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## CBT-I and women's health: Sex as a biological variable

Sara Nowakowski, PhD<sup>a</sup> and Jessica M. Meers, MA<sup>b</sup>

<sup>a</sup>Department of Obstetrics and Gynecology, University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555-0587 sanowako@utmb.edu

<sup>b</sup>Department of Psychology, University of Houston, 4800 Calhoun Road, Houston, TX, 77204 jmmeers@Central.UH.edu

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### Introduction

Several studies have demonstrated that women report more sleep difficulties<sup>1,2</sup> and are at greater risk for a diagnosis of insomnia compared to men.<sup>3,4</sup> In the National Sleep Foundation's 2007 poll, 30% of pregnant women and 42% of postpartum women reported rarely getting a good night's sleep, compared with 15% among all women. Additionally, 25% of perimenopausal women and 30% of postmenopausal women reported getting a good night's sleep only a few nights per month or less.<sup>5,6</sup> In general, there is a higher prevalence of insomnia and dissatisfaction with sleep in women. In contrast, objective measures of sleep, measured by actigraphy and polysomnography (PSG), have demonstrated shorter sleep onset latency, increased sleep efficiency and total sleep time in women compared to men.<sup>7-9</sup> A meta-analysis of sex differences of sleep behaviors in older adults (aged 58+) revealed no sex differences in total sleep time.<sup>10</sup> Although sleep disturbances and insomnia disorder are widespread in the general population, they tend to occur more frequently in women, particularly during times of hormonal fluctuation. In addition to sex differences found in the complaint of sleep disturbances and prevalence of insomnia, sex differences also exist for the treatment of sleep complaints. For example, in 2013 the U.S. Food and Drug Administration (FDA) required the manufacturers of Ambien to lower the recommended dose of zolpidem for women from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release products due to the risk of next-morning impairment and motor vehicle accidents. Women appear to be more susceptible to this risk because they eliminate zolpidem from their bodies more slowly than men. Zolpidem

**Corresponding Author:** Sara Nowakowski, PhD, University of Texas Medical Branch, Department of Obstetrics and Gynecology, 301 University Boulevard, Galveston, TX 77555-0587, Tel: (409) 772-3996, Fax: (409) 747-5129, sanowako@utmb.edu.

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is the first drug in the U.S. to have different recommended doses for women versus men, but it seems likely pharmacokinetic sex differences would lead to differences in rates of absorption, metabolism, and excretion of other medications as well. Other biopsychosocial factors, such as discomfort during pregnancy, breastfeeding and infant/child care during the postpartum period, and potential ongoing nocturnal vasomotor symptoms (hot flashes and night sweats) during peri- and postmenopause, may complicate insomnia treatment and require special treatment considerations for sleep disturbances in women.

## The Menstrual Cycle and Menstrual Cycle Disorders

The menstrual cycle of healthy women is characterized by cyclic changes in production of estradiol, progesterone, luteinizing hormone, follicle stimulating hormone, prolactin, and growth hormone. Reproductive hormones not only regulate reproductive function during the menstrual cycle, but also influence sleep and circadian rhythms. Negative menstrual symptoms are most commonly experienced by women during the last few days of the cycle, as progesterone and estrogen levels decline.<sup>11</sup> (see Figure 1).

Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD) are characterized by emotional, behavioral, and physical symptoms that occur in the premenstrual phase of the menstrual cycle, with resolution at the onset of menses or shortly thereafter. Many women of reproductive age experience some premenstrual symptoms, but 3-8% of women have clinically relevant premenstrual symptoms that they perceive as distressing and that affect daily function and meet diagnostic criteria.<sup>6,12-14</sup> Women with PMS/PMDD typically report sleep-related complaints such as insomnia, frequent awakenings, non-restorative sleep, unpleasant dreams or nightmares, and poor sleep quality associated with their symptoms; and daytime disturbances such as sleepiness, fatigue, decreased alertness, and an inability to concentrate during the premenstrual week and during the first few days of menstruation.<sup>15-24</sup> Women who experience severe premenstrual syndrome report significant declines in sleep quality in association with their symptoms during the late luteal phase compared with early follicular phase of their cycle.<sup>25-27</sup> Changes in progesterone and estrogen, rather than absolute levels, in the late-luteal phase may be an important consideration in determining factors associated with sleep quality. Actigraphic sleep was examined in participants from the Study of Women's Health Across the Nations (SWAN) and investigators found that among later reproductive-age women, sleep efficiency (SE) and total sleep time (TST) declines across the menstrual cycle with the most pronounced decline in the last week of the menstrual cycle.<sup>28</sup> These corresponding changes, however, were not found in PSG sleep.<sup>29-31</sup> Another study demonstrated that a steeper rate of rise in progesterone levels from follicular phase through mid-luteal phase was associated with greater PSG wake after sleep onset (WASO) and sleep fragmentation in the late luteal phase.<sup>32</sup> Sleep studies across the menstrual cycle have been limited by small sample sizes, heterogeneous cycle lengths, lack of ovulation timing controls, and oral contraceptive use. Due to these methodological issues and the limited nature of these studies, much remains unknown about premenstrual sleep.

Most women with PMDD seeking psychiatric help for this disorder present with symptoms of premenstrual depression, anxiety, and/or irritability. A number of treatment strategies

currently exist that target these symptoms and appear beneficial in treating them.<sup>33</sup> The selective serotonin reuptake inhibitors (SSRIs) fluoxetine and sertraline have been approved by the U.S. FDA for the treatment of PMDD. Fluoxetine,<sup>34-37</sup> sertraline,<sup>38</sup> and clomipramine<sup>39,40</sup> appear to be highly effective for treatment of depression, however little data is available on the safety and efficacy of using SSRIs to treat sleep disturbance and insomnia in PMS and PMDD. The evidence for nonpharmacological treatments, such as cognitive behavioral therapy for insomnia (CBT-I) have been summarized in several meta-analyses,<sup>41-43</sup> which led to its recognition as a first-line treatment for insomnia by the NIH Consensus Statement<sup>44</sup> and the American College of Physicians.<sup>45</sup> However, the efficacy of CBT-I in improving sleep and menstrual symptoms has not been examined. It remains unclear if CBT-I is efficacious for women with PMS/PMDD and if special treatment considerations should be made (e.g., targeting other PMS symptoms such as menstrual pain<sup>46</sup> or using CBT-I skills intermittently during late luteal phase of a women's menstrual cycle, as it is done to treat mood symptoms,<sup>47-49</sup> when symptoms are likely to be the most problematic).

## Pregnancy

Pregnancy brings about significant fluctuations in hormones that affect the sleep-wake cycle and cause physiologic changes that lead to sleep disturbance. In addition to the hormonal changes, pregnancy itself causes a multitude of anatomic and physiologic changes; which are essential to maintain the pregnancy, but can also contribute to sleep problems. Common symptoms, such as anxiety, urinary frequency, backache, fetal movement, general abdominal discomfort, breast tenderness, leg cramps, heart burn, and reflux cause sleep disturbance during pregnancy. Complaints of sleep disturbance during pregnancy generally start at the onset of pregnancy and increase in frequency and duration as the pregnancy progresses due to pregnancy-related anatomic, physiologic, and hormonal changes.<sup>50,51</sup> During the first trimester women tend to sleep longer and experience greater daytime sleepiness. Cross sectional and longitudinal studies that use subjective (self-report) and objective (PSG) measures of sleep have consistently documented increased wake after sleep onset and decreased sleep quality during the first trimester relative to pre-pregnancy.<sup>52,53</sup> During the second trimester, daytime sleepiness improves. During the third trimester there is an increase in sleep disruptions with typically 3-5 awakenings per night,<sup>54</sup> diminished daytime alertness, more disturbed dreams,<sup>55</sup> and approximately 21% report disturbed sleep at levels consistent with a diagnosis of insomnia disorder.<sup>52,56</sup> (Fig 2). Decreased sleep efficiency, increased wake after sleep onset, increased total sleep time (decreased by third trimester), increased stage 1 and 2 sleep, and decreased REM sleep (during late pregnancy) have been noted by PSG recordings.<sup>57-60</sup> Poor and insufficient sleep during pregnancy are also associated with increased circulating levels of inflammatory markers involved in poor health<sup>61-65</sup> and adverse pregnancy outcomes, including intrauterine growth restriction and preterm delivery.<sup>66-72</sup> During the third trimester of pregnancy, insufficient and poor sleep may place women at increased risk for prolonged labor and cesarean deliveries<sup>73,74,75</sup> and for having an infant small for gestational age.<sup>76</sup>

