HHS Public Access

Author manuscript

Obstet Gynecol Clin North Am. Author manuscript; available in PMC 2019 December 01.

Published in final edited form as:

Obstet Gynecol Clin North Am. 2018 December ; 45(4): 679–694. doi:10.1016/j.ogc.2018.07.008.

Sleep, Health, and Metabolism in Midlife Women and Menopause: Food for Thought

Howard M. Kravitz, D.O., M.P.H.[1,2], **Rasa Kazlauskaite, M.D., M.Sc., FACE**[3], and **Hadine Joffe, M.D., M.Sc.**[4]

[(1)]Department of Psychiatry, Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, IL,

[(2)]Department of Preventive Medicine, Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, IL,

[(3)]Department of Internal Medicine, Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, IL,

[(4)]Connors Center for Women's Health and Department of Psychiatry, Brigham and Women's Hospital and Dana Farber Cancer Institute, Harvard Medical School, Boston, MA.

Keywords

Sleep Health; Metabolic Health; Immunometabolism; Menopause; Menopausal Transition; Midlife

Introduction

"If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made."[1] In the half-century since Allan Rechtschaffen's declaration, studies of sleep and sleep deprivation have demonstrated that as a universal behavior sleep serves a variety of physiological functions. As a behavior essential for survival, and one in which humans engage in for nearly one third of their life, sleep is as necessary as food and water.[2] Although the function(s) associated with the complex phenomenon of sleep, which involves many interacting regulatory mechanisms, remain to be fully elucidated, one of its key roles is metabolic homeostasis.[3] Moreover, the health of populations is increasingly defined by positive attributes such as wellness, performance, and adaptation, and not merely by the absence of disease,[4] as well as prolongation of healthspan,

Corresponding Author: Dr. Kravitz - mailing address and email address as above.
Author Contact Information:
Howard M. Kravitz: Rush University Medical Center, Rush West Campus, Department of Psychiatry, 2150 West Harrison Street, Room 278, Chicago, IL 60612. hkravitz@rush.edu
Rasa Kazlauskaite: Rush University Medical Center, 1750 West Harrison Street, Suite 604v Jelke, Chicago, IL 60612. rasa_kazlauskaite@rush.edu
Hadine Joffe: Brigham and Women's Hospital, 75 Francis Street, Boston MA 02115. hjoffe@bwh.harvard.edu

not just extension of lifespan.[5] In this article, the authors will examine the concepts of Sleep Health and Metabolic Health, and their relationships to reproductive and chronologic aging in middle aged and older adult women.

Sleep and Sleep Health

The 2007 report of the Sleep in America poll brought national attention to the public health relevance of sleep, particularly for women.[6] Closely inter-related psychological, social, and cultural factors associated with the transition to midlife shape a woman's experience of menopause and contribute to sleep disturbances, a common complaint during the menopausal transition (MT).[7,8] In their review of studies of perceived sleep quality, Shaver and Woods'[7] described that more women in MT stages (i.e., perimenopause) reported poor sleep than did women in late reproductive age to an extent that was beyond anticipated age effects. Menopause-specific factors, aging, stress and other psychological factors, social realities/social transitions and their associated lifestyle changes, coexisting health conditions, and cultural factors can contribute to sleep problems and poor Sleep Health.[9]

Much information has accrued about the impact of sleep and sleep disorders on women's health since the release of the Sleep in America report. Consistent findings have confirmed that women's sleep disturbances increase with age, more so than in men, and the prevalence of their sleep problems increase as they traverse the MT.[10] Both sex (biological and physiological) and gender (environmental, social, and cultural influences on the biological factors) differences may help explain why men and women sleep differently and may underlie their differential risk for sleep disorders.[11,12] However, because menopause is associated with changes in behavior and other biological functions such as mood swings, anxiety/depression, and stress, in addition to sleep disturbances, symptoms that are associated with reproductive aging may be difficult to differentiate from symptoms due to chronological aging. Vasomotor symptoms, hormonal changes, age-associated changes in sleep, comorbid conditions, and psychosocial factors all have been cited as factors that contribute to the increasing prevalence of disturbed sleep in midlife women as they transition to menopause.[13] Recent data from the Study of Women's Health Across the Nation (SWAN)[14] and the Penn Ovarian Aging Study (POAS),[15] which used the final menstrual period (FMP) rather than MT stages, suggest that premenopausal sleep complaints predict poor sleep around the final menstrual period, consistent with a diagnosis of a menopause-related form of sleep disturbance. However, aside from a subgroup of ~ 15% of women whose sleep worsened in the years around the FMP, both the SWAN and the POAS found that following the FMP sleep complaints tended to be stable or increase slowly from pre-FMP to post-FMP from their premenopausal baseline.

In older adults, women as well as men, large variability in sleep characteristics are observed. Sleep is described as lighter, more easily disrupted, and associated with more frequent brief arousals and longer awakenings. It is shorter and less refreshing, and older adults are more likely to take daytime naps and/or adopt earlier bedtimes. In addition, older adults experience a greater burden of general health problems, and sleep problems, such as sleep apnea and restless legs, which become more prevalent, particularly in women during

postmenopause. However, few studies have specifically examined the potential benefits of good sleep/sleep health in older adults.

Sleep Health

Good Sleep Health is important for successful aging. Although sleep complaints are common in older adults, they are commonly associated with physical, environmental, and health factors. Menopause-specific factors, aging, stress and other psychological factors, social realities/social transitions and their associated lifestyle changes, coexisting health conditions, and cultural factors can contribute to sleep problems and poor Sleep Health.[16] Foley and associates[17] found that respondents to the 2003 "Sleep and Aging" survey who were 65 years and older indicated an inverse association between self-perceived quality of sleep and the number of their comorbid conditions. Buysse[4] defined Sleep Health as "a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being." In developing this concept, he found that "Sleep Health" is a term that is mentioned infrequently in the literature, and when it is, it is typically not defined. A PubMed search for this exact term produced 150 results, and Google Scholar over 3,000, but the majority include a comma between the words "sleep" and "health," indicating two items in a list of related concepts. Moreover, Sleep Health consisted of a number of different sleep parameters, including sleep duration, sleep times, awakenings, sleepiness, and specific sleep disorder symptoms. We conducted a more recent Ovid Medline search (December 18, 2017) and obtained 370 documents, of which 302 (82%) were published between 2010 and the search date.

To assess Sleep Health, characteristics of sleep and sleep problems can be measured on a range of key quantifiable dimensions, including subjective sleep satisfaction, appropriate timing of sleep, adequate duration, sleep efficiency or continuity, sustained alertness/sleepiness during waking hours, and sleep regularity.[4,18] This definition does not pertain to any specific sleep disorder, and can be used to characterize sleep multi-dimensionally across all persons. Buysse's[4] conceptual model of Sleep Health recognizes that relationships between sleep-wake function and molecular, cellular, systems and organism-level outcomes are reciprocal; just as sleep affects function and health, so too function and health influence sleep-wake function.

