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# Obstructive Sleep Apnea in Women

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## Introduction

Obstructive sleep apnea (OSA) is a common disease with a large public health burden.[1] Due to several anatomical and physiological differences, OSA has traditionally thought to be much less common in women than in men. These differences include variations in craniofacial anatomy, sex hormone differences, greater peripheral fat distribution, as well as women having shorter and less collapsible airways and less respiratory drive instability.[2] However the recruitment bias from clinical samples in early studies has fostered this sex difference to an exaggerated degree.

One large community-based sample of adults aged 21–80 indicated a point prevalence of OSA with clinically significant sleepiness of 3–7% in males and 2–5% of females.[3] Another much larger worldwide community study indicated a lifetime prevalence of OSA of 27.3% in men and 22.5% in women in a narrower population aged 30–69.[1] Both studies show an approximate 1:5–1 ratio which is much lower than that of previous studies showing a ratio of 9 or 10:1.[4] In pediatric and elderly populations, the male to female prevalence ratio is close to equal.[5]

## Clinical Presentation

Numerous studies have clearly demonstrated that women with OSA are more likely to present with a differential and more nonspecific symptom pattern. While traditionally males present with snoring and apnea, presenting symptoms in women frequently include more non specific symptoms such as fatigue, insomnia, depression, nightmares, nocturia, and use of sleep medications.[6,7]

Due to social stigma, women may have a greater reluctance to present with traditional male OSA symptoms. Women are also less likely to present due to a bed partner noticing symptoms, and their partners are less likely to provide collateral history.[5,8] Even women who present with classic OSA symptoms may not be referred due to lack of clinical suspicion from the physician.[9] Here, we present an approach for the clinician to avoid this scenario.

## Clinical Sleep Study Features and Outcomes

Polysomnography data have clearly demonstrated that OSA in women is characterized by less snoring, a lower apnea hypopnea index (AHI), less severe apneic episodes, and less pronounced oxygen desaturations. A higher frequency of rapid eye movement (REM)-related OSA, longer sleep time and more disturbed sleep has also been noted.[10,11]

In both genders, fatigue and sleepiness in OSA is well known to correlate poorly to the AHI.[12] Thus, women may be significantly symptomatic with lower levels of traditionally measured disease.[13] Compared to men, women with sleep apnea also use more healthcare resources prior to OSA diagnosis[9] and have a lower level of quality of life that is also independent of the AHI.[14,15]

Outcomes associated with OSA may be different in women as well, with greater prominence of chronic diseases including hypertension, Type 2 diabetes (T2DM), hypothyroidism, and asthma, especially in women with severe OSA.[6,16] Untreated severe OSA in women is also linked to greater healthcare usage, more cardiovascular disease (CVD) and worse health status than men with untreated disease.[11]

The same severity of OSA may also be more deleterious to women than men from a CVD perspective.[11] Women have a higher incidence of REM-related AHI, which can itself be associated with adverse CV outcomes.[17] Additionally, moderate OSA is associated with greater endothelial damage to blood vessels in women than in men.[18]

## Women's Health and OSA

### Pregnancy

Large meta-analyses indicate that the pooled worldwide lifetime prevalence of OSA in pregnancy is approximately 15–20%, approximately two to three times the baseline prevalence of women of reproductive age.[19,20] This includes both new onset OSA and exacerbated pre-existing disease. Physiological changes such as generalized weight gain, increased uterine/fetal size, mucosal edema, increased rhinitis of the nose, narrowing upper airway diameter, extra pressure on the chest from breast enlargement, as well as elevation of the diaphragm all contribute to reduced lung capacity, increased effort of breathing, and increased oxygen consumption. Hormonal fluctuations affecting respiratory drive, muscle tone and systemic inflammation are also factors increasing the risk and severity of airway collapse.[21,22]

Extensive literature demonstrates a variety of adverse outcomes for women with pre-existing OSA during pregnancy. Significantly, these include both increased overall morbidity and a fivefold increase in the odds of in-hospital mortality, even after adjusting for obesity.[23,24] Additionally, there are increased risks for maternal gestational hypertension/diabetes, preeclampsia, caesarean sections, postoperative wound complication, and more than six times the risk of pulmonary edema.[19] New onset OSA during pregnancy and even snoring were also associated with increased risk of gestational hypertension/diabetes, and preeclampsia.[25]

For the infant, OSA in the mother has also been related to an increased risk for preterm birth, neonatal intensive care unit admission,[19] intrauterine growth restriction, low birth weight,[26] and congenital anomalies.[27]

Sample sizes are very small, but the use of CPAP in pregnancy appears to be well tolerated and may be associated with a reduction in both blood pressure and pre-eclampsia. Maternal CPAP may also improve birthweight and reduce the risk of preterm birth. Further studies are upcoming, but OSA is a clear risk factor for a difficult pregnancy and delivery.[28]

### Polycystic Ovary Syndrome (PCOS)

PCOS is an underdiagnosed condition associated with hyperandrogenism, insulin resistance, and central obesity that affects anywhere from 5–15% of women worldwide.[29] One meta-analysis showed that over one-third of women with PCOS had OSA, and the risk of having OSA was almost four times greater in women with PCOS compared to controls.[30]

OSA is also associated with obesity and worse metabolic profiles in women with PCOS; however, the nature of this relationship remains unclear.[31] Nevertheless, given the potential mechanisms and strong comorbidity, clinicians should have a very high index of suspicion of OSA in women with PCOS.

