CME

Major Sleep Disorders Among Women

(Women's Health Series)

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Abstract: Disruption of sleep causes adverse health outcomes and poor quality of life. People with sleep disruption have higher levels than people without disrupted sleep of depression and anxiety and increased rates of cardiovascular diseases. Women have a higher incidence than men of insomnia and depression related to poor sleep. The types of complaints differ significantly between the sexes. Women are more likely than men to complain of insomnia, headache, irritability, and fatigue than the "typical" symptoms of loud snoring and breathing cessation during sleep. Hormones play an important role in sleep in women. Reproductive hormones were found to have a protective effect on sleep apnea in women of premenopausal age. Pregnancy is another period when the prevalence of sleep apnea and restless leg syndrome increases from hormonal effect. Cardiovascular mortality is high in women with obstructive sleep apnea. Continuous positive airway pressure therapy improves outcomes in most cases of obstructive sleep apnea. The epidemiology, risk factors, diagnostic criteria, and therapies for the three most common sleep disorders (insomnia, obstructive sleep apnea, and restless leg syndrome), along with effects of menopause, pregnancy, and social factors on sleep in women, are key considerations for clinicians caring for female patients across the adult life span.

Key Words: insomnia, obstructive sleep apnea, restless leg syndrome, sleep disorders, women

Sleep is essential for normal physiologic function. Chronic sleep deprivation and poor-quality, fragmented sleep result in excessive daytime sleepiness, neurocognitive dysfunction, memory impairment, depression, anxiety, dysglycemia, systemic inflammation, heart rhythm abnormalities, atherosclerosis, and cardiovascular events.[1] Although the differences in sleep physiology between men and women are modest, the prevalence and presentation of sleep disorders vary considerably between the sexes. Women with obstructive sleep apnea (OSA) are more likely to present with atypical complaints than with the more classical symptoms usually seen in men.[1a,2] Sleep duration also varies with sex and race. Reproductive hormones play important roles in sleep physiology for women at different ages and times of their lives. The epidemiology, risk factors, and treatment of the most common sleep disorders (insomnia, OSA, and restless leg syndrome [RLS]), complicated by the effects of menopause, pregnancy, and social factors, are essential issues in understanding sleep disorders in women.

Insomnia

Insomnia includes difficulty falling asleep, inability to maintain sleep, and/or early-morning awakening, which negatively affects daytime function. Symptoms should be present for >1 month to diagnose insomnia, which is more common in women than in men. The American Insomnia Survey (7428 respondents) documented a prevalence of 27% in women (vs 19% in men), with substantial associated workplace costs.[2] A range of 10% to 15% of the US population complains of insomnia with resulting impaired daytime function and 30% of the population expresses dissatisfaction with the quality of their sleep.[3] Women are more likely to report sleep disturbances and are 41% more likely than men to experience insomnia.[4]

Key Points

- Sleep disorders are common in women. The clinical presentation of insomnia and obstructive sleep apnea can be atypical in women.
- Hormonal status plays a major determinant role for sleep disorders in women. Postmenopausal women are at high risk for developing sleep apnea as pregnant women are for restless leg syndrome.
- Management of sleep disorders is multimodal and disease specific.

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The reasons for these differences are incompletely understood. Menopause, late-luteal phase of the menstrual cycle, and third trimester of pregnancy are associated with a particularly high prevalence of insomnia,[5] with approximately 50% of perimenopausal woman reporting significant symptoms.[6] Chronic insomnia also is prevalent among cancer patients, especially women with breast cancer.[7]

Women also experience higher rates than men of depression, anxiety, and other psychiatric disorders that can contribute to insomnia, and persistent insomnia itself increases fourfold the likelihood of developing major depressive disorder.[4] Sleep restriction was found to cause aberration of the adrenocortical rhythm, increasing the risk of depression among women.[8–10] Sleep restriction also is associated with a 28% increase in the daytime level of the orexigenic hormone ghrelin, contributing to increased appetite and weight gain among patients with insomnia.[11]

The etiology of insomnia is multifactorial in most women. Insomnia and insomnia-related disorders are classified in the second edition of *The International Classification of Sleep Disorders*.[12]

The duration of sleep also varies between the sexes and whites and blacks. In the cohort of the Coronary Artery Risk Development in Young Adults (CARDIA) study, the average sleep duration was 6.7 hours in white women, 6.1 hours in white men, 5.9 hours in black women, and 5.1 hours in black men. Increasing income level was associated with increased sleep efficiency and low socioeconomic status with decreased sleep efficiency and increased sleep latency.[13]

Psychological and behavioral interventions are effective and recommended to treat insomnia. The American Academy of Sleep Medicine has developed a practice parameter for these treatments (Table 1).[14] Thirty percent of patients with insomnia have contributory poor sleep hygiene. Good sleep hygiene practices should be prescribed for all patients in addition to other treatments (Fig. 1) because sleep hygiene education alone is ineffective.[15]

The current Food and Drug Administration–approved pharmacological treatments for insomnia include benzodiazepine receptor agonists and melatonin receptor agonists. Potential adverse effects of the former include residual sedation, memory and performance impairment, falls, undesired behaviors during sleep, somatic symptoms, and drug interactions. A number of other prescription medications (eg, sedating antidepressants, antiepileptics) also are used off-label, as well as nonprescription drugs (eg, sedating antihistamines) and naturopathic agents (eg, melatonin, valerian) to treat insomnia, although safety and efficacy data are limited.[15]