Healthy People 2020, a U.S. government-sponsored public health initiative, includes a section on Sleep Health that is designed to increase public awareness about the potential adverse consequences associated with sleep loss and sleep disorders.[19] Perturbations in various dimensions of Sleep Health may be manifested as Metabolic Health consequences[20] and psychological health consequences.[18]

Metabolic Health

Metabolic Health is typically approached from the perspective of the metabolic syndrome (MetS), which is clinically defined using diagnostic thresholds (Table 1).[21] Most women with type 2 diabetes meet criteria for MetS, and majority with MetS are obese or overweight. Moreover, Metabolic Health extends to every human body system and relates to

many chronic degenerative diseases and disability, as energy metabolism is involved in every biological function (Figure 1). Thus, metabolism is an essential component of health.

Historically viewed as a product of insulin resistance, MetS has been recognized as a manifestation of *immunometabolic* dysfunction (nutrient-energy stress induced chronic low-grade inflammation, causing loss of metabolic control).[22] It is generally accepted that energy metabolism is in constant dynamic balance between catabolic processes to generate energy for physical and mental productivity (at cellular and global levels), and anabolic processes to generate "biomass" (such as glucose, fatty acids, amino acids, etc.) for repair, maintenance, detoxification, and storage.[23,24] This dynamic coupling of catabolic and anabolic processes is regulated by circadian,[25] neurological and hormonal systems,[26] and tightly intertwined with innate and adaptive immunity (thus referred to as ***immunometabolism***).[22] The dynamic balance interval of energy metabolism (immunometabolic flexibility) narrows with age and other factors, increasing susceptibility to chronic disease, physical and neuropsychological frailty (for conceptual model, see Figure 1).[23]

In midlife women, accelerated reproductive aging is intertwined with chronological aging. Changes in reproductive hormone milieu lead to transformation of body and selfimage, change in psychological and physical functioning, and adaptation (or maladaptation) of lifestyle behaviors. Moreover, immunometabolic changes during MT relate to adipose tissue redistribution, often without changes in the overall body mass[27] with abdominal adiposity (adipose inflammation) being central to immunometabolic dysfunction and MetS.[28]

Metabolic Health largely depends on individual's lifestyle. Among all lifestyle factors, nutrition (nutrient-energy stress) undisputedly has the most impact on metabolic abnormalities.[29] Yet food intake is affected by other lifestyle factors, with a substantial effect of sleep, as nearly one-third of human life is spent sleeping.[30]

Sleep Health and Metabolic Health: Pathobiology of Associations

Sleep can affect immunometabolism directly and through interactions with the other triggers of immunometabolic dysfunction (Figure 1). Menopause-related sleep disturbance may affect eating behaviors and timing. Sleep disturbance is interconnected with mood, regulation of hunger and impulse control, thermoregulatory sensitivity, and other factors related to metabolic flexibility in response to nutrientenergy stress.[31–34] The relationship between sleep and energy metabolism appears to be bidirectional.[35–37]

Vasomotor symptoms and thermoregulation

Vasomotor symptoms (VMS) are associated with more sleep complaints and impaired sleep efficiency and continuity, with VMS primarily interrupting sleep but not shortening total sleep duration.[14,15,38] A narrow temperature sensitivity interval and core body temperature oscillations during the menopausal transition may explain the transitional nature of VMS, and in late postmenopause when women have lower body temperature, on average, compared to premenopausal women, these symptoms (hot flashes/flushes, night sweats) may subside.[39] A lower thermoregulatory threshold relative to an elevated core body temperature may plausibly prolong the duration of night sweats (and VMS), which in turn may be

associated with extended exposure to an elevated amount of wake after sleep onset (WASO) time.

During sleep, changes in respiratory quotient (RQ), reflecting energy metabolism, appear to follow the time course of core body temperature (decreases during the first half of sleep and increases during the second half), as energy metabolism and thermoregulation are closely associated.[40,41] Specifically, RQ and glucose oxidation decreases during the first half of the nighttime sleep cycle, particularly the last hour of sleep, when the REM sleep propensity is high. As such, MT-related sleep changes produce RQ shifts negatively affecting glucose and lipid utilization and storage, characteristic of MetS.

Circadian timing and insulin resistance

Circadian timing influences the regulation of many body functions, including sleep propensity, appetite/feeding, hormonal rhythms, and the rhythmicity of glucose and lipid metabolism.[42] Age-related changes in sleep and circadian rhythms may contribute to and interact with changes in nutrient intake, energy expenditure and resting metabolic rate, physical activity (exercise, nonexercise, sedentary time), and ultimately sarcopenia and higher body adiposity.[9] Misalignment of the sleep-wake cycle and melatonin rhythm may promote insulin resistance through regulation of the endocrine system, of peripheral clock genes, and of mitochondrial respiratory function. Sleep disturbances, including insufficient total sleep time, poor sleep quality and insomnia, and obstructive sleep apnea, are independent risk factors for the development and exacerbation of insulin resistance.[43] Dietary intake may modulate the effect of sleep loss on insulin resistance,[44] whereas exercise may potentially mitigate some of the metabolic damage and may improve sleep quality.[45] Thus, as older adults continue to work and engage in shiftwork, the incidence of metabolic disease may increase.[46]

In a sample of midlife women participating in SWAN, circadian misalignment beyond shift work (i.e., greater variability in bedtime advance and delay) in non-shift-working midlife women was associated with adverse Metabolic Health.[47] Sex differences in agerelated sleep and circadian rhythm disturbances and age-related changes in sex hormones also may contribute to metabolic disease in older adults, and the relationships between metabolic disease and sleep and circadian rhythm disturbance may be bidirectional.[48]

Metabolic flexibility (the capacity for the organism to adapt fuel oxidation to fuel availability, maintaining normal metabolic function)

Sleep typically represents a state of a relative quiescence from external environmental stressors (as sleep-related fasting), a state that allows for cell maintenance, repair, detoxification, cellular downscaling and memory consolidation, required for daily maintenance of metabolic flexibility.[49] Evidence suggests that chronic exposure to environmental factors can shape the metabolic pathways directed by specific transcriptional programs that tightly regulate the enzymes involved in cell metabolism and dictate cell fate contributing to metabolic flexibility.[50] The studies of transcriptome indicate that sleep loss affects metabolic adaptation and flexibility from the neurocognitive perspective,[51] and from

the peripheral circadian regulation perspective.[52] Likewise, sleep may affect immunological adaptation.[53,54] These restorative processes prevent the organism from disintegration (the entropy of the living systems tends to a maximum, while repair requires time and additional energy). As such, sleep is a fundamental biological necessity.