For most women, sleep disruptions are caused by factors related to pregnancy, such as frequent need for urination during pregnancy.<sup>56</sup> Some women, however, have difficulties

initiating sleep and/or returning to sleep, which may be unrelated to perinatal factors. When sleep disturbances are substantial (occur for 3+ nights per week for a period of 3+ months) and are associated with clinically significant distress or impairment of performance or other aspects of functioning, a diagnosis of insomnia disorder diagnosis is warranted. Insomnia may be experienced as a continuation or exacerbation of insomnia disorder that predates pregnancy or it may develop during pregnancy. The prevalence of sleep disturbance among perinatal women is as high as 58%<sup>77-79</sup> and a probable diagnosis of perinatal insomnia is estimated at 10%.<sup>80</sup> Daytime coping strategies such as napping, spending more time in bed, or increasing caffeine intake can perpetuate sleep difficulties. The presence of insomnia has a significant impact on quality of life and daytime functioning and its management is imperative.

Pharmacological treatment for insomnia during pregnancy is typically avoided because of the potential for adverse effects such as low birth weight, preterm deliveries, and cesarean sections in pregnancy.<sup>81-84</sup> Concerns regarding use of sleep medication during pregnancy and lactation make non-pharmacological treatment options for insomnia particularly attractive. CBT-I is a promising intervention for insomnia during pregnancy. A recent study of 187 pregnant women recruited from a low-risk maternity clinic and trade show, revealed that pregnant women preferred CBT-I over pharmacotherapy or acupuncture for treatment of insomnia.<sup>86</sup> Preliminary evidence in an open-pilot trial of 13 pregnant women with insomnia revealed improvements in diary and actigraphy-assessed sleep onset latency, sleep efficiency, and total sleep time.<sup>87</sup> In addition, symptoms of depression, pregnancy-specific anxiety, and fatigue also improved following treatment.<sup>87</sup> In this trial, CBT-I consisted of five weekly 90-minute group sessions and was adapted for pregnant women using the ORBIT model<sup>88</sup> from a treatment protocol that was previously validated for oncology patients with comorbid insomnia.<sup>89</sup> The final CBT-I session included a booklet on how to maintain gains in the postpartum period and how to foster optimal infant sleep.<sup>90</sup> Future studies could examine CBT-I tailored further for pregnancy symptoms (e.g., overcoming fatigue, strategies to reduce pain/discomfort during pregnancy, minimizing sleep disruption due to urinary frequency at night, increased stress management/relaxation, challenging maladaptive thoughts related to pregnancy and impending labor and delivery, and role transition).

## Postpartum

Sleep disturbance during the postpartum period and its effects on maternal role functioning and mother-infant interactions are not well understood. Both self-report and actigraphy studies have demonstrated that nearly 30% of mothers have disturbed sleep after the birth of their baby. The precipitous drop in hormone levels after the birth and unpredictable infant sleep patterns can affect a new mother's sleep. Longitudinal studies have documented that the first six months postpartum are associated with a significant increase in wake after sleep onset and a decrease in sleep efficiency compared to the last trimester of pregnancy.<sup>51,60,79,91,92</sup> Fatigue and lack of energy remain high from pregnancy into the postpartum period through the first year after delivery. Sleep begins to normalize around 3-6 months postpartum, around the time when infants begin to establish their own circadian rhythm, distinguishing between day and night, and sleep for longer periods of time during the night. Some women may also react to infant waking with catastrophic predictions about the

consequences of these disruptions that, in turn, lead to hyperarousal and prolonged wakefulness even after the baby is content and asleep. The response to sleep disruption with distress and urgency to get back to sleep inevitably increase arousal and reduce the likelihood of returning to sleep easily. Other factors such as the mother's age, type of delivery, type of infant feeding, infant temperament, return-to-work issues, prior birth experience, number of other children at home, and availability of nighttime support from the partner or other family member can have an impact on quality and quantity of sleep in new mothers. Many women compensate for their sleep disruptions by spending more time napping during the early postpartum period and going to bed earlier than pre-pregnancy habitual bedtime.<sup>93</sup> Sleep disruptions that may have begun with pregnancy or postpartum related stressors develop into an insomnia disorder, maintained by maladaptive compensatory behaviors<sup>94</sup> and conditioned hyperarousal.

Negative effects of poor and insufficient sleep during the postpartum period are also associated with mood disturbance and interfere with bonding. Mothers with poorer sleep (lower self-reported sleep quality and a higher number of night waking resulting from infant awakenings) perceived their infants as having lower mood and as being more distressed and tearful.<sup>95</sup> Moreover, insufficient sleep and more time tending to the infant at night predicted poorer maternal-infant attachment. Several studies have documented the relationship between sleep disturbance and subsequent reports of depressive symptoms at a later time among perinatal women (later in pregnancy<sup>96,97,98</sup> or in the early postpartum<sup>97,99, 100-102</sup>). The association between poor sleep and subsequent depressive symptoms also holds when sleep disturbance is experienced during the early postpartum period and postpartum depression develops at a later postpartum time.<sup>103,104,105</sup>

Interventions to improve maternal sleep and fatigue are limited, perhaps because of the universal nature of the experience and the belief that disturbed sleep is an unavoidable part of motherhood. In general, pharmacological interventions are seldom used in postpartum women who are breastfeeding. Even for women who are not breastfeeding, many choose not to take sedatives or other pharmacological options due to the need to have a more flexible sleep schedule for infant care. Therefore, behavioral interventions are the primary treatment options. Two pilot studies provide preliminary evidence for the efficacy of CBT-I for postpartum insomnia and both studies demonstrated that the benefits of CBT-I extended beyond improvement in sleep to other domains. One study provided five CBT-I sessions, between the second and seventh postpartum weeks, to women who stopped smoking during pregnancy and found a significant decrease in time awake in the middle of the night and a significant increase in nocturnal (as well as per 24-hour) sleep time. Importantly, compared to women who did not receive the sleep intervention, those who did undergo CBT-I had lower average daily cigarettes smoked and higher percent cigarette-free days.<sup>106</sup> The second study provided CBT-I to women with postpartum depression who also had disturbed sleep and reported pre to post treatment improvement in insomnia severity, sleep quality, sleep efficiency (% time asleep relative to time in bed), mood, and daytime fatigue.<sup>107</sup> In addition, several RCTs have evaluated interventions promoting infant sleep by providing education and training on infant sleep strategies to limit the development of unwanted sleep associations, increase the infant's ability to self soothe, and recommend environmental modifications to consolidate infant sleep at night. These trials demonstrated longer and more

consolidated sleep periods compared to infants in control conditions.<sup>108-110</sup> Future studies examining CBT-I across pregnancy and into the postpartum period and combining interventions for maternal and infant sleep are still needed. Future studies and interventions could also include the impact of partners or significant others to enhance support for maternal sleep and nighttime parenting responsibilities.

## Menopause

Menopause is a natural process that occurs in women's lives as part of normal aging. Menopause is defined as the cessation of menstruation due to degeneration of ovaries and follicles accompanied by changing ovarian hormone levels (estrogen and progesterone). The World Health Organization<sup>111</sup> characterizes menopause as the permanent cessation of menstrual periods that occurs naturally or is induced by surgery, chemotherapy, or radiation. More recently menopause has been categorized in stages such as menopausal transition (defined by standardized criteria<sup>112</sup> as variable cycle length seven days different from the normal cycle or >2 skipped cycles and an interval of amenorrhea of 2-12 months) or postmenopausal (defined as >12 months since last menstrual period). (Fig. 3). Menopause occurs between 50 and 52 years of age for Western women, but the range can vary based on race and ethnicity as well as lifestyle factors.<sup>113</sup> The worldwide population of 470 million postmenopausal women is expected to increase, as 1.5 million women enter menopause each year, reaching a total of 1.2 billion by the year 2030.<sup>111</sup> Most women now live long enough to become menopausal and can expect to live at least another 30 years beyond their final menstrual period.