In general, symptom pattern, previous treatment failure, comorbid conditions, adverse effects, and medication costs should be considered before starting a hypnotic regimen. Short- to intermediate-acting benzodiazepine receptor agonists or melatonin receptor agonists can be started initially. Medications can be changed or dosages increased based upon the degree of symptom improvement and adverse effects experienced (Fig. 2).[15] Because depression and insomnia are present more frequently in women than in men, selective serotonin reuptake inhibitors appear to be uniquely effective in their treatment.[16] Cognitive-behavioral therapy appears to improve insomnia in women with breast cancer[17]; however, there is no consensus on sex-specific insomnia treatment strategies for women.[16]

OSA

OSA is a common disorder characterized by repetitive upper-airway collapse during sleep. The diagnosis is made by nocturnal polysomnography, which measures the total number of apneic and hypopneic episodes per hour of sleep (the Apnea-Hypopnea Index [AHI]). The American Academy of Sleep Medicine has defined OSA as mild (AHI 5–15), moderate

Table 1. CBT for insomnia[14]

Elements	Description
Cognitive therapy	Aimed at changing patient's belief and attitudes about insomnia
CBTI	Combined cognitive therapy and behavioral techniques; the behavioral component may include stimulus control and/or sleep restriction therapy with or without use of relaxation therapy
Sleep hygiene education	Making patient aware of health practices and environment, but not a standard recommendation for using it as single therapy.
Relaxation training	Progressive muscle relaxation and guided imagery rehearsal
Stimulus-control therapy	Training patient to reassociate bed and bedroom with sleep and reestablish a consistent sleep-wake schedule
Sleep-restriction therapy	Limiting time in bed, creating mild sleep deprivation, and then lengthening sleep time as sleep efficiency improves
Paradoxical intention	Instructing patient to passively remain awake and avoid any effort to fall asleep; the goal is to eliminate performance anxiety
Biofeedback	Visual or auditory feedback to help control physiological variable to reduce arousal
Multicomponent therapy	Multiple behavioral techniques without cognitive therapy

CBT, cognitive-behavioral therapy; CBTI, cognitive-behavioral therapy for insomnia.

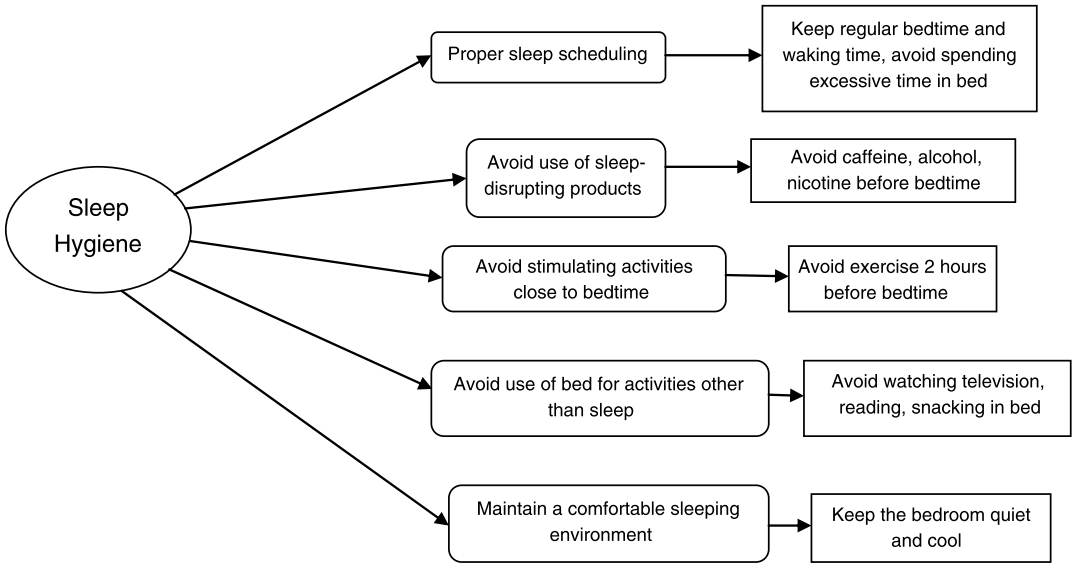

Fig. 1. Sleep hygiene practices.[12]

(AHI 15–30), or severe (AHI >30) based on the frequency of these events.[18]

The disorder is associated with conditions that contribute to excess mortality in adults, including cardiovascular disease, stroke, neurocognitive dysfunction, and motor vehicle crashes.[19] The estimated prevalence of OSA is 9% in women (vs 24% in men).[20,21] The Wisconsin Sleep Cohort Study estimated that sleep apnea was undiagnosed in >90% of women with moderate to severe sleep apnea[21] and suggested that underdiagnosis related to atypical symptomatology may explain much of the perceived disparity.[22]

Loud snoring, breathing pauses during sleep, and excessive daytime sleepiness are classic symptoms seen in most men with OSA, whereas atypical symptoms such as insomnia, morning headache, fatigue, tiredness, depression, and anxiety are more common presentations in women. Women are two to three times less likely than men to report classic OSA symptoms,[23] with approximately 20% of women presenting primarily with complaints of insomnia, supporting the position of frequently missed diagnoses. As such, women are more likely to be treated inappropriately for depression, anxiety, or hypothyroidism than are men with the same severity of OSA.[24]