In experimental settings sleep-related fasting is modeled as time-restricted feeding, which is contrasted with random around-the clock feeing time, representing disrupted sleep-wake cycle. Time-restricted feeding exerts profound effect on hepatic gene expression and metabolites, particularly related to glucose and lipid metabolism,[55] including cyclic adenosine monophosphate (AMP) response element binding protein (CREBP), mechanistic target of rapamycin (mTOR), and AMP-activated protein kinase (AMPK) nutrient sensing pathways.[42] In addition, compared to random around-the-clock feeding time, restricted feeding results in smaller adipocyte size, less macrophage infiltration of adipose, lower inflammatory cytokine production, and more mitochondria. As such, time-restricted feeding may be associated with better adipose tissue function and immunometabolism.

Appetite, mood and nutrient-energy stress

Sleep restriction does not significantly affect 24-hour energy expenditure.[33,40] In contrast, sleep disturbance relates to positive energy balance due to increased food intake, suggesting an additional indirect mechanism for sleep's effect on Metabolic Health.[35,40,56]

In experimental settings with controlled eucaloric diet, sleep restriction results in significantly decreased concentrations of leptin, fasting peptide YY levels, glucagon-like peptide 1 and fullness, with significantly increased ghrelin, hunger and appetite.[40,56–58] Experimental sleep restriction studies paired with ad libitum eating opportunities further demonstrate that sleep restriction increases food intake, especially in the evening, and in excess of that required for energy balance, resulting in weight gain despite changes in hunger and satiety hormones signaling excess energy stores. Relative to men, women maintain weight during adequate sleep, but increase food consumption and experience weight gain during insufficient sleep.[59] Thus, excess energy intake secondary to sleep restriction is driven by both adverse changes in orexigenic and anorexigenic hormones and food consumption.[31,60,61] However, only a small number of women have been included in experimental sleep restriction studies, so less is known about the role of adipokines in women's Metabolic Health. In addition, it is not known whether sleep fragmentation concurrent with normal sleep duration, the most common type of sleep problem linked with menopause and VMS, has the same metabolic and eating behavior consequences as observed in sleep restriction.

Menopause-related sleep disturbance is associated with negative changes in mood.[32,62,63] Moreover, negative memory bias exacerbates this association.[64] The proposed mechanisms to explain the association between sleep, mood and excessive ad libitum food intake include sensitivity to food reward, disinhibited eating and psychological distress.[65] The relation of emotions and sleep is bi-directional: emotional processing can affect sleep, and sleep disturbance can be associated with stress reactivity and maladaptive coping including

excessive food intake, alcohol consumption, and reduced physical activity – all factors that directly affect metabolism.

Menopausal hormonal milieu

The association of sleep with immunometabolic changes is stronger in midlife women than in men. Specifically, actigraphy assessed sleep latency in women was associated with insulin resistance and partially explained by the indirect effect of inflammatory cytokines.[66] Loss of ovarian estradiol (E2) leads to much lower E2 concentrations in postmenopausal women than in midlife men of the same age,[67] partially explaining sex disparities in sleep and immunometabolism. Evidence suggests that there may be a significant bidirectional relationship in which sleep-wake cycles influence ovarian steroids and gonadotropins, and ovarian steroids and gonadotropin hormones influence sleep-wake cycles.[68–71] Marked fluctuations and changes in ovarian steroids and gonadotropins during the MT may contribute to the risks for and mechanism(s) involved in the development of menopause-related sleep disturbances and disorders.[72,73]

The estrogen action on immunometabolism has been extensively reviewed.[74] As estrogens decrease food intake and upturn energy expenditure, menopausal loss of ovarian estrogen narrows the interval of metabolic flexibility, increasing susceptibility to metabolic abnormalities when exposed to sleep disturbances and nutrient-energy stress.[75] Menopausal hormone therapy appears to restore Sleep Health[68] and facilitates Metabolic Health.[76] E2 in the physiological range mitigates immunometabolic dysfunction in adipose, cardiovascular, and neural in vitro systems,[77,78] partially explaining pleiotropic effects of menopausal E2 loss on chronic degenerative conditions.

Sleep Apnea, Metabolic Health and Menopause

The direct relationship between Sleep Health and immunometabolism is well established,[79] with chronic hypoxia affecting oxidative metabolism and apnea-induced sleep fragmentation affecting appetite regulation, neurohormonal regulation, adipose tissue distribution, epigenetic phenomena and immunometabolism overall. Multiple mechanisms link obstructive sleep apnea with abnormal immunometabolism.[80] Menopause is associated with increased risk of sleep apnea.[81] Specifically, at the perimenopause each additional year in the MT was associated with 4% greater apneahypopnea index.[82] Moreover, metabolic markers improve with treatment of obstructive sleep apnea,[83] and treatment of MetS using lifestyle modifications or bariatric surgery improve sleep apnea indices.[84,85]

Metabolic Outcomes

Associations between sleep and metabolic outcomes have been explored in cross-sectional and longitudinal studies.[37] The prototypical metabolic outcomes pertaining to midlife women include obesity, diabetes, and MetS.

Obesity

A meta-analysis of 14 adult longitudinal studies reported overall 25% higher odds of obesity with short (≤ 5 – 6 hours) sleep duration, but not with the long (≥ 7 – 9 hours) sleep duration.[86] The meta-analysis of cross-sectional studies reported negative relationship between sleep duration and abdominal adiposity.[87] These meta-analyses were not specific to midlife women, nor do they address the specific menopause- and VMS-related sleep problem of sleep interruption paired with normal sleep duration.

It is becoming increasingly recognized that sleep and nutrition are related, though the studies of these associations in clinical and community samples generally have been cross-sectional and have not involved midlife or older adults. Among 310 midlife women (mean 49.7, SD 2.0 years) who participated in the SWAN Sleep Study, cross-sectional associations between sleep duration and current BMI were independent of sleep-disordered breathing, but longitudinal associations between sleep duration and annual BMI change were not prospectively associated over ~ 4.6 years of follow-up in unadjusted and adjusted models.[88] Shortened sleep and sleep disturbances appear to be related to accumulation of visceral adipose tissue in a study that included midlife women.[89] Although longitudinal studies, which are limited by reliance on self-reported duration and generally do not account for potential confounding by sleep disordered breathing, demonstrate no consistent association between sleep and BMI in midlife women, the evidence suggests a potential relation between sleep and adipose tissue redistribution (visceral adiposity, increase in total body fat and decrease in muscle), which is characteristic of MetS.[27] These limitations highlight the need for a longitudinal investigation of sleep and adipose tissue distribution (with or without changes in total body fat) during the MT.