### Menopause

Premenopausal protection from OSA is thought to be due to effects of progesterone and estrogen on both overall respiratory stability and peripheral fat distribution.[10] These advantages decline throughout menopause, increasing OSA prevalence 2–3 times in the peri- and post-menopausal period even after adjusting for age and weight.[32,33] To a lesser extent, early and surgical menopause also show an increased risk of OSA,[34] which indicates that OSA increase in menopausal women is likely an interaction between age, weight and various hormonal changes. Studies also indicate that menopause hormonal therapy (MHT) is inconsistent at directly reducing OSA, confirming the role of non hormonal factors.[35] Nonetheless, given the multiple additional benefits to biological and psychological factors in menopause including improved sleep, MHT should always be considered early in the peri-menopausal period.

## A Clinical Approach to OSA in Women

### Assessment

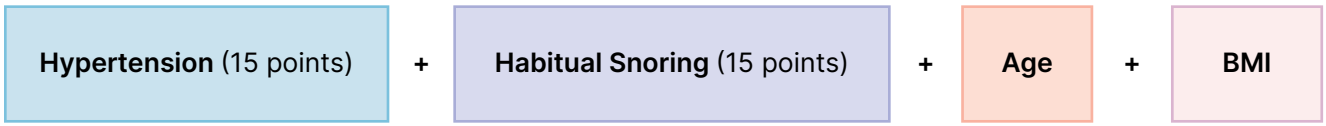
OSA in women can be challenging to diagnose and often may not be the primary issue given the higher rate of comorbidities. Clinicians should have a high index of clinical suspicion for OSA.

Unfortunately, as in many areas of medicine, teaching and clinical guidelines for evaluation and diagnosis of OSA are based on studies of male patients. In particular, OSA should always be considered in women during peri- and post-menopause, during pregnancy, and in patients with PCOS, CVD risk, mood disorders, insomnia, and those taking sleep medications (**Table 1**).

Standard predictive sleep apnea questionnaires are derived from symptom patterns predominantly present in men and

| Symptoms | Key Indicators |
|---|---|
| • Depression<br>• Anxiety<br>• Insomnia<br>• Sleep medication use<br>• Non-specific fatigue<br>• Hypothyroidism | • Peri-post menopause<br>• Pregnancy<br>• PCOS<br>• Metabolic and cardiovascular disease onset (especially hypertension and Type 2 diabetes) |

**Table 1.** Nontraditional symptoms and indicators for OSA screening in women; *courtesy of Atul Khullar, MD, MSc, FRCPC, DABPN (Cert sleep medicine), DABOM, FAASM, and Jennifer Swainson, MD, FRCPC, DABOM.*




**Scores exceeding 75 should prompt consideration of OSA screening.**

**Table 2.** Proposed alternative scoring to screen women with OSA; *adapted from Facco, FL et al., 2014.*

alternative predictive scoring for women may be considered when using these.[36,37] A simple, practical four variable model that has been useful in pregnancy (**Table 2**)[38] could potentially be considered for women overall.

## Testing and Referrals

Testing and referrals for OSA vary according to jurisdiction, coverage, and availability. In some parts of Canada, sleep apnea must be referred to a sleep centre or for specialist consultation, and in others it is managed by the family physician and a respiratory home care company.

The two current major types of testing include home sleep testing and polysomnography (PSG), which is conducted in a sleep laboratory with more measurements and a greater degree of observation. Though PSG testing is more accurate, home testing is more convenient and available. Remote tracking technology such as watches or phones show promise, but lack clinical validation at this time. Unfortunately, even when referred, only one-half to two-thirds of individuals follow through for testing.[39,40] Therefore, education about the reason for testing and the potential deleterious effects of OSA needs to be part of the patient visit.

Home sleep testing is less likely to pick up the shorter, less pronounced respiratory events and the less severe oxygen desaturations characteristic of OSA in women, which often leads to a missed diagnosis. This is especially true in younger, non-obese women. Under treatment of women can easily occur if an overall AHI from a home study is used. For example, clusters of REM-related apnea, usually only seen accurately on full PSG, can be very fatiguing and are associated with increased cardiac risk. Therefore, home sleep testing can rule in but cannot rule out sleep apnea. Full PSG should be considered in any female patient with a negative home study.