In women at risk for OSA, other less typical symptoms, including memory loss, poor concentration, decreased libido, irritability, worsening unexplained fatigue, and tiredness, should be appraised using a comprehensive sleep evaluation. An large neck size (>16 in.), a body mass index (BMI) >30 kg/m^2, and the presence of structural abnormalities (oropharyngeal narrowing, retrognathia, macroglossia, uvula elongation, high arched hard palate, nasal septal deviation) should be sought during physical examination; each anatomic finding increases the probability of OSA.[25]

Obesity may be the most important risk factor for OSA. Women with OSA are more likely to be obese than are men with OSA of similar severity.[26] In a study of women with BMI >30 kg/m,^{2} one-third of asymptomatic women were found to have OSA by polysomnographic criteria, and a significant correlation was identified between AHI and BMI in this cohort.[27]

Hormonal status also contributes to sleep abnormalities in women. A study in a general population evaluated the effects of menopause and hormone therapy (HT) on polysomnographic findings in women and compared the female cohorts to the male cohorts.[28] The study found that women slept objectively better than men and that sleep in young women is more resistant to external stressors. Menopause showed a negative effect on sleep: Postmenopausal women had longer sleep latency, less slow-wave sleep, and less deep sleep as compared with premenopausal subjects. Postmenopausal women not receiving HT had longer sleep latency than did those on treatment, suggesting that estrogens may exert a protective effect on sleep integrity. Bixler et al found a low prevalence of OSA (0.6%) among premenopausal women and postmenopausal women receiving HT (0.5%) compared with postmenopausal women not receiving HT (2.7%).[29]

Vasomotor symptoms (VMS), particularly hot flashes, correlate strongly with subjective sleep complaints.[30] Declining estradiol levels during the climacterium demonstrates an association with increased VMS, trouble sleeping, and diminished sexual response.[31] Worse mood associates with poorer sleep and concurrent VMS, explaining in part the increased anxiety, depression, and mental health issues seen in some postmenopausal women. In a prospective crossover study, postmenopausal women with OSA were treated with estrogen alone, and with an estrogen-progestin combination.[32] Polysomnography was performed at baseline and repeated after 3 to 4 weeks of each regimen. Both treatment strategies reduced OSA, with a 50% reduction of AHI following estrogen-progesterone treatment and a 25% reduction following estrogen-only therapy.[32] Estrogen effects