Diabetes Mellitus

A meta-analysis of 15 studies suggest a parabolic dose-response relationship in persons with diabetes between sleep duration and hemoglobin A1c, and a direct association between poor sleep quality and hemoglobin A1c.[90] Meta-analysis of ten prospective studies with follow-up of at least three years revealed an unambiguous and consistent parabolic relationship between sleep duration (both short, i.e., less than 6 hours, or long, i.e., more than 8 hours) or difficulties maintaining sleep and the risk of incident type 2 diabetes.[91] Moreover, a meta-analysis of 36 studies revealed that sleep disturbances, including difficulty initiating and maintaining sleep and obstructive sleep apnea, were associated with risk for incident diabetes, with the effect sizes comparable to having family history of diabetes or being overweight, and exceeding the effect size of sedentary lifestyle on diabetes risk.[30] The magnitude of the sleep effect highlights the importance of sleep in diabetes risk.

The recently published results from three studies including midlife women – the Nurses' Health Study,[92] the Whitehall II study,[93] and the West of Scotland study[94] – suggest parabolic associations between sleep duration or quality and incident diabetes, with confounding effects of obesity and behavioral factors. The majority of studies involving individuals without diabetes, which are not limited to midlife or menopausal women, have reported independent associations between obstructive sleep apnea (OSA) and insulin

resistance or sensitivity and/or other measures of glycemic health, with dose-dependent effect of OSA on such measures of metabolic impairment, though some studies were confounded by obesity.[95]

Although the steepest increase in diabetes prevalence occurs at midlife, the relationship between ovarian aging and incident diabetes proved to be difficult to ascertain. Neither natural nor surgical menopause per se has been reported to have strong associations with diabetes risk.[76,96] Likewise, the evidence linking menopausal reproductive hormone changes with increased diabetes risk is weak, although rapid changes as observed with oophorectomy may increase risk, and menopausal hormone therapy appears to reduce the diabetes risk. Moreover, diabetes may increase the risk of ovarian failure, although studied less extensively.[76] The effects of ovarian aging may be difficult to disentangle from the effects of chronological aging in relation to incident diabetes due to the insidious nature (leading to imprecise timing of diagnosis) and heterogeneity of diabetes. Moreover, results of longitudinal studies may be confounded by methodological constraints, related to limited glycemic outcomes across the glycemic spectrum. Also, instead of long-term glycemic markers (e.g., hemoglobin A1c or glycated albumin) most studies use short-term glycemic markers such as fasting glucose, which tend to have relatively poor reproducibility. The definitions of menopausal staging may also affect the associations between MT, metabolic outcomes and sleep factors.

Metabolic Syndrome

MetS (Table 1) is more prevalent in midlife women than in men,[97] and adversely affects women more than men.[98] Women typically transition from prediabetes to diabetes with a worse cardiovascular risk profile and a higher BMI than men. The steepest progression of MetS to diabetes occurs at midlife.

The increased risk for the MetS during the MT[28] may be linked to dimensions of sleep affected by MT, including subjective sleep complaints such as difficulty initiating or maintaining sleep,[99] and sleep disordered breathing.[100,101] A meta-analysis of 3 longitudinal and 12 cross-sectional studies reported higher odds of MetS with short (≤ 5 – 6 hours), and long (≥ 8 – 10 hours) sleep duration,[102] and the associations of short sleep duration with MetS are stronger in women than in men.[103] SWAN investigators examined cross-sectional associations of subjective and objective measures of sleep with the MetS in a multi-ethnic sample of midlife women and found that objective indices of sleep continuity, depth, and sleep disordered breathing were significant correlates of the MetS independent of race/ethnicity, menopausal status, and other factors that might otherwise account for these relationships, and these relationships did not differ by race/ethnicity.[20]

Summary/Discussion

Sleep is a biological necessity, a complex phenomenon that involves many interacting regulatory mechanisms, and one of its key roles is metabolic homeostasis. Sleep problems are common complaints of midlife women, particularly as they traverse the MT. Menopause-specific factors, aging, general health, psychosocial factors and lifestyle changes are typical

contributors to sleep problems and suboptimal Sleep Health. Sleep Health, as defined and conceptualized by Buysse, is a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being. Consisting of a number of different parameters, including sleep duration, sleep times, awakenings, sleepiness, and specific sleep disorder symptoms, Sleep Health can be used to characterize sleep multi-dimensionally. The conceptual model recognizes that relationships between sleep-wake function and molecular, cellular, systems and organism-level outcomes are reciprocal – sleep affects function and health, and function and health influence sleep-wake function.

Metabolism, too, is an essential component of health, extending as it does to every human body system, because energy metabolism is involved in every biological function. Whereas Metabolic Health depends largely on individual's lifestyle, disturbances in dimensions of Sleep Health may be manifested as Metabolic Health consequences. Aging in women, both chronologic and reproductive, are associated with the onset and progression of chronic degenerative diseases and disability, as accelerated reproductive aging is intertwined with chronologic aging. The dynamic balance interval of energy metabolism, termed "immunometabolic flexibility" narrows with age and other factors, increasing the susceptibility to chronic disease, physical and neuropsychological frailty. Both sleep and metabolism are influenced by circadian timing, and age-related changes in sleep and circadian rhythms may contribute to and interact with changes in orexigenic and anorexigenic hormones, nutrient intake, energy expenditure, resting metabolic rate, physical activity (exercise, non-exercise, sedentary time), and ultimately lead to and higher body adiposity.

To examine associations between sleep and metabolism, we have reviewed hot flashes and sleep apnea as important causes of sleep disruption during the menopause transition together with common Metabolic Health conditions relevant to midlife women – obesity, diabetes, and MetS. By addressing women's healthcare needs for these conditions, and encouraging healthy lifestyle behaviors and activities, clinicians will be assisting them to achieve Sleep and Metabolic Health as well as help them on the path to successful aging beyond midlife.

ACKNOWLEDGMENTS

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). Dr. Joffe also has support from R01AG053838. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

Disclosure Statement: Dr. Kravitz and Dr. Kazlauskaite report no relationship with a commercial company that has a direct financial interest in subject matter or materials discussed in this article or with a company making a competing product. Hadine Joffe reports research grants from Merck, Pfizer and SAGE, and consulting fees from Merck, Mitsubishi Tanabe, and KaNDy.

References

1. Rechtschaffen A The control of sleep. Proceedings of the Symposium on Human Behavior and its Control. Meeting of the American Association for the Advancement of Science, Chicago, Ill,

December 1970 [cited in Aldrich MS. Normal human sleep In: Sleep medicine. New York: Oxford University Press; 1999 p. 3–26 (p.20)].

