

Three Decades of Progress in Sleep Disorders and Sleep Health for Women

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Abstract

Over the past 3 decades, significant strides have been made in the field of sleep medicine for women. The impact of sex and gender on sleep health and sleep disorders received little attention in the early 1990s, but driven by policies ensuring inclusion of women in medical research, more recent studies have identified sex differences in sleep and investigated gender differences in sleep disorders. Nevertheless, disparities remain: diagnosis of sleep disorders, such as obstructive sleep apnea, narcolepsy, and rapid eye movement (REM) sleep behavior disorder are often delayed and underdiagnosed in women. Future research should continue to examine how biological sex and identity across the gender spectrum influence sleep health and sleep disorders, allowing for more personalized health care for all patients.

Keywords

sex differences, sleep disorders, sleep health, women

The year is 1993 and women are making strides toward equity. Janet Reno was sworn in as the first woman Attorney General of the United States and the US Defense Secretary ordered military chiefs to allow women pilots to fly in combat. You are a 46-year-old woman who has started having trouble sleeping. You've gained weight and family members complain that your snoring wakes them up at night. During the day, you feel irritable and have trouble remembering things. You decide it is time to do something about your sleep. But is the health care system prepared to help?

In 1993, there were fewer than 10 sleep medicine training programs and just over 500 physicians in the United States with sleep medicine board certification.¹ Women comprised over 40% of entering US medical students, but only 3% of medical school deans were women.² A PubMed literature search for papers on sleep in humans that year yields over 1500 publications, but fewer than 2% focused on sleep in women or sex differences and many papers included only men as participants, even though the study topic pertained to both sexes.

So, what were the options for a woman with a sleep disorder in 1993? And what was her prognosis? The higher prevalence of insomnia in women was recognized at that time³ and non-benzodiazepine hypnotics were a relatively new treatment option, yet most patients with insomnia were not treated. Gender disparities in the identification and treatment of obstructive sleep apnea were the norm in 1993,⁴ and unfortunately persist today.⁵ So, chances are, if you were a woman with a sleep

disorder in 1993, accurate, timely diagnosis and effective treatment would have been elusive.

There was, however, a bright spot for a woman with a sleep disorder in the 1990s. Based on recommendations from the National Commission on Sleep Disorders Research to Congress in 1992,⁶ the National Center on Sleep Disorders Research was established within the National Heart, Lung, and Blood Institute in 1993. Another positive milestone was the National Institutes of Health (NIH) Revitalization Act of 1993, which established guidelines addressing the inclusion of women and underrepresented groups in clinical research.⁷

The last 3 decades of sleep research has produced actionable data. We know that healthy sleep is associated with a myriad of optimal outcomes across the life span regardless of sex or gender. We have established that key components of healthy sleep include sufficient duration for age, consistent timing, and

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alignment with endogenous circadian phase. There is increased recognition that sleep disorders can present differently in women and men. However, gender disparities remain in diagnosis of sleep disorders; in a 2017 study of 1000 patients ranging from age 11 to 90 years old, men and boys were twice as likely to be referred for a sleep disorder evaluation compared with women and girls.⁸ Changes in sleep across the menstrual cycle have been documented, but are understudied, particularly among women with sleep disorders. For example, patient-reported sleep disturbances are increased in the late luteal and early follicular phases and polysomnographic studies show more sleep disturbances during the luteal phase compared to the follicular phase.^{9–11} Whether these fluctuations impact the severity of sleep disorders and treatment efficacy in women is unknown.

The diagnosis of narcolepsy is delayed by ~2 years in women compared to men.^{12,13} One study showed women with narcolepsy had different comorbid conditions (neurologic disorders, fibromyalgia, and autoimmune disorders) than men, which may contribute to the testing delay.¹² Once tested, however, women have greater objective sleepiness on the multiple sleep latency test.^{12,13} Delay in diagnosis can affect many aspects of women's lives. For instance, women with narcolepsy are older when they start their families and face difficult decisions regarding treatment during pregnancy and lactation.^{14,15}

Sleep apnea in women is vastly underrecognized with an estimated 90% of women with severe sleep apnea going undiagnosed.⁴ Phenotypic differences between men and women are often cited as contributing to this disparity, and indeed many women with sleep apnea present with insomnia, which may discourage testing.⁸ Nevertheless, phenotypic differences alone do not explain the gender imbalance in referral and diagnosis; no gender differences in reports of snoring or witnessed apneas were found between women and men with moderate or severe sleep apnea in a large study of patients referred for sleep-disordered breathing.¹⁶ Gender bias also is inherent in common questionnaires used to screen for sleep apnea such as the Epworth Sleepiness Scale, which is more sensitive in detecting sleepiness in men than women.^{17,18} Furthermore, once tested, women have more electroencephalogram arousals rather than oxygen desaturations with respiratory events, potentially lowering the apnea–hypopnea index, and more REM-related obstructive sleep apnea, which could be underrepresented in sleep laboratory settings where studies end prior to women completing their REM cycles.^{19,20} Thus, sleep apnea diagnoses in women are significantly underestimated. This disparity also includes pregnant women with obstructive sleep apnea, who are underdiagnosed and undertreated, leading to increased risk of gestational diabetes, pregnancy-induced hypertension, and intrauterine growth retardation.²¹ However, strides toward improved diagnosis and treatment for women are emerging. Tailoring the scoring rubrics of sleep apnea screening tools using gender-specific cutoffs can improve diagnosis in women.²² Additionally, auto-titrating continuous positive airway pressure (CPAP) algorithms accounting for

gender differences allow for better control of sleep apnea at lower pressures for women compared to traditional algorithms.²³

Among older adults, sleep disorders, including sleep apnea and sleep-related movement disorders, appear to precede dementia more in women than men.²⁴ REM sleep behavior disorder (RBD) has historically been thought to be more prevalent in men, but an investigation in a community-based cohort (n = 1997) studied with polysomnography found no sex difference in the prevalence of RBD.²⁵ Women are underdiagnosed due to less violent dreams and tendency toward a less observant bed partner or no bed partner at all.²⁶ Among elders without sleep disorders, women's sleep is more likely to be disrupted in the caregiving role.²⁷

Public health studies have documented troubling disparities in the US population's knowledge about sleep and access to diagnosis and treatment based not only on gender but also on race and ethnicity, exposure to racism, socioeconomic status, and geography. Along with including sex as a biological variable, gender, including nonbinary genders, must be considered in research on healthy sleep and sleep disorders. Sex and gender *both* affect health care decision-making in patients and clinicians.²⁸ We have made some progress: women are now included in more research studies, and in 2015, NIH extended and strengthened its mandate by requiring inclusion of sex as a biological variable in human and vertebrate animal research study design, analyses, and data reporting. However, the effects of these policies are not yet reflected in the sleep literature—although the overall number of studies focused on sex, gender, or women's health have increased, these papers still represent a small percentage of the sleep field's science. To advance more rapidly, culture change and accountability are needed at multiple levels across a range of stakeholders, from enforcement of existing policies,⁷ to enhanced monitoring by research gatekeepers such as institutional review boards and editorial boards,²⁹ to ensuring that women who volunteer as research participants do not experience bias and discrimination.³⁰ Building on the progress of the last 3 decades, sleep research and sleep medicine are poised to make further gains and work toward personalized and precision health care for all patients regardless of gender.

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