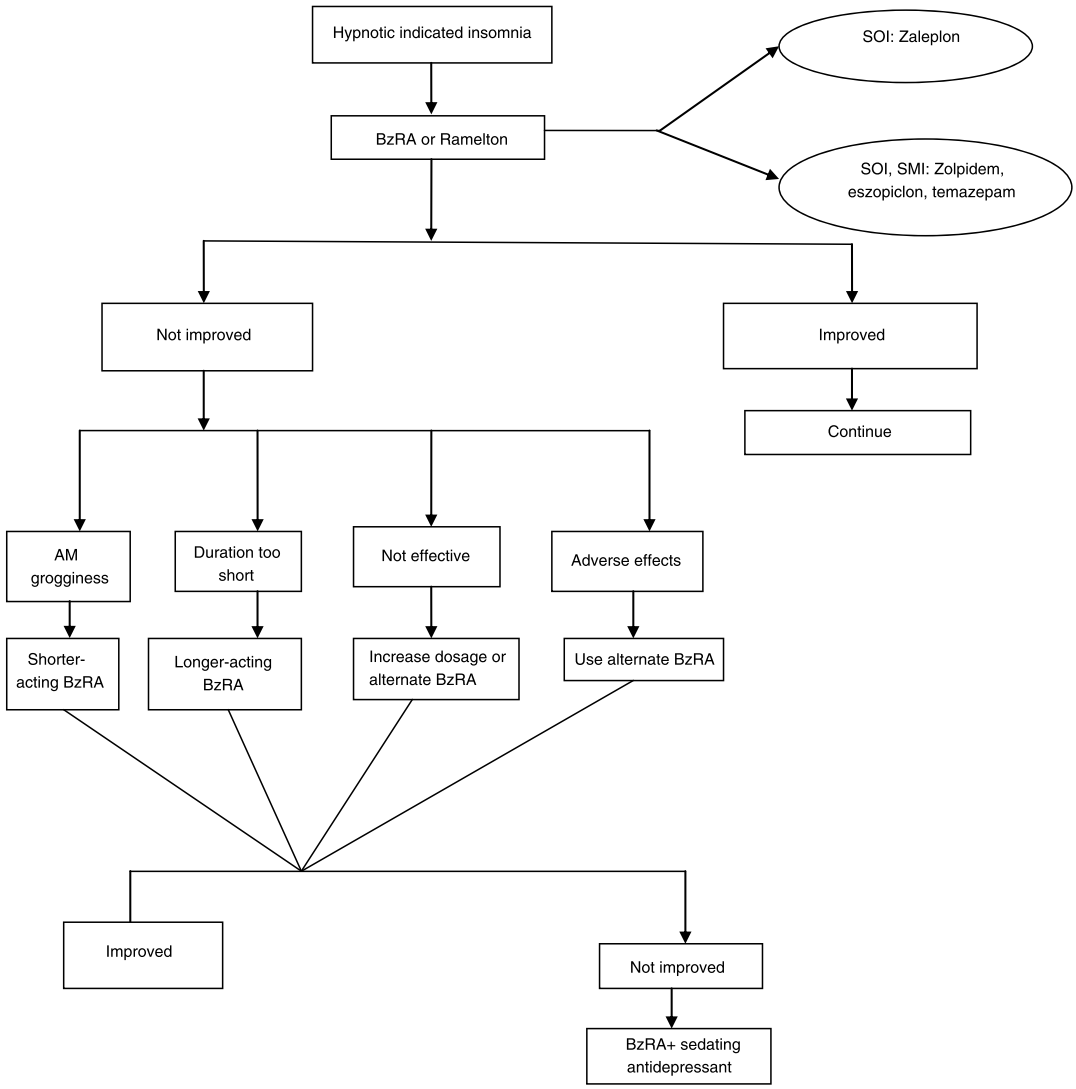

Fig. 2. **Hypnotic management of insomnia. BzRA, benzodiazepine receptor agonist; SMI, sleep maintenance insomnia, SOI, sleep-onset insomnia. Adapted with permission from the American Academy of Sleep Medicine.[12]**

were further studied in two groups of postmenopausal women (one receiving HT and the other untreated); treated women had lower free cortisol levels and better polysomnographic sleep parameters than untreated subjects.[33]

Despite these data, HT is not a recommended treatment for perimenopausal OSA at this time.[32,33] Women with established cardiovascular disease experience more coronary and thromboembolic events and greater mortality when prescribed HT,[34] and with the higher incidence of major cardiovascular risk determinants in OSA patients overall, the potential for harm is significant. Further long-term outcomes studies are needed to evaluate the net effect of HT on postmenopausal women with OSA.

Cardiovascular complications associated with untreated OSA include hypertension, myocardial infarction, congestive heart failure, atrial fibrillation, and stroke.[35] Upper airway collapse during sleep results in intrathoracic pressure swings, which cause myocardial transmural pressure gradients, stretching thin atrial walls. Over time, this combined with secondary pulmonary hypertension from hypoxic vasoconstriction may result in atrial enlargement, impaired intraatrial conduction, enhanced atrial automaticity, and subsequent atrial fibrillation.[36,37] Repetitive intermittent hypoxia from OSA also produces oxidative stress and inflammation (with release of cytokines, interleukins, and tumor necrosis factor) and promotes fibrosis and endothelial dysfunction, which results in pathologic vasoconstriction and an increased incidence of atherosclerosis.[38]

In a prospective study of 1116 women for 88 months, the hazard ratio for cardiovascular mortality in patients with untreated severe OSA was 3.50 (95% confidence interval 1.23–9.98); adequate continuous positive airway pressure (CPAP) therapy reduced the relative risk to 0.55 (95% confidence interval 0.17–1.74) after controlling for age, BMI, previous cardiovascular history, hypertension, and diabetes. These data strongly suggest that severe OSA independently associates with cardiovascular

mortality and that CPAP therapy may reduce cardiovascular death in these patients.[39]

Many metabolic conditions also demonstrate an association with OSA. Impaired glucose metabolism, demonstrated by elevated HbA1C concentrations, correlates with increasing AHI among patients with OSA.[40] Diabetics have a high prevalence of OSA, and CPAP improves glucose control in these patients.[41] Women with a history of witnessed OSA have a threefold increased risk of diabetes.[42] Insulin-resistant women with polycystic ovary syndrome are at high risk for OSA, early-onset diabetes, and cardiovascular disease; CPAP treatment improves insulin sensitivity, decreases sympathetic nervous system outflow, and decreases diastolic blood pressure in these patients.[43] Secretion of growth hormone and prolactin are regulated by processes occurring during stage 3 and rapid-eye-movement sleep; when these sleep components are disturbed by OSA, hormone concentrations fall and symptomatic deficiency states develop.[44]

Neurocognitive dysfunction, including dementia, memory loss, depression, and anxiety, also can result from untreated OSA. There is a strong association between depression and OSA, although it is unclear whether depression is triggered by sleep deprivation and subsequent sleepiness or whether OSA itself causes this mood disorder.[43]

OSA should be approached as a chronic disease requiring long-term, multidisciplinary management. Medical, behavioral, and surgical treatment options are available and patients should be active participants in the treatment decision process. Positive airway pressure therapy (PAP), the treatment of choice for all degrees of OSA, provides pneumatic splinting of the upper airway and is effective in reducing AHI.[48] It may be delivered in CPAP, bilevel PAP, or autotitrating PAP modes. Full-night, provider-observed polysomnography performed in a sleep laboratory is the preferred approach to titrate to optimal PAP parameters.[44] Compliance is a major challenge. Ye[56] found that CPAP improved functional status and OSA symptoms in both sexes, but CPAP compliance was not different between women and men. Nino-Murcia[45] confirmed that CPAP compliance rates (65%–83%) were similar between the sexes, whereas a population-based prospective study found that female patients used CPAP more frequently than their male counterparts.[46]

Behavioral therapy, including sleep hygiene (Fig. 1), weight reduction, exercise, alcohol avoidance, and bedtime sedatives are important adjuncts to PAP. Oral appliances (mandibular repositioning or tongue retaining devices) may improve upper airway patency.[47] Surgical therapy is site directed and patient based. Nasal (septoplasty, turbinate reduction, nasal polypectomy), oropharyngeal (uvulopalatoplasty, tonsillectomy, adenoidectomy), and global (maxilla-mandibular advancement) airway procedures can be considered based upon patient anatomy in individuals who fail less-invasive treatment. Bariatric surgery may be needed for patients with refractory obesity.[25]

To date, most treatment trials have been conducted in male patients and few trials have included enough women to define differences in the efficacy of various modalities in female patients.[48,49] Selected clinical studies including female patients are presented in Table 2.