2. Ross JJ. Neurological findings after prolonged sleep deprivation. Arch Neurol 1965;12:399–403. [PubMed: 14264871]
3. Upender RP. Sleep medicine, public policy, and public health In: Kryger M, Roth T, Dement WC, editors. Principles and practice of sleep medicine, 6th edition Philadelphia, PA: Elsevier, Inc.; 2017 p.638–45.
4. Buysse DJ. Sleep health: Can we define it? Does it matter? Sleep 2014;37:9–17. [PubMed: 24470692]
5. World Health Organization. WHO methods for life expectancy and healthy life expectancy. In: Global Health Estimates Technical Paper WHO/HIS/HSI/GHE/2014.5. March 2014. Available at: http://www.who.int/healthinfo/statistics/LT_method_1990_2012.pdf. Accessed January 18, 2018.
6. 2007 Women and Sleep. Sleep in America Polls. National Sleep Foundation Web site. Available at http://www.sleepfoundation.org/article/sleep-america-polls/2007women-and-sleep. Accessed August 11, 2017.
7. Shaver JL, Woods NF. Sleep and menopause: a narrative review. Menopause 2015;22:899–915. [PubMed: 26154276]
8. Xu Q, Lang CP, Rooney N. A systematic review of the longitudinal relationships between subjective sleep disturbance and menopausal stage. Maturitas 2014;79:401–12. [PubMed: 25449825]
9. Fung CH, Vitiello MV, Alessi CA, et al. Report and research agenda of the American Geriatrics Society and National Institute on Aging bedside-to-bench conference on sleep, circadian rhythms, and aging: new avenues for improving brain health, physical health, and functioning. J Am Geriatr Soc 2016;64:e238–47. [PubMed: 27858974]
10. Jehan S, Masters-Isarilov A, Salifu I, et al. Sleep disorders in postmenopausal women. J Sleep Disord Ther 2015;4:1000212. [PubMed: 26512337]
11. Krishnan V, Collop NA. Gender differences in sleep disorders. Curr Opin Pulm Med 2006;12:383–9. [PubMed: 17053485]
12. Mallampalli MP, Carter CL. Exploring sex and gender differences in sleep health: a Society for Women's Health Research Report. J Women's Health 2014;23:553–62.
13. Joffe H, Massler A, Sharkey KM. Evaluation and management of sleep disturbance during the menopause transition. Semin Reprod Med 2010;28:404–21. [PubMed: 20845239]
14. Kravitz HM, Janssen I, Bromberger JT, et al. Sleep trajectories before and after the final menstrual period in the Study of Women's Health Across the Nation (SWAN). Curr Sleep Medicine Rep 2017;3:235–50.
15. Freeman EW, Sammel MD, Gross SA, et al. Poor sleep in relation to natural menopause: a population-based 14-year follow-up of midlife women. Menopause. 2015;22:719–26. [PubMed: 25549066]
16. Society for Women's Health Research Interdisciplinary Network on Sleep. Women & Sleep A Guide for Better Health. Washington, DC: Society for Women's Health Research, 2017.
17. Foley D, Ancoli-Israel S, Britz P, et al. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res 2004;56:497–502. [PubMed: 15172205]
18. Furihata R, Hall MH, Stone KL, et al. An aggregate measure of sleep health is associated with prevalent and incident clinically significant depression symptoms among community-dwelling older women. Sleep 2017;40:zsw075.
19. HealthyPeople.gov. Sleep health. Available at: http://www.healthypeople.gov/2020/topicsobjectives2020/overview.aspx?topicid=38. Accessed December 25, 2017.
20. Hall M, Okun ML, Sowers M, et al. Sleep is associated with the metabolic syndrome in a multi-ethnic cohort of midlife women: the SWAN Sleep Study. Sleep 2012;35:783–90. [PubMed: 22654197]
21. Alberti K, Eckel R, Grundy S, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation;

International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–5. [PubMed: 19805654]

22. Hotamisligil GS. Foundations of immunometabolism and implications for metabolic health and disease. Immunity 2017;47:406–20. [PubMed: 28930657]
23. Feng Z, Hanson RW, Berger NA, et al. Reprogramming of energy metabolism as a driver of aging. Oncotarget 2016;7:15410–20. [PubMed: 26919253]
24. Vander Heiden MG, Cantley LC, Thompson CB. Understanding the Warburg effect: the metabolic requirements of cell proliferation. Science 2009;324:1029–33. [PubMed: 19460998]
25. Asher G, Sassone-Corsi P. Time for food: the intimate interplay between nutrition, metabolism, and the circadian clock. Cell 2015;161:84–92. [PubMed: 25815987]
26. Samuel VT, Shulman GI. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. J Clin Invest 2016;126:12–22. [PubMed: 26727229]
27. Janssen I, Powell LH, Kazlauskaite R, et al. Testosterone and visceral fat in midlife women: the Study of Women's Health Across the Nation (SWAN) fat patterning study. Obesity (Silver Spring). 2010;18:604–10. [PubMed: 19696765]
28. Janssen I, Powell LH, Crawford S, et al. Menopause and the metabolic syndrome: The Study of Women's Health Across the Nation. Arch Intern Med 2008;168:1568–75. [PubMed: 18663170]
29. Hall KD, Heymsfield SB, Kemnitz JW, et al. Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 2012;95:989–94. [PubMed: 22434603]
30. Anothaisintawee T, Reutrakul S, Van Cauter E, et al. Sleep disturbances compared to traditional risk factors for diabetes development: systematic review and metaanalysis. Sleep Med Rev 2016;30:11–24. [PubMed: 26687279]
31. Chaput J-P, St-Onge M-P. Increased food intake by insufficient sleep in humans: Are we jumping the gun on the hormonal explanation? Front Endocrinol (Lausanne) 2014;5:116. [PubMed: 25076940]
32. Kahn M, Sheppes G, Sadeh A. Sleep and emotions: bidirectional links and underlying mechanisms. Int J Psychophysiol 2013;89:218–28. [PubMed: 23711996]
33. Klingenberg L, Sjodin A, Holmback U, et al. Short sleep duration and its association with energy metabolism. Obes Rev 2012;13:565–77. [PubMed: 22440089]
34. Wilckens KA, Woo SG, Kirk AR, et al. Role of sleep continuity and total sleep time in executive function across the adult lifespan. Psychol Aging 2014;29:658–65. [PubMed: 25244484]
35. Chapman CD, Benedict C, Brooks SJ, et al. Lifestyle determinants of the drive to eat: a meta-analysis. Am J Clin Nutr 2012;96:492–7. [PubMed: 22836029]
36. Depner CM, Stothard ER, Wright KP. Metabolic consequences of sleep and circadian disorders. Curr Diab Rep 2014;14:507. [PubMed: 24816752]
37. Schmid SM, Hallschmid M, Schultes B. The metabolic burden of sleep loss. Lancet Diabetes Endocrinol 2015;3:52–62. [PubMed: 24731536]
38. Joffe H, Crawford S, Economou N, et al. A gonadotropin-releasing hormone agonist model demonstrates that nocturnal hot flashes interrupt objective sleep. Sleep 2013;36:1977–85. [PubMed: 24293774]
39. Neff LM, Hoffmann ME, Zeiss DM, et al. Core body temperature is lower in postmenopausal women than premenopausal women: potential implications for energy metabolism and midlife weight gain. Cardiovasc Endocrinol 2016;5:151–4. [PubMed: 28111609]
40. Hibi M, Kubota C, Mizuno T, et al. Effect of shortened sleep on energy expenditure, core body temperature, and appetite: a human randomised crossover trial. Sci Rep 2017;7:39640. [PubMed: 28071649]
41. Park I, Kayaba M, Iwayama K, et al. Relationship between metabolic rate and core body temperature during sleep in human. [Abstract]. Sleep Med 2015:16(Supplement 1);S186–7.
42. Manoogian ENC, Panda S. Circadian rhythms, time-restricted feeding, and healthy aging. Ageing Res Rev 2017;39:59–67. [PubMed: 28017879]
43. Van Cauter E Sleep disturbances and insulin resistance. Diabet Med 2011;28:1455–62. [PubMed: 21950773]