Many women go through the menopausal transition with few or no symptoms, while a small percentage of women suffer from symptoms severe enough to interfere with their ability to function effectively at home, work, or school. Common complaints include hot flashes, night sweats, insomnia, mood changes, fatigue, and excessive daytime sleepiness. In the 2005 NIH State-of-the-Science Conference panel report on menopause-related symptoms, sleep disturbance was identified as a core symptom of menopause.<sup>114</sup> The prevalence of insomnia, defined as disturbed sleep associated with distress or impairment, is estimated at 38-60% in peri- and postmenopausal women.<sup>115-117</sup> Troubled sleep was reported by 54-58% of women between 40 and 60 years of age in the Ohio Midlife Women's study.<sup>118</sup> The Wisconsin Sleep Cohort found that perimenopausal women and postmenopausal women were twice as likely to be dissatisfied with their sleep as premenopausal women.<sup>119</sup> The Study of Women's Health Across the Nation (SWAN) has shown that difficulty sleeping is reported by 38% of women between 40 and 55 years of age, with higher levels among late perimenopausal (45.4%) and surgical postmenopausal (47.6%) women.<sup>116</sup>

The prevalence on nocturnal hot flashes/night sweats is generally believed to occur in 60 to 80% of women during the menopausal transition<sup>120</sup> and persist for 4 to 5 years on average.<sup>121,122</sup> When hot flashes occur during the night, they frequently awaken women from sleep; although not every nocturnal flash is associated with an awakening. Women with nocturnal flashes may also experience awakenings that are unrelated to a vasomotor event. Indeed, insomnia can occur during menopause independent of nocturnal flashes. Although self-reported nocturnal flashes correlate with poor subjective sleep quality, such association is



less clear when objective sleep measures are used.<sup>119,123,124</sup> There is only limited and contradictory evidence supporting an association between nocturnal flashes and sleep disturbance when both variables were measured objectively.<sup>119,123–129</sup> This may be, in part, due to the stage of sleep hot flashes are occurring. When taking sleep stage into account, several studies have demonstrated a relatively low incidence hot flashes during REM sleep, which has been postulated to be due to the inhibition of thermoregulatory responses during REM sleep.<sup>130</sup> Contradictory evidence may also be due to how investigators characterized hot flashes associated with awakenings and the duration of the window for detecting an awakening before or after the hot flash occurred.

Vasomotor symptoms, including nocturnal hot flashes and night sweats, may be a precipitating factor in the development of insomnia, but physiological arousals, behavioral conditioning, and misguided coping attempts appear to prolong insomnia.<sup>131</sup> CBT-I targets these behaviors and has been shown to be efficacious for the treatment of chronic insomnia in randomized trials of older adults<sup>132</sup> and for midlife women.<sup>133–135</sup> Telephone-delivered CBT-I has recently been evaluated for insomnia during the menopausal transition in a randomized clinical trial of perimenopausal and postmenopausal women with insomnia symptoms as well as daily hot flashes.<sup>135,136</sup> Compared with a menopause education control condition, 8 weeks of telephone-delivered CBT-I led to a greater reduction in insomnia symptoms, with improvements maintained at 6 months posttreatment.<sup>135</sup> Another randomized clinical trial of 150 postmenopausal women with insomnia were randomized to one of three conditions: face-to-face CBT-I, sleep restriction only, or sleep hygiene education control. The investigators found that the participants treated with CBT-I had a decrease in the insomnia severity index by 7.7 point, sleep restriction by 6.5 points, and sleep hygiene control by 1.1 points. Participants who received CBT-I were generally more likely to remit than participants who received sleep restriction alone.<sup>134</sup> These studies have examined traditional CBT-I or sleep restriction component of CBT-I in midlife women.

By focusing on distress following the hot flash experience, the principles of CBT can also be used to reduce suffering from hot flashes. Psychological factors, such as reaction to stress, appear to play a role; with past findings that higher levels of perceived control and lower distress were associated with fewer hot flashes.<sup>137–139</sup> Women who perceive greater control over their reactions to hot flashes tend to regard their flashes as less problematic and report fewer hot flashes.<sup>138</sup> This suggests that addressing reactions to hot flashes and providing strategies for coping with hot flashes could reduce distress associated with hot flashes. Indeed, several studies have provided empirical support demonstrating CBT as an effective strategy for coping with hot flashes and other menopausal symptoms.<sup>140–147</sup> Future studies combining CBT for insomnia and hot flashes could prove to be beneficial for women bothered by multiple symptoms during menopause, including insomnia and hot flashes.

## Conclusion

Sleep disturbances and disorders are common across a woman's lifespan. Important biological events, often mediated by hormones and physiological changes, such as menstruation, pregnancy, and menopause commonly impact and often cause dissatisfaction with sleep. (see Figure 4).

Given the fact that the negative impacts of poor sleep extend beyond tiredness and fatigue but also impair daytime functioning and mood, identification and treatment of these disorders is vital to a woman's quality of life. Women looking to treat their sleep problems have many options. Nonpharmacological treatments, such as CBT-I, offer longer-lasting improvements for insomnia without the side-effects that are often accompanied by medications.

Despite advancing research in sleep and women's health, there are several areas that deserve more focused research. In studies examining sex differences, the menstrual phase should be considered and documented. While it is known that the hormones are linked to sleep and that the variability across the menstrual cycle causes changes in sleep quality, there are few studies that have explored insomnia treatment options in women with PMS and PMDD and the interaction of sleep and mood disturbances and menstrual pain. There are a greater number of published studies examining CBT-I in perinatal and perimenopausal women. However, few studies have tailored CBT-I to multiple symptoms women may be experiencing. In addition, the high prevalence of women experiencing insomnia during times of reproductive hormonal change relative to the low number of trained providers able to effectively deliver CBT-I remains unbalanced.<sup>148</sup> Thus, future research should focus on dissemination and implementation of CBT-I in order to improve access to care, with particular attention on utilizing health technologies to reach more patients. Examining the effectiveness of CBT-I and its downstream effects on immune functioning, chronic health conditions, and recovery is also greatly needed.

## References

1. Akerstedt T, Knutsson A, Westerholm P, Theorell T, Alfredsson L, Kecklund G. Sleep disturbances, work stress and work hours: a cross-sectional study. *J Psychosom Res.* 2002;53(3):741–748. [PubMed: 12217447]
2. Lindberg E, Janson C, Gislason T, Bjornsson E, Hetta J, Boman G. Sleep disturbances in a young adult population: can gender differences be explained by differences in psychological status? *Sleep.* 1997;20(6):381–387. [PubMed: 9302720]
3. Jaussent I, Dauvilliers Y, Ancelin ML, et al. Insomnia symptoms in older adults: associated factors and gender differences. *Am J Geriatr Psychiatry.* 2011;19(1):88–97. [PubMed: 20808113]
4. Singareddy R, Vgontzas AN, Fernandez-Mendoza J, et al. Risk factors for incident chronic insomnia: a general population prospective study. *Sleep Med.* 2012;13(4):346–353. [PubMed: 22425576]
5. Baker FC, Wolfson AR, Lee KA. Association of sociodemographic, lifestyle, and health factors with sleep quality and daytime sleepiness in women: findings from the 2007 National Sleep Foundation "Sleep in America Poll". *J Womens Health (Larchmt).* 2009;18(6):841–849. [PubMed: 19514826]
6. Ferguson KA, Ono T, Lowe AA, Ryan CF, Fleetham JA. The relationship between obesity and craniofacial structure in obstructive sleep apnea. *Chest.* 1995;108(2):375–381. [PubMed: 7634870]
7. Carrier J, Land S, Buysse DJ, Kupfer DJ, Monk TH. The effects of age and gender on sleep EEG power spectral density in the middle years of life (ages 20–60 years old). *Psychophysiology.* 2001;38(2):232–242. [PubMed: 11347869]
8. Bixler EO, Papaliaga MN, Vgontzas AN, et al. Women sleep objectively better than men and the sleep of young women is more resilient to external stressors: effects of age and menopause. *J Sleep Res.* 2009;18(2):221–228. [PubMed: 19302341]
9. Jean-Louis G, Mendlowicz MV, Von Gizycki H, Zizi F, Nunes J. Assessment of physical activity and sleep by actigraphy: examination of gender differences. *J Womens Health Gend Based Med.* 1999;8(8):1113–1117. [PubMed: 10565670]