Restless Leg Syndrome

This movement disorder is characterized by an urge to move the legs, typically during rest, which is relieved by activity. Symptoms are often accompanied by sensations of "creeping," "pulling," "itching," or "tingling," and the diagnosis requires the presence of sensory symptoms.[58] The International Restless Leg Syndrome Study Group developed standardized criteria for the diagnosis of RLS (Fig. 3),[12] which were modified by a consensus conference in 2002 (Fig. 4).[58] The prevalence ranges from 4% to 29% in the general population[59,60] and increases with age. Prospective cohort data suggest that 11.7% of women are affected,[61] and overall prevalence is higher among women (13.9%) than men (6.1%) in another cohort analysis.[62] Although 80% of patients with RLS will have nocturnal periodic limb movements, many patients with these abnormal movements do not have RLS. Periodic limb movements are characterized by episodic repetitive, highly stereotyped limb movements that occur during sleep and by resulting clinical sleep disturbances that cannot be explained by another sleep disorder.[10] Although periodic limb movements may be observed during polysomnography in patients with RLS, the diagnosis is made on the basis of clinical symptoms (Fig. 4) and a sleep study is not necessary.

Although the mechanism of this disease is unknown, dopaminergic dysfunction is thought to be an underlying component.[63–65] The current consensus theory on the pathophysiology of RLS is the "iron dopamine hypothesis." Iron is a cofactor for the enzyme tyrosine hydroxylase, which performs a rate-limiting enzymatic step in the formation of dopamine. Patients with RLS show a greater circadian variation of dopamine metabolites, consistent with the circadian (evening concentrated) symptom clustering in this disorder.[44]

In addition to reducing quality of life, RLS may predispose to significant morbidity and excess mortality. A positive correlation between RLS and coronary artery disease was found in a large number of women (n = 70,694) in a prospective study. Women with RLS for ≥3 years demonstrated an elevated risk for nonfatal myocardial infarction and fatal coronary heart diseases.[66]

Iron-deficiency anemia, pregnancy, smoking, neuropathy, rheumatoid arthritis, multiple sclerosis, diabetes, kidney disease, caffeine and alcohol consumption, and use of H_2-receptor blockers and some antidepressant medications have been linked to RLS.[44,63] In a cohort study of women studied during and after pregnancy, 26% were found to have RLS during pregnancy (with symptoms being most common during the third trimester), which tended to disappear after delivery. Affected women had lower hemoglobin concentrations compared with nonaffected women,[67] supporting the theory that iron status may contribute to RLS.

Table 2. Selected sleep apnea clinical trials in which the majority of participants were women

Authors	Type of study	Study participants	N	Length of study	Study outcome
Mortality					
Campose-Rodroguez et al 2012[48]	Prospective observational	CPAP treated vs untreated	1116 women	72 mo	Severe OSA is associated with CV death in women and CPAP reduces death rate ($P < 0.001$)
Yeboah J et al 2011[50]	Prospective observational	Sleep apnea vs snorers vs normal participants	5338: 2643 men, 2695 women	7.5 y	Physician-diagnosed sleep apnea but not habitual snoring was associated with high CV events and all-cause mortality
Punjabi NM et al 2009[51]	Prospective observational	Sleep apnea vs nonsleep apnea with baseline PSG, followed for mortality	6441, 53.3% women	8.2 y	Sleep apnea is associated with all-cause mortality; men had a higher mortality rate than women (24.8 vs 16.5; $P < 0.0001$)
PCOS					
Tasali et al 2011[43]	Prospective observational	CPAP	19 women	8 wk	Young obese women with PCOS improves in cardiometabolic function by using CPAP
Diabetes					
Valham F. et al 2009[42]	Prospective observational	Questions on snoring and witnessed apnea	4047 women, 3858 men	Random selection for 1 visit	58% of the women who snored had diabetes and women with history of witnessed sleep apnea had threefold increase in frequency of diabetes mellitus.
Foster GD et al 2009[52]	RCT	Intensive lifestyle modification vs diabetes support and education	264, 59% women	1 y	Weight loss improves OSA among obese diabetic patients
Preeclampsia					
Blyton DM et al 2013[53]	Prospective observational	CPAP	40 women	2 nights	CPAP improves fetal activity and fetal hiccups among patients with preeclampsia
Menopause					
Tom et al 2011[54]	RCT	Hormone therapy suspension and hormone therapy continuation	1704 women	3 mo	Suspension of hormone therapy increases frequency of sleep problems
Polo-Kantola et al 2003[30]	RCT (double-blind crossover)	Estrogen vs placebo on postmenopausal women who underwent PSG	62 women	3 mo	Estrogen therapy decreased the occurrence ($P = 0.047$) and frequency of sleep apnea ($P = 0.049$), but had no effect on partial upper airway obstruction among postmenopausal women.
Pregnancy					
Maasilta P. 2001[55]	Prospective observational	Overnight PSG at 12 weeks (early) and 30 weeks (late) of pregnancy	11 obese and 11 non-obese pregnant women	30 wk	AHI, 4% O_2 desaturation and snoring occurs more in obese mothers than mothers of normal weight ($P < 0.05$, <0.005, <0.001, respectively) when compared with early and late pregnancy readings
CPAP treatment					
Ye et al 2009[56]	Prospective observational	CPAP treatment response across sexes	152 men, 24 women	3 mo	CPAP improved OSA symptoms and functional status in both men and women; average CPAP use in women was not different from men ($P = 0.265$).
Jayaraman et al 2011[57]	Retrospective	CPAP treatment	56 women and 39 men	6 mo	Pressure requirement for CPAP was higher in men than in women ($P < 0.0001$)
Don Sin et al 2002[46]	Prospective	CPAP treatment	296, 18.9% women	6 mo	Women used CPAP more frequently than men
Battagel et al 1999[47]	Prospective observational	Mandibular advancement device	45 men and 13 women with mild–moderate OSA		Despite smaller faces and narrower pharynxes than men, women enlarge their pharynx more than men in different measurements of protrusion

