2.0 hours vs. 13.3 hours \pm 1.9 hours in non-shift workers, $p = 0.02$) [135]. Additionally, a randomized crossover trial revealed that food consumption was distributed almost continuously during night shifts in contrast to day shifts [62].

Shift work has the potential to disturb the energy distribution throughout the 24-hour period, as indicated by various studies, even without a corresponding increase in overall energy intake. Several meta-analyses have been conducted, and they have not consistently revealed uniform outcomes in energy distribution when comparing night shifts to day shifts. This inconsistency is likely attributed to the insufficient adjustment for crucial covariates, unmeasured confounding variables, or variations in the shift structures and designs across the studies underlying these analyses [124, 122, 133]. A meta-analysis revealed that night shift workers tended to adhere to the three-meals-a-day structure, albeit with less regularity, especially during nighttime hours [18]. Additionally, individuals working night and rotating shifts exhibited a higher tendency to skip meals, with a particular emphasis on skipping breakfast [140]. Additionally, an investigation of American nurses revealed that 10% had no chance to take a break or have a meal during their shift, attributed to the demanding workload [141]. Among the 393 participants, 43% had some time for a meal break but were not relieved from patient care responsibilities [142]. Flight attendants had limited control over meal timings during their shifts, and their eating patterns were dictated by the demands of the flight [143]. In Australia, nurses have reported overeating during breaks, seizing the opportunity to consume as much as possible when given the chance [112]. Long-distance truck drivers, facing unpredictable and varied work hours, mentioned eating whenever it was convenient, fearing they might not have another opportunity to eat [144]. Paramedics stated that they consumed meals whenever there was a chance between emergency call-outs [145]. When 44 rotating shift workers and their spouses were interviewed to explore the impact of work routines on family life, meals emerged as a significant source of conflict between couples when integrating a shiftwork routine into the family lifestyle [146]. Families had to adjust the timing of the family meal to accommodate the shift worker's schedule, disrupting the family routine. Dinner preparation was also frequently disrupted, as workers faced the dilemma of choosing between sleeping and contributing to or participating in the family dinner [147].

Similarly, mine workers with rotating shifts find it challenging to adhere to regular meal patterns [148]. There's also evidence suggesting that night shift workers might skip breakfast when on duty in the morning, prioritizing sleep upon returning home, or may have breakfast outside the typical morning hours [115]. The temporal variations in the eating behavior of shift workers underscore the growing interest in chrononutrition [63, 124] and chronotypes, which refer to an individual's inclination toward early sleep and activity (morningness) versus late sleep and activity (eveningness) [71]. The individual chronotype may

also influence the tolerance to shift work, its impact on cardio-metabolic health [100], and the eating behavior within the general population [149, 150].

In certain workplace settings, there are designated break times during which workers can have meals [18]. However, increasing evidence suggests that these breaks are not consistently utilized for food consumption. Workers, especially in care settings, frequently forgo break opportunities and skip meals to attend to patient needs or fulfill other responsibilities. For instance, in a study involving 20 nurses, all participants reported being unable to take their full breaks, primarily due to prioritizing patient care [151]. The irregularity in working hours can affect food consumption patterns, with hunger showing a decrease during the night compared to daytime [18]. Hunger follows an endogenous circadian rhythm, decreasing at night [50] when homeostatic processes promote sleep [52]. This could explain why some workers report not eating during a night shift compared to day shifts [18]. Furthermore, in a study involving both night and day workers, male employees on night shifts were more prone to skipping breakfast, while female workers were more likely to skip lunch [152]. Another potential avenue of exploration lies in the central regulation of eating behavior, where appetite-regulating hormones could govern hedonic pathways, thereby playing a role in the alterations of eating patterns and, consequently, the metabolic effects of shift work [153, 102]. Instead of forgoing meals with the family, firefighters mentioned having dinner meal with the family before a night shift and then eating again at the firehouse [154]. This practice could influence the total energy consumed within a 24-hour period during a night shift. Likewise, in studies involving nurses and train drivers, participants reported that work hours conflicted with their families' eating habits [151, 155].

The timing of food intake among shift workers is heavily influenced by the irregularity of their work schedules. The extended eating duration, shortened fasting periods, and irregular meal patterns are common characteristics observed across various professions. These disruptions in eating schedules, coupled with the challenges of balancing work and personal life, contribute to the complexity of dietary behaviors in shift workers. Understanding these temporal variations in food consumption is crucial for developing targeted interventions that can help mitigate the adverse health effects associated with shift work. Further research is needed to explore the interactions between meal timing, chronotypes, and the metabolic health of shift workers to provide more effective dietary guidelines tailored to their unique needs.

7 CONCLUSIONS

The complex interplay among shift work, circadian cycles, and mealtime has a significant impact on cardiometabolic health. Disruptions in circadian alignment due to shift work and irregular eating patterns contribute to increased risks of obesity, type 2 diabetes, and cardiovascular diseases. Individual susceptibility to these risks is largely influenced by chronotype, with evening chronotypes generally better adapted to shift work than morning chronotypes. The review highlights the significance of synchronizing internal biological clocks with external environmental cues, particularly through appropriate meal timing, to maintain metabolic homeostasis. Moving forward, there is a pressing need for comprehensive research to further elucidate these relationships and for the development of evidence-based guidelines and interventions. Such measures will be crucial in mitigating the adverse health effects experienced by shift workers, ultimately fostering improved health outcomes and quality of life for those subjected to irregular work schedules.

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