10. Rediehs MH, Reis JS, Creason NS. Sleep in old age: focus on gender differences. *Sleep*. 1990;13(5):410–424. [PubMed: 2287853]
11. Driver HS, Baker FC. Menstrual factors in sleep. *Sleep Med Rev*. 1998;2(4):213–229. [PubMed: 15310493]
12. Halbreich U, Borenstein J, Pearlstein T, Kahn LS. The prevalence, impairment, impact, and burden of premenstrual dysphoric disorder (PMS/PMDD). *Psychoneuroendocrinology*. 2003;28 Suppl 3:1–23.
13. Halbreich U, Backstrom T, Eriksson E, et al. Clinical diagnostic criteria for premenstrual syndrome and guidelines for their quantification for research studies. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*. 2007;23(3):123–130. [PubMed: 17454164]
14. de Carvalho AB, Cardoso TA, Mondin TC, et al. Prevalence and factors associated with Premenstrual Dysphoric Disorder: A community sample of young adult women. *Psychiatry Res*. 2018;268:42–45. [PubMed: 29986177]
15. Khazaie H, Ghadami MR, Khaledi-Paveh B, Chehri A, Nasouri M. Sleep Quality in University Students with Premenstrual Dysphoric Disorder. *Shanghai Arch Psychiatry*. 2016;28(3):131–138. [PubMed: 28638182]
16. Liu X, Chen H, Liu ZZ, Fan F, Jia CX. Early Menarche and Menstrual Problems Are Associated with Sleep Disturbance in a Large Sample of Chinese Adolescent Girls. *Sleep*. 2017;40(9).
17. Kim T, Nam GE, Han B, et al. Associations of mental health and sleep duration with menstrual cycle irregularity: a population-based study. *Arch Womens Ment Health*. 2018.
18. Kang W, Jang KH, Lim HM, Ahn JS, Park WJ. The menstrual cycle associated with insomnia in newly employed nurses performing shift work: a 12-month follow-up study. *Int Arch Occup Environ Health*. 2018.
19. Baker FC, Driver HS. Self-reported sleep across the menstrual cycle in young, healthy women. *J Psychosom Res*. 2004;56(2):239–243. [PubMed: 15016584]
20. Cohen LS, Soares CN, Otto MW, Sweeney BH, Liberman RF, Harlow BL. Prevalence and predictors of premenstrual dysphoric disorder (PMDD) in older premenopausal women. The Harvard Study of Moods and Cycles. *J Affect Disord*. 2002;70(2):125–132. [PubMed: 12117624]
21. Hachul H, Andersen ML, Bittencourt LR, Santos-Silva R, Conway SG, Tufik S. Does the reproductive cycle influence sleep patterns in women with sleep complaints? *Climacteric*. 2010;13(6):594–603. [PubMed: 20001564]
22. Lamarche LJ, Driver HS, Wiebe S, Crawford L, DEK JM. Nocturnal sleep, daytime sleepiness, and napping among women with significant emotional/behavioral premenstrual symptoms. *J Sleep Res*. 2007;16(3):262–268. [PubMed: 17716275]
23. Smith MJ, Schmidt PJ, Rubinow DR. Operationalizing DSM-IV criteria for PMDD: selecting symptomatic and asymptomatic cycles for research. *J Psychiatr Res*. 2003;37(1):75–83. [PubMed: 12482472]
24. Woosley JA, Lichstein KL. Dysmenorrhea, the menstrual cycle, and sleep. *Behavioral medicine (Washington, DC)*. 2014;40(1):14–21.
25. Lee KA, Baker FC, Newton KM, Ancoli-Israel S. The Influence of reproductive status and age on women's sleep. *J Womens Health (Larchmt)*. 2008;17(7):1209–1214. [PubMed: 18774898]
26. Moline ML, Broch L, Zak R. Sleep in women across the life cycle from adulthood through menopause. *The Medical clinics of North America*. 2004;88(3):705–736, ix. [PubMed: 15087212]
27. Schmidt PJ, Martinez PE, Nieman LK, et al. Premenstrual Dysphoric Disorder Symptoms Following Ovarian Suppression: Triggered by Change in Ovarian Steroid Levels But Not Continuous Stable Levels. *Am J Psychiatry*. 2017;174(10):980–989. [PubMed: 28427285]
28. Zheng H, Harlow SD, Kravitz HM, et al. Actigraphy-defined measures of sleep and movement across the menstrual cycle in midlife menstruating women: Study of Women's Health Across the Nation Sleep Study. *Menopause*. 2014.
29. Baker FC, Kahan TL, Trinder J, Colrain IM. Sleep quality and the seep electroencephalogram in women with severe premenstrual syndrome. *Sleep*. 2007;30(10):1283–1291. [PubMed: 17969462]