AHI, Apnea-Hypopnea Index; CPAP, continuous positive airway pressure; CV, cardiovascular; OSA, obstructive sleep apnea; PCOS, polycystic ovary syndrome; PSG, polysomnography; RCT, randomized clinical trial.

A. The patient reports an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.

B. The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or sitting.

C. The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, as long as the activity continues.

D. The urge to move or sensations are worse, or only occur, in the evening or at night.

E. The condition is not better explained by another current sleep disorder, medical or neurological disorder, medication use, or substance use disorder.

Fig. 3. ***International Classification of Sleep Disorders-2*** **restless leg syndrome diagnostic criteria.[12]**

1. An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. (Sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs.)

2. The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or sitting.

3. The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.

4. The urge to move or unpleasant sensations are worse in the evening or at night than during the day or only occur in the evening or at night. (When symptoms are extremely severe, the worsening at night may not be noticeable but must have been present previously.)

Fig. 4. International Restless Leg Syndrome Study Group criteria for restless leg syndrome. Adapted with permission from the American Academy of Sleep Medicine.[58]

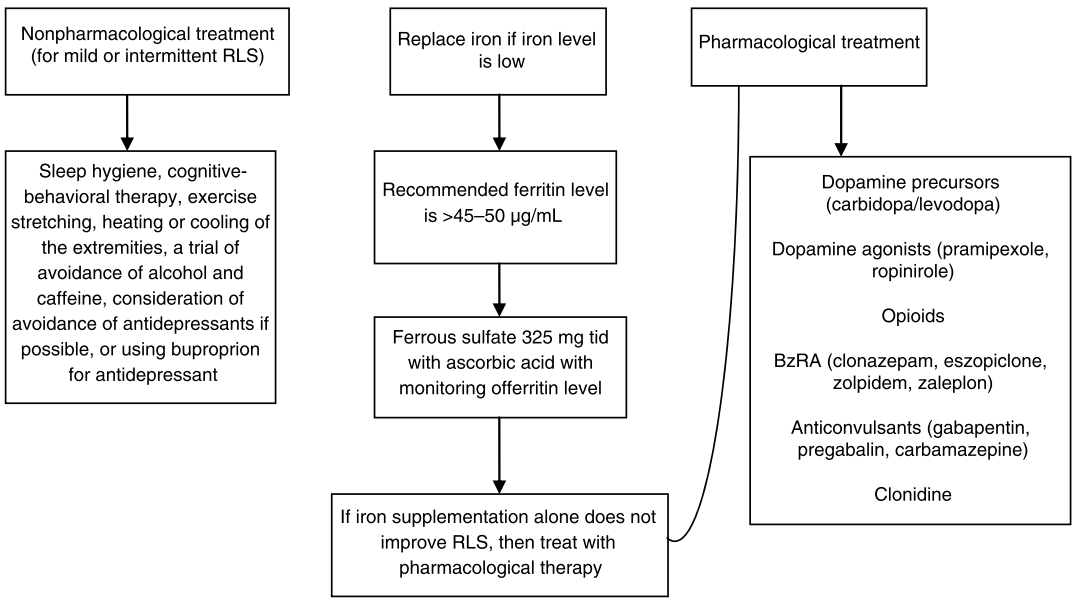

Fig. 5. Treatment of restless leg syndrome (RLS) and periodic leg movement. BzRA, benzodiazepine receptor agonist.[44,68]

The treatment of RLS is multimodal. The American Academy of Sleep Medicine developed recommendations for pharmacotherapy.[45,68] A treatment algorithm (Fig. 5) describes an organized strategy.[68] Avoidance of certain foods (eg, caffeine, alcohol) and drugs (eg, antihistamines, neuroleptics, some dopamine antagonists) can be helpful. Selective serotonin receptor blockers, tricyclic antidepressants, and lithium may worsen RLS symptoms and also should be avoided whenever possible.[69]

RLS often is underdiagnosed. In a large multinational primary care population of 23,052 patients, 68% of women had RLS; however, only 12.9% received the diagnosis, despite 64.8% reporting their RLS symptoms to a physician. Published data on women with RLS are few and more research focusing on the symptoms and treatment options for women is needed to tailor both diagnostic and treatment strategies.[60]

Conclusions

Sleep disorders are far more common in women than previously appreciated and presenting symptoms often differ from those in men. Although insomnia itself is more prevalent among women, it can constitute an atypical presentation of other sleep disorders such as OSA in women. Women often are incorrectly diagnosed as having and been treated for anxiety, depression, chronic fatigue, and psychosomatic disorders when having OSA instead. Postmenopausal women carry a higher risk for OSA and should be screened with a comprehensive sleep evaluation and sleep study if these symptoms are present. Cardiovascular risks of untreated OSA are high and women should be aware of their individual risks. PAP therapy should be offered to women with OSA and other treatment options should be discussed if they fail to improve with optimal PAP therapy. RLS is common among women of all ages, but it is more frequent during pregnancy. Correction of iron deficiency and use of dopaminergic medications can be helpful for treatment.