44. Nedeltcheva AV, Imperial JG, Penev PD. Effects of sleep restriction on glucose control and insulin secretion during diet-induced weight loss. Obesity 2012;20:1379–86. [PubMed: 22513492]
45. Saner NJ, Bishop DJ, Bartlett JD. Is exercise a viable therapeutic intervention to mitigate mitochondrial dysfunction and insulin resistance induced by sleep loss? Sleep Med Rev 2018;37:60–8. [PubMed: 29056415]
46. Tucker P, Marquie JC, Folkard S, et al. Shiftwork and metabolic dysfunction. Chronobiol Int 2012;29:549–55. [PubMed: 22621350]
47. Taylor BJ, Matthews KA, Hasler BP, et al. Bedtime variability and metabolic health in midlife women: the SWAN Sleep Study. Sleep 2016;39:457–65. [PubMed: 27091639]
48. Aurora RN, Punjabi NM. Obstructive sleep apnoea and type 2 diabetes mellitus: a bidirectional association. Lancet Respir Med 2013;1:329–38. [PubMed: 24429158]
49. Cronise RJ, Sinclair DA, Bremer AA. Oxidative priority, meal frequency, and the energy economy of food and activity: Implications for longevity, obesity, and cardiometabolic disease. Metab Syndr Relat Disord 2017;15:6–17. [PubMed: 27869525]
50. Gluckman PD, Hanson MA, Buklijas T, et al. Epigenetic mechanisms that underpin metabolic and cardiovascular diseases. Nat Rev Endocrinol 2009;5:401–8. [PubMed: 19488075]
51. Lane JM, Liang J, Vlasac I, et al. Genome-wide association analyses of sleep disturbance traits identify new loci and highlight shared genetics with neuropsychiatric and metabolic traits. Nat Genet 2017;49:274–81. [PubMed: 27992416]
52. Archer SN, Oster H. How sleep and wakefulness influence circadian rhythmicity: effects of insufficient and mistimed sleep on the animal and human transcriptome. J Sleep Res 2015;24:476–93. [PubMed: 26059855]
53. Westermann J, Lange T, Textor J, et al. System consolidation during sleep – A common principle underlying psychological and immunological memory formation. Trends Neurosci 2015;38:585–97. [PubMed: 26442693]
54. O'Neill LAJ, Kishton RJ, Rathmell J. A guide to immunometabolism for immunologists. Nat Rev Immunol 2016;169):553–65.
55. Robinson SL, Hattersley J, Frost GS, et al. Maximal fat oxidation during exercise is positively associated with 24-hour fat oxidation and insulin sensitivity in young, healthy men. J Appl Physiol 2015;118:1415–22. [PubMed: 25814634]
56. St-Onge M-P. Impact of sleep duration on food intake regulation: Different mechanisms by sex? [Commentary]. Obesity (Silver Spring, Md.) 2016;24:11.
57. Spiegel K, Leproult R, L'hermite-Balériaux M, et al. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. J Clin Endocrinol Metab 2004;89:5762–71. [PubMed: 15531540]
58. Spiegel K, Tasali E, Penev P, et al. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med 2004;141:846–50. [PubMed: 15583226]
59. Markwald RR, Melanson EL, Smith MR, et al. Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain. PNAS 2013;110:5695–5700. [PubMed: 23479616]
60. Capers PL, Fobian AD, Kaiser KA, et al. A systemic review and meta-analysis of randomized controlled trials of the impact of sleep duration on adiposity and components of energy balance. Obes Rev 2015;16: 771–82. [PubMed: 26098388]
61. Nedeltcheva AV, Kilkus JM, Imperial J, Kasza K, Schoeller DA, Penev PD. Sleep curtailment is accompanied by increased intake of calories from snacks. The Am J Clin Nutr 2009;89:126–33. [PubMed: 19056602]
62. Joffe H, Crawford SL, Freeman MP, White DP, Bianchi MT, Kim S, Economou N, Camuso J, Hall JE, Cohen LS. Independent Contributions of Nocturnal Hot Flashes and Sleep Disturbance to Depression in Estrogen-Deprived Women. J Clin Endocrinol Metab. 2016;101:3847–3855. [PubMed: 27680875]
63. Prairie BA, Wisniewski SR, Luther J, et al. Symptoms of depressed mood, disturbed sleep, and sexual problems in midlife women: cross-sectional data from the Study of Women's Health Across the Nation. J Women's Health 2015;24:119–26.