30. Baker FC, Sassoos SA, Kahan T, et al. Perceived poor sleep quality in the absence of polysomnographic sleep disturbance in women with severe premenstrual syndrome. *J Sleep Res.* 2012;21(5):535–545. [PubMed: 22417163]
31. Parry BL, Mostofi N, LeVeau B, et al. Sleep EEG studies during early and late partial sleep deprivation in premenstrual dysphoric disorder and normal control subjects. *Psychiatry Res.* 1999;85(2):127–143. [PubMed: 10220004]
32. Sharkey KM, Crawford SL, Kim S, Joffe H. Objective sleep interruption and reproductive hormone dynamics in the menstrual cycle. *Sleep Med.* 2014;15(6):688–693. [PubMed: 24841109]
33. Altshuler LL, Hendrick V, Parry B. Pharmacological management of premenstrual disorder. *Harv Rev Psychiatry.* 1995;2(5):233–245. [PubMed: 9384908]
34. Menkes DB, Taghavi E, Mason PA, Spears GF, Howard RC. Fluoxetine treatment of severe premenstrual syndrome. *Bmj.* 1992;305(6849):346–347. [PubMed: 1392887]
35. Steiner M, Steinberg S, Stewart D, et al. Fluoxetine in the treatment of premenstrual dysphoria. Canadian Fluoxetine/Premenstrual Dysphoria Collaborative Study Group. *N Engl J Med.* 1995;332(23):1529–1534. [PubMed: 7739706]
36. Stone AB, Pearlstein TB, Brown WA. Fluoxetine in the treatment of late luteal phase dysphoric disorder. *J Clin Psychiatry.* 1991;52(7):290–293. [PubMed: 2071558]
37. Wood SH, Mortola JF, Chan YF, Moossazadeh F, Yen SS. Treatment of premenstrual syndrome with fluoxetine: a double-blind, placebo-controlled, crossover study. *Obstet Gynecol.* 1992;80(3 Pt 1):339–344. [PubMed: 1495689]
38. Yonkers KA, Halbreich U, Freeman E, et al. Symptomatic improvement of premenstrual dysphoric disorder with sertraline treatment. A randomized controlled trial. Sertraline Premenstrual Dysphoric Collaborative Study Group. *Jama.* 1997;278(12):983–988. [PubMed: 9307345]
39. Sundblad C, Modigh K, Andersch B, Eriksson E. Clomipramine effectively reduces premenstrual irritability and dysphoria: a placebo-controlled trial. *Acta Psychiatr Scand.* 1992;85(1):39–47. [PubMed: 1546547]
40. Sundblad C, Hedberg MA, Eriksson E. Clomipramine administered during the luteal phase reduces the symptoms of premenstrual syndrome: a placebo-controlled trial. *Neuropsychopharmacology.* 1993;9(2):133–145. [PubMed: 8216696]
41. Morin CM, Culbert JP, Schwartz SM. Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *Am J Psychiatry.* 1994;151(8):1172–1180. [PubMed: 8037252]
42. Murtagh DR, Greenwood KM. Identifying effective psychological treatments for insomnia: a meta-analysis. *J Consult Clin Psychol.* 1995;63(1):79–89. [PubMed: 7896994]
43. Smith MT, Perlis ML, Park A, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry.* 2002;159(1):5–11. [PubMed: 11772681]
44. NIH. National Institutes of Health State of the Science Conference statement on Manifestations and Management of Chronic Insomnia in Adults, June 13–15, 2005. *Sleep.* 2005;28(9):1049–1057. [PubMed: 16268373]
45. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD. Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med.* 2016;165(2):125–133. [PubMed: 27136449]
46. Araujo P, Hachul H, Santos-Silva R, Bittencourt LR, Tufik S, Andersen ML. Sleep pattern in women with menstrual pain. *Sleep Med.* 2011;12(10):1028–1030. [PubMed: 22030206]
47. Freeman EW, Rickels K, Sondheim SJ, Polansky M, Xiao S. Continuous or intermittent dosing with sertraline for patients with severe premenstrual syndrome or premenstrual dysphoric disorder. *Am J Psychiatry.* 2004;161(2):343–351. [PubMed: 14754784]
48. Halbreich U, Bergeron R, Yonkers KA, Freeman E, Stout AL, Cohen L. Efficacy of intermittent, luteal phase sertraline treatment of premenstrual dysphoric disorder. *Obstet Gynecol.* 2002;100(6):1219–1229. [PubMed: 12468166]
49. Kornstein SG, Pearlstein TB, Fayyad R, Farfel GM, Gillespie JA. Low-dose sertraline in the treatment of moderate-to-severe premenstrual syndrome: efficacy of 3 dosing strategies. *J Clin Psychiatry.* 2006;67(10):1624–1632. [PubMed: 17107257]
50. Little SE, McNamara CJ, Miller RC. Sleep changes in normal pregnancy. *Obstet Gynecol.* 2014;123 Suppl 1:153S.

51. Hertz G, Fast A, Feinsilver SH, Albertario CL, Schulman H, Fein AM. Sleep in normal late pregnancy. *Sleep*. 1992;15(3):246–251. [PubMed: 1621025]
52. Hedman C, Pohjasvaara T, Tolonen U, Suhonen-Malm AS, Myllyla VV. Effects of pregnancy on mothers' sleep. *Sleep Med*. 2002;3(1):37–42. [PubMed: 14592252]
53. Santiago JR, Nollado MS, Kinzler W, Santiago TV. Sleep and sleep disorders in pregnancy. *Ann Intern Med*. 2001;134(5):396–408. [PubMed: 11242500]
54. Tsai SY, Lin JW, Kuo LT, Thomas KA. Daily sleep and fatigue characteristics in nulliparous women during the third trimester of pregnancy. *Sleep*. 2012;35(2):257–262. [PubMed: 22294816]
55. Lara-Carrasco J, Simard V, Saint-Onge K, Lamoureux-Tremblay V, Nielsen T. Disturbed dreaming during the third trimester of pregnancy. *Sleep Med*. 2014;15(6):694–700. [PubMed: 24780135]
56. Baratte-Beebe KR, Lee K. Sources of midsleep awakenings in childbearing women. *Clinical nursing research*. 1999;8(4):386–397. [PubMed: 10855105]
57. Kizilirmak A, Timur S, Kartal B. Insomnia in pregnancy and factors related to insomnia. *The Scientific World Journal*. 2012;2012:197093. [PubMed: 22623880]
58. Driver HS, Shapiro CM. A longitudinal study of sleep stages in young women during pregnancy and postpartum. *Sleep*. 1992;15(5):449–453. [PubMed: 1455129]
59. Pien GW, Schwab RJ. Sleep disorders during pregnancy. *Sleep*. 2004;27(7):1405–1417. [PubMed: 15586794]
60. Lee KA, Zaffke ME, McEnany G. Parity and sleep patterns during and after pregnancy. *Obstet Gynecol*. 2000;95(1):14–18. [PubMed: 10636494]
61. von Kanel R, Dimsdale JE, Ancoli-Israel S, et al. Poor sleep is associated with higher plasma proinflammatory cytokine interleukin-6 and procoagulant marker fibrin D-dimer in older caregivers of people with Alzheimer's disease. *J Am Geriatr Soc*. 2006;54(3):431–437. [PubMed: 16551309]
62. Vgontzas AN, Zoumakis E, Bixler EO, et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. *J Clin Endocrinol Metab*. 2004;89(5):2119–2126. [PubMed: 15126529]
63. McDade TW, Hawkey LC, Cacioppo JT. Psychosocial and behavioral predictors of inflammation in middle-aged and older adults: the Chicago health, aging, and social relations study. *Psychosom Med*. 2006;68(3):376–381. [PubMed: 16738067]
64. Meier-Ewert HK, Ridker PM, Rifai N, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J Am Coll Cardiol*. 2004;43(4):678–683. [PubMed: 14975482]
65. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med*. 2006;166(16):1756–1762. [PubMed: 16983055]
66. Dudley D. Cytokines in preterm and term parturition In: Hill J, ed. *Cytokines in Human Reproduction*. New York, NY: John Wiley & Sons, Inc.; 2000:171–202.
67. Holst RM, Mattsby-Baltzer I, Wennerholm UB, Hagberg H, Jacobsson B. Interleukin-6 and interleukin-8 in cervical fluid in a population of Swedish women in preterm labor: relationship to microbial invasion of the amniotic fluid, intra-amniotic inflammation, and preterm delivery. *Acta Obstet Gynecol Scand*. 2005;84(6):551–557. [PubMed: 15901266]
68. Menon R, Merialdi M, Lombardi SJ, Fortunato SJ. Differences in the placental membrane cytokine response: a possible explanation for the racial disparity in preterm birth. *Am J Reprod Immunol*. 2006;56(2):112–118. [PubMed: 16836613]
69. Vogel I, Thorsen P, Curry A, Sandager P, Uldbjerg N. Biomarkers for the prediction of preterm delivery. *Acta Obstet Gynecol Scand*. 2005;84(6):516–525. [PubMed: 15901257]
70. Bartha JL, Romero-Carmona R, Comino-Delgado R. Inflammatory cytokines in intrauterine growth retardation. *Acta Obstet Gynecol Scand*. 2003;82(12):1099–1102. [PubMed: 14616253]
71. Holcberg G, Huleihel M, Sapir O, et al. Increased production of tumor necrosis factor-alpha TNF-alpha by IUGR human placentae. *Eur J Obstet Gynecol Reprod Biol*. 2001;94(1):69–72. [PubMed: 11134828]