Sleep is essential for women to live a functional, productive life. Diagnostic evaluations should be performed and, if needed, treatment prescribed when sleep is disturbed.

References

1. Mullington JN, Haack M, Toth M, et al. Cardiovascular, inflammatory and metabolic consequences of sleep deprivation. *Prog Cardiovasc Dis* 2009; 51:294–302.

1a. Redline S, Kump K, Tishler PV, et al. Gender differences in sleep disordered breathing in a community-based sample. *Am J Respir Crit Care Med* 1994;149:722–726.

2. Kessler RC, Berglund PA, Coulouvrat C, et al. Insomnia and the performance of US workers: results from the America insomnia survey. *Sleep* 2011;34:1161–1171.

3. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev* 2002;6:97–111.

4. Zhang B, Wing YK. Sex differences in insomnia: a meta-analysis. *Sleep* 2006;29:85–93.

5. Krystal AD, Edinger J, Wohlgemuth W, et al. Sleep in peri-menopausal and post-menopausal women. *Sleep Med Rev* 1998;2:243–253.

6. Hachul H, Bittencourt LR, Soares JM Jr, et al. Sleep in post-menopausal women: differences between early and late post-menopause. *Eur J Obstet Gynecol Reprod Biol* 2009;145:81–84.

7. Palesh OG, Roscoe JA, Mustian KM, et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol* 2010;28:292–298.

8. Omisade A, Buxton OM, Rusak B. Impact of acute sleep restriction on cortisol and leptin levels in young women. *Physiol Behav* 2012;99: 651–656.

9. Van Cauter E, Copinschi GL, Turek FW. Endocrine and other biological rhythms. in DeGroot LJ, Jameson JL (eds): *Endocrinology.* Philadelphia, WB Saunders, 2001, Vol 1, 4th ed, pp341–372.

10. Gold PW, Goodwin FK, Chrousos GP. Clinical and biochemical manifestations of depression. Relation to the neurobiology of stress (1). *N Engl J Med* 1988;319:348–353.

11. 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;141:846–850.

12. *International Classification of Sleep Disorders), Second Edition: Diagnostic and Coding Manual*. Westchester, IL, American Academy of Sleep Medicine, 2005.

13. Lauderdale DS, Knutson KL, Yan LL, et al. Objectively measured sleep characteristics among early-middle-aged adults: the CARDIA study. *Am J Epidemiol* 2006;164:5–16.

14. Morgenthaler T, Kramer M, Alessi C, et al. Practice parameters for the psychological and behavioral treatment of insomnia: an update. An American Academy of Sleep Medicine report. *Sleep* 2006;29:1415–1419.

15. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. *J Clin Sleep Med* 2008;4:487–504.

16. Krystal AD. Insomnia in women. *Clin Cornerstone* 2003;5:41–50.

17. Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. *Oncol Nurs Forum* 2007;34:E51–E59.

18. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine task force. *Sleep* 1999;22: 667–689.

19. Young T, Blustein J, Finn L, et al. Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. *Sleep* 1997;20:608–613.

20. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230–1235.

21. Young T, Evans L, Finn L, et al. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep* 1997;20:705–706.

22. Young T, Peppard PE. Clinical presentation of OSAS: gender does matter. *Sleep* 2005;28:293–295.

23. Young T, Shahar E, Nieto FJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med* 2002;162:893–900.

24. Shepertycky MR, Banno K, Kryger MH. Differences between men and women in the clinical presentation of patients diagnosed with obstructive sleep apnea syndrome. *Sleep* 2005;28:309–314.

25. Epstein LJ, Kristo D, Strollo PJ Jr, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009;5:263–276.

26. Walker RP, Durazo-Arvizu R, Wachter B, et al. Preoperative differences between male and female patients with sleep apnea. *Laryngoscope* 2001;111:1501–1505.

27. Richman RM, Elliott LM, Burns CM, et al. The prevalence of obstructive sleep apnoea in an obese female population. *Int J Obes Relat Metab Disord* 1994;18:173–177.