64. Hussain D, Shams W, Brake W. Estrogen and memory system bias in females across the lifespan. Translational Neuroscience. 2014;5:35.
65. Chaput J-P. Sleep patterns, diet quality and energy balance. Physiol Behav 2014;134:86–91. [PubMed: 24051052]
66. Kim TH, Carroll JE, An SK, et al. Associations between actigraphy-assessed sleep, inflammatory markers, and insulin resistance in the Midlife Development in the United States (MIDUS) study. Sleep Med 2016;27–28:72–9.
67. Vandenput L, Ohlsson C. Estrogens as regulators of bone health in men. Nat Rev Endocrinol 2009;5:437–43. [PubMed: 19528961]
68. Mong JA, Baker FC, Mahoney MM, et al. Sleep, rhythms, and the endocrine brain: influence of sex and gonadal hormones. J Neurosci 2011;31:16107–16. [PubMed: 22072663]
69. Shaw ND, Gill S, Lavoie HB, et al. Persistence of sleep-associated decrease in GnRH pulse frequency in the absence of gonadal steroids. J Clin Endocrinol Metab 2011;96:2590–5. [PubMed: 21646369]
70. Kravitz HM, Janssen I, Santoro N, et al. Relationship of day-to-day reproductive hormone levels to sleep in midlife women. Arch Intern Med 2005;165:2370–6. [PubMed: 16287766]
71. Sowers MF, Zheng H, Kravitz HM, et al. Sex steroid hormone profiles are related to sleep measures from polysomnography and the Pittsburgh Sleep Quality Index. Sleep 2008;31:1339–49. [PubMed: 18853931]
72. Polo-Kantolo P Sleep problems in midlife and beyond. Maturitas 2011;68:224–32. [PubMed: 21295422]
73. Paul KN, Turek, Kryger MH. Influence of sex on sleep regulatory mechanisms. J Womens Health 2008;17:1201–8.
74. Monteiro R, Teixeira D, Calhau C. Estrogen signaling in metabolic inflammation. Mediators Inflamm 2014;2014:Article ID 615917 (20 pages).
75. Jones MEE, Thorburn AW, Britt KL, et al. Aromatase-deficient (ArKO) mice have a phenotype of increased adiposity. Proc Natl Acad Sci 2000;97:12735–40. [PubMed: 11070087]
76. Karvonen-Gutierrez CA, Park SK, Kim C. Diabetes and menopause. Curr Diab Rep 2016;16:20. [PubMed: 26879303]
77. Ghisletti S, Meda C, Maggi A, et al. 17beta-estradiol inhibits inflammatory gene expression by controlling NF-kappaB intracellular localization. Mol Cell Biol. 2005;25:2957–68. [PubMed: 15798185]
78. Turgeon JL, Carr MC, Maki PM, et al. Complex actions of sex steroids in adipose tissue, the cardiovascular system, and brain: insights from basic science and clinical studies. Endocr Rev 2006;27:575–605. [PubMed: 16763155]
79. Gileles-Hillel A, Kheirandish-Gozal L, Gozal D. Biological plausibility linking sleep apnoea and metabolic dysfunction. Nat Rev Endocrinol 2016;12:290–8. [PubMed: 26939978]
80. Farr OM, Mantzoros CS. Sleep apnea in relation to metabolism: an urgent need to study underlying mechanisms and to develop novel treatments for this unmet clinical need. Metabolism 2017;69:207–10. [PubMed: 28190524]
81. Tufik S, Santos-Silva R, Taddei JA, et al. Obstructive sleep apnea syndrome in the Sao Paulo Epidemiologic Sleep Study. Sleep Med 2010;11:441–6. [PubMed: 20362502]
82. Mirer AG, Young T, Palta M, et al. Sleep-disordered breathing and the menopausal transition among participants in the Sleep in Midlife Women Study. Menopause 2017;24:157–62. [PubMed: 27760083]
83. Jullian-Desayes I, Joyeux-Faure M, Tamisier R, et al. Impact of obstructive sleep apnea treatment by continuous positive airway pressure on cardiometabolic biomarkers: a systematic review from sham CPAP randomized controlled trials. Sleep Med Rev 2015;21:23–38. [PubMed: 25220580]
84. Anandam A, Akinnusi M, Kufel T, et al. Effects of dietary weight loss on obstructive sleep apnea: a meta-analysis. Sleep Breath 2013;17:227–34. [PubMed: 22374151]
85. Greenburg DL, Lettieri CJ, Eliasson AH. Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. Am J Med 2009;122:535–42. [PubMed: 19486716]

86. Wu Y, Zhai L, Zhang D. Sleep duration and obesity among adults: a meta-analysis of prospective studies. Sleep Med 2014;15:1456–62. [PubMed: 25450058]
87. Sperry SD, Scully ID, Gramzow RH, et al. Sleep duration and waist circumference in adults: a meta-analysis. Sleep 2015;38:1269–76. [PubMed: 25581918]
88. Appelhans BM, Janssen I, Cursio JF, et al. Sleep duration and weight change in midlife women: the SWAN Sleep Study. Obesity 2013;21:77–84. [PubMed: 23505171]
89. Chaput J-P, Bouchard C, Tremblay A. Change in sleep duration and visceral fat accumulation over 6 years in adults. Obesity (Silver Spring) 2014;22:E9–12. [PubMed: 24420871]
90. Lee SWH, Ng KY, Chin WK. The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: a systematic review and meta-analysis. Sleep Med Rev 2017;31:91–101. [PubMed: 26944909]
91. Cappuccio FP, D'Elia L, Strazzullo P, et al. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care 2010;33:414–20. [PubMed: 19910503]
92. Cespedes EM, Bhupathiraju SN, Li Y, et al. Long-term changes in sleep duration, energy balance and risk of type 2 diabetes. Diabetologia 2016;59:101–9. [PubMed: 26522276]
93. Ferrie JE, Kivimäki M, Akbaraly TN, et al. Change in sleep duration and type 2 diabetes: the Whitehall II Study. Diabetes Care 2015;38:1467–72. [PubMed: 26068863]
94. Green MJ, Espie CA, Popham F, et al. Insomnia symptoms as a cause of type 2 diabetes incidence: a 20 year cohort study. BMC Psychiatry 2017;17:94. [PubMed: 28302102]
95. Lui MM, Ip MS. Disorders of glucose metabolism in sleep-disordered breathing. Clin Chest Med 2010;31:271–85. [PubMed: 20488286]
96. Kim C Does menopause increase diabetes risk? Strategies for diabetes prevention in midlife women. Womens Health (Lond). 2012;8:155–67. [PubMed: 22375719]
97. Beigh SH, Jain S. Prevalence of metabolic syndrome and gender differences. Bioinformation 2012;8(13):613–616. [PubMed: 22829741]
98. Rossi MC, Cristofaro MR, Gentile S, et al. Sex disparities in the quality of diabetes care: biological and cultural factors may play a different role for different outcomes: a cross-sectional observational study from the AMD Annals initiative. Diabetes Care 2013;36:3162–8. [PubMed: 23835692]
99. Akbaraly TN, Jaussent I, Besset A, et al. Sleep complaints and metabolic syndrome in an elderly population: the Three-City Study. Am J Geriatr Psychiatry 2015;23:818–28. [PubMed: 25499672]
100. Resta O, Bonfitto P, Sabato R, et al. Prevalence of obstructive sleep apnoea in a sample of obese women: effect of menopause. Diabetes Nutr Metab 2004;17:296–303. [PubMed: 16295052]
101. Young T, Finn L, Austin D, et al. Menopausal status and sleep-disordered breathing in the Wisconsin Sleep Cohort Study. Am J Respir Crit Care Med 2003;167:1181–5. [PubMed: 12615621]
102. Ju SY, Choi WS. Sleep duration and metabolic syndrome in adult populations: a meta-analysis of observational studies. Nutr Diabetes 2013;3:e65. [PubMed: 23670223]
103. Xi B, He D, Zhang M, et al. Short sleep duration predicts risk of metabolic syndrome: A systematic review and meta-analysis. Sleep Med Rev 2014;18: 293–7. [PubMed: 23890470]