72. Romero R, Espinoza J, Goncalves LF, Kusanovic JP, Friel LA, Nien JK. Inflammation in preterm and term labour and delivery. *Semin Fetal Neonatal Med.* 2006;11(5):317–326. [PubMed: 16839830]
73. Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. *Am J Obstet Gynecol.* 2004;191(6):2041–2046. [PubMed: 15592289]
74. Okun ML, Roberts JM, Marsland AL, Hall M. How disturbed sleep may be a risk factor for adverse pregnancy outcomes. *Obstetrical & gynecological survey.* 2009;64(4):273–280. [PubMed: 19296861]
75. Okun ML, Luther JF, Wisniewski SR, Sit D, Prairie BA, Wisner KL. Disturbed sleep, a novel risk factor for preterm birth? *J Womens Health (Larchmt).* 2012;21(1):54–60. [PubMed: 21967121]
76. Chang J, Chien L, Duntley S, Pien G. Sleep duration during pregnancy and maternal and fetal outcomes: a pilot study using actigraphy Sleep. 2011;34(A317).
77. Dorheim SK, Bondevik GT, Eberhard-Gran M, Bjorvatn B. Sleep and depression in postpartum women: a population-based study. *Sleep.* 2009;32(7):847–855. [PubMed: 19639747]
78. Swanson LM, Pickett SM, Flynn H, Armitage R. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. *J Womens Health (Larchmt).* 20(4):553–558. [PubMed: 21417746]
79. Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. *J Obstet Gynecol Neonatal Nurs.* 2000;29(6):590–597.
80. Manber R, Steidtmann D, Chambers AS, Ganger W, Horwitz S, Connelly CD. Factors associated with clinically significant insomnia among pregnant low-income Latinas. *J Womens Health (Larchmt).* 2013;22(8):694–701. [PubMed: 23863074]
81. Okun ML, Ebert R, Saini B. A review of sleep-promoting medications used in pregnancy. *Am J Obstet Gynecol.* 2015;212(4):428–441. [PubMed: 25448509]
82. Wang LH, Lin HC, Lin CC, Chen YH, Lin HC. Increased risk of adverse pregnancy outcomes in women receiving zolpidem during pregnancy. *Clinical pharmacology and therapeutics.* 2010;88(3):369–374. [PubMed: 20686480]
83. Ibrahim S, Foldvary-Schaefer N. Sleep disorders in pregnancy: implications, evaluation, and treatment. *Neurologic clinics.* 2012;30(3):925–936. [PubMed: 22840797]
84. McLafferty LP, Spada M, Gopalan P. Pharmacologic Treatment of Sleep Disorders in Pregnancy. *Sleep Med Clin.* 2018;13(2):243–250. [PubMed: 29759274]
85. Zammit G. Comparative tolerability of newer agents for insomnia. *Drug safety : an international journal of medical toxicology and drug experience.* 2009;32(9):735–748.
86. Sedov ID, Goodman SH, Tomfohr-Madsen LM. Insomnia Treatment Preferences During Pregnancy. *Journal of obstetric, gynecologic, and neonatal nursing : JOGNN / NAACOG.* 2017;46(3):e95–e104.
87. Tomfohr-Madsen LM, Clayborne ZM, Rouleau CR, Campbell TS. Sleeping for Two: An Open-Pilot Study of Cognitive Behavioral Therapy for Insomnia in Pregnancy. *Behav Sleep Med.* 2017;15(5):377–393. [PubMed: 27124405]
88. Czajkowski SM, Powell LH, Adler N, et al. From ideas to efficacy: The ORBIT model for developing behavioral treatments for chronic diseases. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* 2015;34(10):971–982.
89. Garland SN, Carlson LE, Stephens AJ, Antle MC, Samuels C, Campbell TS. Mindfulness-based stress reduction compared with cognitive behavioral therapy for the treatment of insomnia comorbid with cancer: a randomized, partially blinded, noninferiority trial. *J Clin Oncol.* 2014;32(5):449–457. [PubMed: 24395850]
90. Stremler R, Hodnett E, Kenton L, et al. Effect of behavioural-educational intervention on sleep for primiparous women and their infants in early postpartum: multisite randomised controlled trial. *BMJ.* 2013;346:f1164. [PubMed: 23516146]
91. Montgomery-Downs HE, Insana SP, Clegg-Kraynok MM, Mancini LM. Normative longitudinal maternal sleep: the first 4 postpartum months. *Am J Obstet Gynecol.* 2010;203(5):465 e461–467. [PubMed: 20719289]
92. Brunner DP, Munch M, Biedermann K, Huch R, Huch A, Borbely AA. Changes in sleep and sleep electroencephalogram during pregnancy. *Sleep.* 1994;17(7):576–582. [PubMed: 7846455]

93. Swain AM, O'Hara MW, Starr KR, Gorman LL. A prospective study of sleep, mood, and cognitive function in postpartum and nonpostpartum women. *Obstet Gynecol.* 1997;90(3):381–386. [PubMed: 9277648]
94. Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. *Psychiatr Clin North Am.* 1987;10(4):541–553. [PubMed: 3332317]
95. Tikotzky L, Chambers AS, Gaylor E, Manber R. Maternal sleep and depressive symptoms: links with infant Negative Affectivity. *Infant Behav Dev.* 2010;33(4):605–612. [PubMed: 20723998]
96. Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. *J Sleep Res.* 2008;17(2):217–220. [PubMed: 18482110]
97. Park EM, Meltzer-Brody S, Stickgold R. Poor sleep maintenance and subjective sleep quality are associated with postpartum maternal depression symptom severity. *Arch Womens Ment Health.* 2013;16(6):539–547. [PubMed: 23733081]
98. Kamysheva E, Skouteris H, Wertheim EH, Paxton SJ, Milgrom J. A prospective investigation of the relationships among sleep quality, physical symptoms, and depressive symptoms during pregnancy. *J Affect Disord.* 2010;123(1-3):317–320. [PubMed: 19822370]
99. Dorheim SK, Bjorvatn B, Eberhard-Gran M. Can insomnia in pregnancy predict postpartum depression? A longitudinal, population-based study. *PloS one.* 2014;9(4):e94674. [PubMed: 24732691]
100. Wolfson AR, Crowley SJ, Anwer U, Bassett JL. Changes in sleep patterns and depressive symptoms in first-time mothers: last trimester to 1-year postpartum. *Behav Sleep Med.* 2003;1(1):54–67. [PubMed: 15600137]
101. Bei B, Milgrom J, Ericksen J, Trinder J. Subjective perception of sleep, but not its objective quality, is associated with immediate postpartum mood disturbances in healthy women. *Sleep.* 2010;33(4):531–538. [PubMed: 20394323]
102. Wilkie G, Shapiro CM. Sleep deprivation and the postnatal blues. *J Psychosom Res.* 1992;36(4):309–316. [PubMed: 1593506]
103. Doering J, Szabo A. Sleep quality and depression symptoms in disadvantaged postpartum women. *Sleep.* 2011; 34:A319.
104. Okun ML, Luther J, Prather AA, Perel JM, Wisniewski S, Wisner KL. Changes in sleep quality, but not hormones predict time to postpartum depression recurrence. *J Affect Disord.* 130(3):378–384. [PubMed: 20708275]
105. Tsai SY, Thomas KA. Sleep disturbances and depressive symptoms in healthy postpartum women: a pilot study. *Res Nurs Health.* 2012;35(3):314–323. [PubMed: 22431157]
106. Stone K. Effects of a behavioral sleep intervention on postpartum sleep. *Sleep.* 2011;34:A320.
107. Swanson L, Arnedt J, Adams J, Armitage R, Flynn H. An open pilot of cognitive behavioral therapy for insomnia in women with postpartum depression. *Sleep.* 2011;34:A319.
108. St James-Roberts I, Sleep J, Morris S, Owen C, Gillham P. Use of a behavioural programme in the first 3 months to prevent infant crying and sleeping problems. *J Paediatr Child Health.* 2001;37(3):289–297. [PubMed: 11468047]
109. Symon BG, Marley JE, Martin AJ, Norman ER. Effect of a consultation teaching behaviour modification on sleep performance in infants: a randomised controlled trial. *Med J Aust.* 2005;182(5):215–218. [PubMed: 15748130]
110. Wolfson A, Lacks P, Futterman A. Effects of parent training on infant sleeping patterns, parents' stress, and perceived parental competence. *J Consult Clin Psychol.* 1992;60(1):41–48. [PubMed: 1556284]
111. WHO. Research on the menopause in the 1990s. 1996.
112. Soules MR, Sherman S, Parrott E, et al. Executive summary: Stages of Reproductive Aging Workshop (STRAW). *Climacteric.* 2001;4(4):267–272. [PubMed: 11770182]
113. Gold EB. The timing of the age at which natural menopause occurs. *Obstet Gynecol Clin North Am.* 2011;38(3):425–440. [PubMed: 21961711]
114. NIH. National Institutes of Health State-of-the-Science Conference statement: management of menopause-related symptoms. *Ann Intern Med.* 2005;142(12 Pt 1):1003–1013. [PubMed: 15968015]