28. 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;18:221–228.
29. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 2001; 163:608–613.
30. Polo-Kantola P, Rauhala E, Helenius H, et al. Breathing during sleep in menopause: a randomized, controlled, crossover trial with estrogen therapy. *Obstet Gynecol* 2003;102:68–75.
31. Dennerstein L, Lehert P, Guthrie JR, et al. Modeling women's health during the menopausal transition: a longitudinal analysis. *Menopause* 2007;14:53–62.
32. Keefe DL, Watson R, Naftolin F. Hormone replacement therapy may alleviate sleep apnea in menopausal women: a pilot study. *Menopause* 1999;6:196–200.
33. Prinz P, Bailey S, Moe K, et al. Urinary free cortisol and sleep under baseline and stressed conditions in healthy senior women: effects of estrogen replacement therapy. *J Sleep Res* 2001;10:19–26.
34. Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/Progestin Replacement Study (HERS) Research Group. *JAMA* 1998;280:605–613.
35. Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. *Lancet* 2009;373:82–93.
36. Gami AS, Pressman G, Caples SM, et al. Association of atrial fibrillation and obstructive sleep apnea. *Circulation* 2004;110:364–367.
37. Neuberger HR, Schotten U, Verheule S, et al. Development of a substrate of atrial fibrillation during chronic atrioventricular block in the goat. *Circulation* 2005;111:30–37.
38. Kohler M, Stradling JR. Mechanisms of vascular damage in obstructive sleep apnea. *Nat Rev Cardiol* 2010;7:677–685.
39. Campos-Rodriguez F, Martinez-Garcia MA, de la Cruz-Moron I, et al. Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: a cohort study. *Ann Intern Med* 2012;156:115–122.
40. Aronsohn RS, Whitmore H, Van Cauter E, et al. Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. *Am J Respir Crit Care Med* 2010;181:507–513.
41. Hassaballa HA, Tulaimat A, Herdegen JJ, et al. The effect of continuous positive airway pressure on glucose control in diabetic patients with severe obstructive sleep apnea. *Sleep Breath* 2005;9:176–180.
42. Valham F, Stegmayr B, Eriksson M, et al. Snoring and witnessed sleep apnea is related to diabetes mellitus in women. *Sleep Med* 2009;10: 112–117.
43. Tasali E, Chapotot F, Leproult R, et al. Treatment of obstructive sleep apnea improves cardiometabolic function in young obese women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2011;96:365–374.
44. Berry RB. *Fundamentals of Sleep Medicine*. Philadelphia, Elsevier Saunders, 2012.
45. Nino-Murcia G, McCann CC, Bliwise DL, et al. Compliance and side effects in sleep apnea patients treated with nasal continuous positive airway pressure. *West J Med* 1989;150:165–169.
46. Sin DD, Mayers I, Man GC, et al. Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study. *Chest* 2002;121:430–435.
47. Battagel JM, Johal A, L'Estrange PR, et al. Changes in airway and hyoid position in response to mandibular protrusion in subjects with obstructive sleep apnoea (OSA). *Eur J Orthod* 1999;21:363–376.
48. Campos-Rodriguez F, Martinez-Garcia MA, et al. Gender differences in treatment recommendations for sleep apnea. *Clin Pract* 2012;9:565–578.
49. Deleted in proof.
50. Yeboah J, Redline S, Johnson C, et al. Association between sleep apnea, snoring, incident cardiovascular events and all-cause mortality in an adult population: MESA. *Atherosclerosis* 2011;219:963–968.
51. Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009;6:e1000132.
52. Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med* 2009;169: 1619–1626.
53. Blyton DM, Skilton MR, Edwards N, et al. Treatment of sleep disordered breathing reverses low fetal activity levels in preeclampsia. *Sleep* 2013; 36:15–21.
54. Tom SE, Anderson ML, Landis CA, et al. Sleep problems after short-term hormone therapy suspension: secondary analysis of a randomized trial. *Menopause* 2011;18:1184–1190.
55. Maasilta P, Bachour A, Teramo K, et al. Sleep-related disordered breathing during pregnancy in obese women. *Chest* 2001;120:1448–1454.
56. Ye L, Pien GW, Ratcliffe SJ, et al. Gender differences in obstructive sleep apnea and treatment response to continuous positive airway pressure. *J Clin Sleep Med* 2009;5:512–518.
57. Jayaraman G, Majid H, Surani S, et al. Influence of gender on continuous positive airway pressure requirements in patients with obstructive sleep apnea syndrome. *Sleep Breath* 2011;15:781–784.
58. Allen RP, Picchietti D, Hening WA, et al. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101–119.
59. Berger K, Kurth T. RLS epidemiology—frequencies, risk factors and methods in population studies. *Mov Disord* 2007;22:S420–S423.
60. Hening W, Walters AS, Allen RP, et al. Impact, diagnosis and treatment of restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. *Sleep Med* 2004;5:237–246.
61. Winter AC, Schurks M, Glynn RJ, et al. Restless legs syndrome and risk of incident cardiovascular disease in women and men: prospective cohort study. *BMJ Open* 2012;2:e000866.
62. Rothdach AJ, Trenkwalder C, Haberstock J, et al. Prevalence and risk factors of RLS in an elderly population: the MEMO study. Memory and Morbidity in Augsburg Elderly. *Neurology* 2000;54:1064–1068.
63. Paulus W, Dowling P, Rijsman R, et al. Pathophysiological concepts of restless legs syndrome. *Mov Disord* 2007;22:1451–1456.
64. Earley CJ, Allen RP, Beard JL, et al. Insight into the pathophysiology of restless legs syndrome. *J Neurosci Res* 2000;62:623–628.
65. Allen RP. Race, iron status and restless legs syndrome. *Sleep Med* 2002;3:467–468.
66. Li Y, Walters AS, Chiuve SE, et al. Prospective study of restless legs syndrome and coronary heart disease among women. *Circulation* 2012; 126:1689–1694.
67. Manconi M, Govoni V, De Vito A, et al. Restless legs syndrome and pregnancy. *Neurology* 2004;63:1065–1069.
68. Littner MR, Kushida C, Anderson WM, et al. Practice parameters for the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. *Sleep* 2004;27:557–559.
69. Picchietti D, Winkelman JW. Restless legs syndrome, periodic limb movements in sleep, and depression. *Sleep* 2005;28:891–898.