Key Points:

- Sleep Health comprises quantifiable dimensions that include subjective sleep satisfaction, regularity, appropriate timing of sleep, adequate duration, sleep efficiency/continuity, and sustained alertness during waking hours.
- Metabolic Health depends largely on lifestyle and extends to every human body system as energy metabolism is involved in every biological function.
- Circadian rhythms regulate many functions related to sleep and metabolism, including sleep propensity, hormonal rhythms, feeding behavior/appetite, and the glucose and lipid metabolism rhythmicity.
- Changes in sleep patterns associated with menopause and aging may reflect voluntary lifestyle modifications, and disturbances in Sleep Health may result in Metabolic Health consequences.
- Menopause-related sleep disturbance may affect eating behaviors and timing, directly affect immunometabolism, and interact with other triggers of immunometabolic dysfunction, particularly abdominal adiposity (adipose inflammation).

Synopsis:

Sleep and Metabolism are essential components of health. Metabolic Health depends largely on individual's lifestyle. Disturbances in Sleep Health, such as changes in sleep patterns that are associated with menopause/reproductive aging and chronological aging, may have Metabolic Health consequences. Sleep restriction and age-related changes in sleep and circadian rhythms may influence changes in appetite and reproductive hormones, energy expenditure, and body adiposity. In this article, the authors describe how menopause-related sleep disturbance may affect eating behavior patterns, immunometabolism, immunometabolic dysfunction, and associations between sleep and metabolic outcomes.

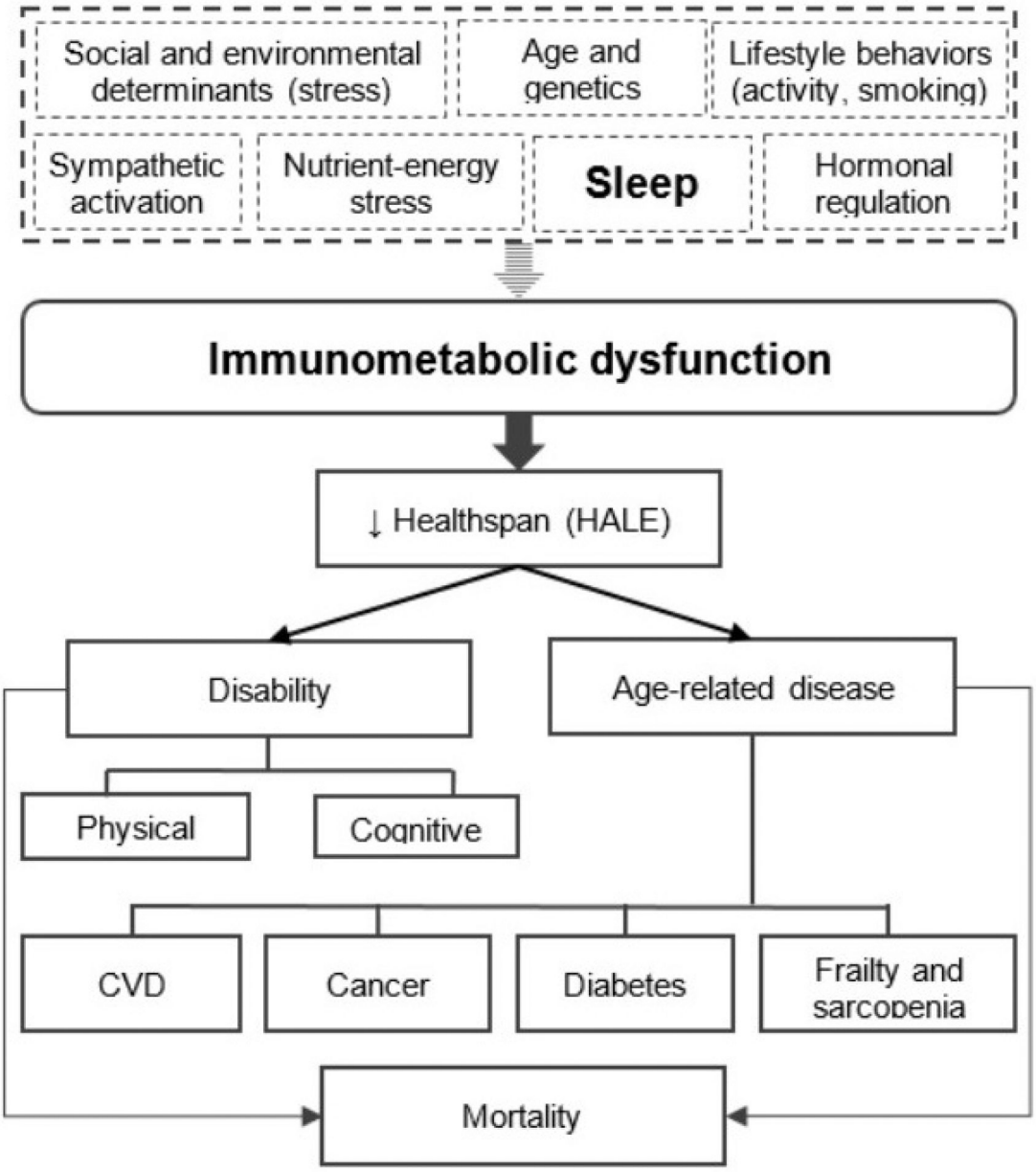

Figure 1:

Sleep with other triggers of immunometabolic dysfunction and relation to healthspan, disease, and disability in midlife women. Sleep can affect immunometabolism directly and through interactions with other triggers.

Hormonal regulation: reproductive hormones, adipokines, and other hormones.

HALE= healthy life expectancy[5]

CVD = cardiovascular disease

Courtesy of R. Kazlauskaite, MD, MSc, FACE, Chicago, IL.

Table 1.

Diagnostic criteria for metabolic syndrome

Criteria	Thresholds
Central obesity	Waist circumference [1] • Men: ≥ 102 cm (90 cm in Asians/Hispanics) • Women: ≥ 88 cm (80 cm in Asians/Hispanics)
Hypertension	≥ 130/85 mm Hg or hypertension treatment
Fasting blood glucose	≥ 100 mg/dL
High Density Lipoprotein (HDL) cholesterol	• Men: < 40 mg/dL • Women: < 50 mg/dL
Triglyceridemia	≥ 150 mg/dL

Diagnosis requires meeting threshold for at least 3 of the 5 criteria.

[1]Note that Asian and Hispanic men and women have different waist circumference thresholds than Whites and non-Hispanic Blacks (this is partially related to body size; they tend to be shorter on average).

Modified from Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120(16):1642.