115. Kravitz HM, Ganz PA, Bromberger J, Powell LH, Sutton-Tyrrell K, Meyer PM. Sleep difficulty in women at midlife: a community survey of sleep and the menopausal transition. *Menopause*. 2003;10(1):19–28. [PubMed: 12544673]
116. Kravitz HM, Zhao X, Bromberger JT, et al. Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. *Sleep*. 2008;31(7):979–990. [PubMed: 18652093]
117. NIH. State-of-the Science Conference statement. Management of menopause-related symptoms. *Ann Intern Med*. 2005;142(12):1003–1013. [PubMed: 15968015]
118. Glazer G, Zeller R, Delumba L, et al. The Ohio Midlife Women's Study. *Health Care Women Int*. 2002;23(6-7):612–630. [PubMed: 12418983]
119. Young T, Rabago D, Zgierska A, Austin D, Laurel F. Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in the Wisconsin Sleep Cohort Study. *Sleep*. 2003;26(6):667–672. [PubMed: 14572118]
120. Gold EB, Sternfeld B, Kelsey JL, et al. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40–55 years of age. *Am J Epidemiol*. 2000;152(5):463–473. [PubMed: 10981461]
121. Col NF, Guthrie JR, Politi M, Dennerstein L. Duration of vasomotor symptoms in middle-aged women: a longitudinal study. *Menopause*. 2009;16(3):453–457. [PubMed: 19188852]
122. Politi MC, Schleinitz MD, Col NF. Revisiting the duration of vasomotor symptoms of menopause: a meta-analysis. *J Gen Intern Med*. 2008;23(9):1507–1513. [PubMed: 18521690]
123. Shaver J, Giblin E, Lentz M, Lee K. Sleep patterns and stability in perimenopausal women. *Sleep*. 1988;11(6):556–561. [PubMed: 3148991]
124. Ensrud KE, Stone KL, Blackwell TL, et al. Frequency and severity of hot flashes and sleep disturbance in postmenopausal women with hot flashes. *Menopause*. 2009;16(2):286–292. [PubMed: 19002015]
125. Savard J, Davidson JR, Ivers H, et al. The association between nocturnal hot flashes and sleep in breast cancer survivors. *J Pain Symptom Manage*. 2004;27(6):513–522. [PubMed: 15165649]
126. Freedman RR, Roehrs TA. Lack of sleep disturbance from menopausal hot flashes. *Fertil Steril*. 2004;82(1):138–144. [PubMed: 15237002]
127. Erlik Y, Tataryn IV, Meldrum DR, Lomax P, Bajorek JG, Judd HL. Association of waking episodes with menopausal hot flushes. *Jama*. 1981;245(17):1741–1744. [PubMed: 7218488]
128. Freedman RR, Benton MD, Genik RJ 2nd, Graydon FX. Cortical activation during menopausal hot flashes. *Fertil Steril*. 2006;85(3):674–678. [PubMed: 16500337]
129. Woodward S, Freedman RR. The thermoregulatory effects of menopausal hot flashes on sleep. *Sleep*. 1994;17(6):497–501. [PubMed: 7809562]
130. Freedman RR, Roehrs TA. Effects of REM sleep and ambient temperature on hot flash-induced sleep disturbance. *Menopause*. 2006;13(4):576–583. [PubMed: 16837879]
131. Krystal AD, Edinger J, Wohlgenuth W, Marsh GR. Sleep in peri-menopausal and postmenopausal women. *Sleep Med Rev*. 1998;2(4):243–253. [PubMed: 15310495]
132. Sivertsen B, Omvik S, Pallesen S, et al. Cognitive behavioral therapy vs zopiclone for treatment of chronic primary insomnia in older adults: a randomized controlled trial. *Jama*. 2006;295(24):2851–2858. [PubMed: 16804151]
133. Arnedt JT, Cuddihy L, Swanson LM, Pickett S, Aikens J, Chervin RD. Randomized controlled trial of telephone-delivered cognitive behavioral therapy for chronic insomnia. *Sleep*. 2013;36(3):353–362. [PubMed: 23450712]
134. Drake CL, Kalmbach DA, Arnedt JT, et al. Treating Chronic Insomnia in Postmenopausal Women: A Randomized Clinical Trial Comparing Cognitive-Behavioral Therapy for Insomnia (CBTI), Sleep Restriction Therapy, and Sleep Hygiene Education. *Sleep*. 2018.
135. McCurry SM, Guthrie KA, Morin CM, et al. Telephone-Based Cognitive Behavioral Therapy for Insomnia in Perimenopausal and Postmenopausal Women With Vasomotor Symptoms: A MsFLASH Randomized Clinical Trial. *JAMA Intern Med*. 2016;176(7):913–920. [PubMed: 27213646]
136. Guthrie KA, Larson JC, Ensrud KE, et al. Effects of Pharmacologic and Nonpharmacologic Interventions on Insomnia Symptoms and Self-reported Sleep Quality in Women With Hot



- Flashes: A Pooled Analysis of Individual Participant Data From Four MsFLASH Trials. *Sleep*. 2018;41(1).
137. Hunter MS, Liao KL. A psychological analysis of menopausal hot flushes. *Br J Clin Psychol*. 1995;34 (Pt 4):589–599. [PubMed: 8563666]
138. Reynolds FA. Perceived control over menopausal hot flushes: exploring the correlates of a standardised measure. *Maturitas*. 1997;27(3):215–221. [PubMed: 9288693]
139. Hunter MS, Mann E. A cognitive model of menopausal hot flushes and night sweats. *J Psychosom Res*. 69(5):491–501. [PubMed: 20955869]
140. Adler JEBK, Armbruster U, Decio R, Gairing A, Kang A et al. Cognitive-behavioural group intervention for climacteric syndrome. *Psychother Psychosom*. 2006;75(5):298–303. [PubMed: 16899966]
141. Atema V, van Leeuwen M, Oldenburg HSA, van Beurden M, Hunter MS, Aaronson NK. An Internet-based cognitive behavioral therapy for treatment-induced menopausal symptoms in breast cancer survivors: results of a pilot study. *Menopause*. 2017;24(7):762–767. [PubMed: 28195994]
142. Hunter M, Smith In Collaboration With The British Menopause Society M. Cognitive Behaviour Therapy (CBT) for menopausal symptoms: Information for GPs and health professionals. *Post Reprod Health*. 2017;23(2):83–84. [PubMed: 28643610]
143. Stefanopoulou E, Grunfeld EA. Mind-body interventions for vasomotor symptoms in healthy menopausal women and breast cancer survivors. A systematic review. *J Psychosom Obstet Gynaecol*. 2017;38(3):210–225. [PubMed: 27832718]
144. Hunter MS, Hardy C, Norton S, Griffiths A. Study protocol of a multicentre randomised controlled trial of self-help cognitive behaviour therapy for working women with menopausal symptoms (MENOS@Work). *Maturitas*. 2016;92:186–192. [PubMed: 27621258]
145. Norton S, Chilcot J, Hunter MS. Cognitive-behavior therapy for menopausal symptoms (hot flushes and night sweats): moderators and mediators of treatment effects. *Menopause*. 2014;21(6):574–578. [PubMed: 24149919]
146. Stefanopoulou E, Hunter MS. Telephone-guided Self-Help Cognitive Behavioural Therapy for menopausal symptoms. *Maturitas*. 2014;77(1):73–77. [PubMed: 24144959]
147. Carpenter JS, Neal JG, Payne J, Kimmick G, Storniolo AM. Cognitive-behavioral intervention for hot flashes. *Oncol Nurs Forum*. 2007;34(1):37. [PubMed: 17562629]
148. Thomas A, Grandner M, Nowakowski S, Nesom G, Corbitt C, Perlis ML. Where are the Behavioral Sleep Medicine Providers and Where are They Needed? A Geographic Assessment. *Behav Sleep Med*. 2016;14(6):687–698. [PubMed: 27159249]

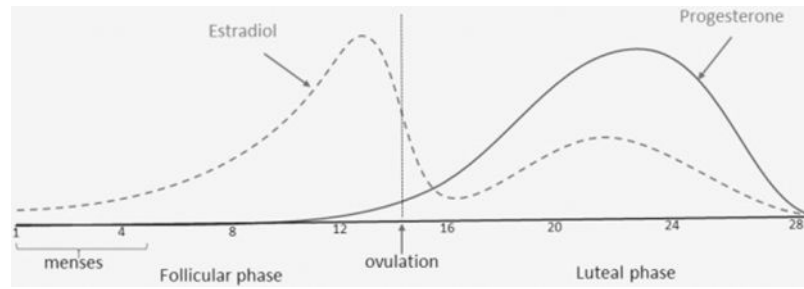
**Synopsis:** Differences in sleep for men and women begin at a very early age, with women reporting poorer sleep and having a higher risk for insomnia compared to men. Women are particularly vulnerable to developing insomnia during times of reproductive hormonal change. Sleep across the woman's lifespan and special treatment considerations for using cognitive behavioral therapy for insomnia (CBT-I) in women will be addressed in this review.

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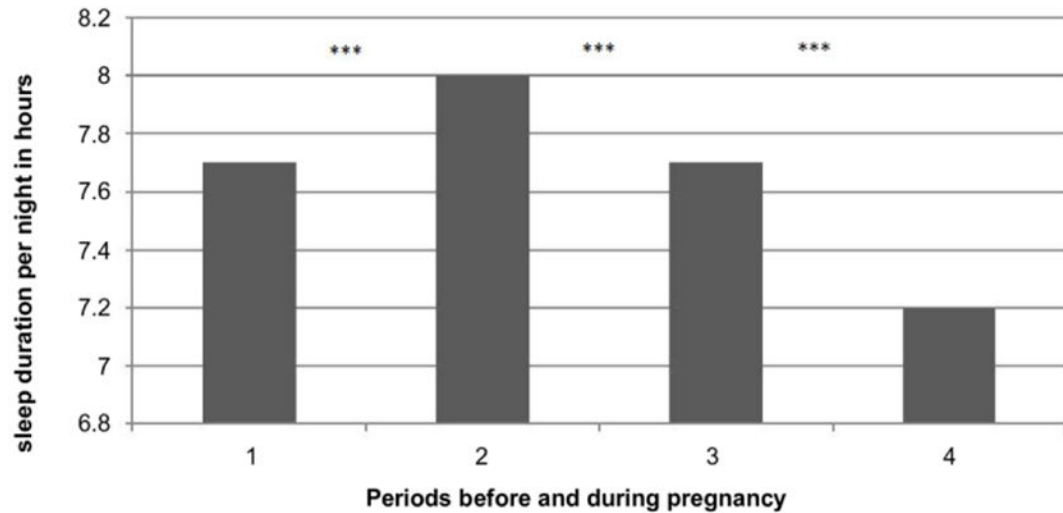
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**Figure 1.**

Changes in estradiol and progesterone across a typical 28-day ovulatory menstrual cycle, where day 1 represents the first day of bleeding. From Baker, FC, Lee KA. Menstrual Cycle Effects on Sleep. *Sleep Med Clin* 13 (2018) 283-94; with permission.



**Figure 2.**

Evolution of women's sleep duration per night before and during pregnancy. 1: Before pregnancy, 2: First trimester of pregnancy, 3: Second trimester of pregnancy, 4: Third trimester of pregnancy. \*\*\*  $P < 0.001$ . Data from Bat-Pitault et al. Sleep Pattern During Pregnancy and Maternal Depression: Study of Aube Cohort. *J Sleep Disord Manag* 2015, 1:1

Menarche					FMP (0)					
Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	variable				variable	1-3 years	2 years (1+1)	3-6 years	Remaining lifespan	
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	Variable Length Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Normal Low Low	Variable* Low Low	↑ Variable* Low Low	↑>25 IU/L** Low Low	↑ Variable* Low Low	Stabilizes Very Low Very Low		
Antral Follicle Count 2-10 mm			Low	Low	Low	Low	Very Low	Very Low		
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms Likely	Vasomotor symptoms Most Likely		Increasing symptoms of urogenital atrophy	

\* Blood draw on cycle days 2-5 = elevated

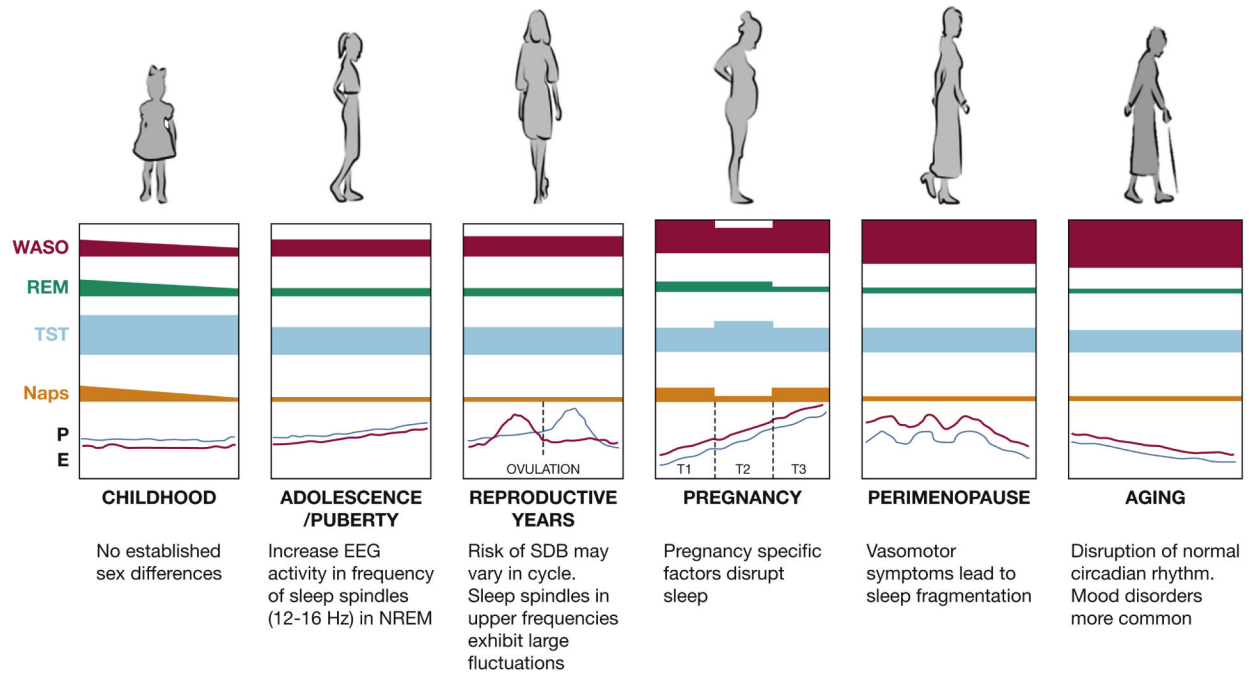
\*\*Approximate expected level based on assays using current pituitary standard<sup>67-69</sup>

\* Blood draw on cycle days 2-5 = elevated

\*\*Approximate expected level based on assays using current pituitary standard<sup>57,69</sup>

**Figure 3.**

The STRAW+10 Staging System for Reproductive Aging in Women. From Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. *Climacteric* 15(2). 2012 105-14; with permission.



**Figure 4.**

Sleep in women across the life span. E = estrogen; NREM = non-rapid eye movement; P = progesterone; REM = rapid eye movement; SDB = sleep-disordered breathing; T = trimester; TST = total sleep time; WASO = wake after sleep onset. From Pegno et al. CHEST 2018; 154(1): 196-206; with permission.