Even if OSA is detected, its clinical severity and implications of untreated disease may be underestimated by the clinician. Canadian insurance companies and some provincial social welfare plans have reinforced this by basing coverage for CPAP treatment on an AHI definition of moderate-to-severe OSA, even though it is clear that mild disease can have deleterious effects, particularly for women.[41]

Given the evolving pathophysiology of OSA over the female life span, repeat testing is often necessary. While there is no consistent guideline for when to repeat sleep testing, it should be

considered when there are new symptoms, significant weight gain, peri- or post-menopausal transitions, or if a number of years have passed. Often patients who did not have significant OSA prior to peri-menopause, develop it in their mid-to-late forties. Disturbed sleep often predates the vasomotor symptoms by months to years. It is important to assess for OSA and other sleep disorders at this time, with strong consideration of MHT therapy.

In terms of pregnancy, time is of the essence. A history of OSA must be reviewed as soon as pregnancy is confirmed. In higher risk patients, testing can be considered as part of preconception counselling. Home studies may be required given limited access to full PSG and treatment may need to be aggressive. One guideline recommended assessment and testing at 12–18 weeks gestation.[40]

## Treatment

Proper screening for OSA will yield numerous cases of mild-to-moderate disease. Given that women commonly have a high degree of insomnia and depressive symptoms, OSA may not be the primary clinical focus, but a treatment trial (not purchase) of CPAP or other conservative measures is always reasonable.

## Conservative Measures

Weight loss has been shown to improve OSA treatment and some of the newer weight loss drugs have clear effects in improving OSA.[42,43] However, weight loss may be less effective in treating OSA in women than men,[44] perhaps due to differences in peripheral vs. central fat distribution. It is also unclear if there are sex-related differences in OSA improvement with bariatric surgery. Nevertheless, given the multiple other benefits of weight loss, this strategy should be pursued aggressively independent of OSA.

Positional therapy (i.e., finding ways or devices to reduce supine sleep) is often used to reduce the impact of sleep apnea particularly in patients who have supine predominant OSA. No sex differences have been seen in the limited reports of this treatment.

## Continuous Positive Airway Pressure (CPAP)

CPAP is the first-line therapy for moderate-to-severe OSA. Typically, it is delivered as straight pressure, or an automatic range of pressures based on an algorithm in the device that detects airway flow limitations. These automatic algorithms have been designed and tested primarily on uncomplicated male patients with greater flow limitations; therefore, automatic pressure ranges may not be as accurate in treating the characteristics of OSA in women.

On average, women require lower CPAP pressures, so the range of the automatic pressure settings should reflect this. If patients have been diagnosed with a home sleep study, they may need full PSG to correctly set the CPAP if they remain symptomatic with the automatic pressures.

Long-term adherence to CPAP may be limited for multiple physical and social reasons. An estimated 20–50% of patients simply will not or cannot use the machine.[45] Given the higher rates of comorbid insomnia in women than in men, this may need to be treated first or in conjunction with sleep apnea therapy. Short courses of hypnotics can support CPAP adherence and newer agents with superior safety profiles can be considered for long-term usage as necessary. Although younger women in particular are often perceived as less adherent to CPAP,[45] there is no clear overall difference between CPAP compliance and functional outcomes between women and men.

## Oral Advancement Therapy (OAT)

OAT is a second-line treatment for OSA that guards against airway collapse by repositioning the jaw and tongue. Women may achieve superior results with OAT treatment given their average lower AHI, smaller necks and reduced upper airway collapse.[46] However, access in Canada is often limited to private plans and frequently requires a prior failure of CPAP therapy.

### Airway Surgery

Numerous types of nasal, oropharyngeal and jaw surgeries have been designed as second- or third-line treatment of OSA. No sex differences have been noted in efficacy studies of OSA surgery, but samples are disproportionately male.[21] Newer implanted upper airway stimulators (UAS)[21] for OSA may achieve superior results in females. Again, access to OAS surgery in Canada is quite limited and, to our knowledge, is nonexistent for UAS.

| Clinical Takeaways |
| --- |
| Always keep a high suspicion of OSA in women. |
| Depending on the region and resources, home sleep studies may be first-line testing, but they can only rule in and not rule out sleep apnea. They may underestimate and miss disease, especially in younger and non-obese women. |
| If a high index of suspicion remains with a negative or borderline home study, or the patient is struggling with OSA therapy, refer for full observed polysomnography. |
| Even with the presence of OSA, other mood, anxiety, or insomnia treatment may take precedence, especially if a trial of CPAP has not been successful |
| The adverse maternal and fetal health outcomes of OSA in pregnancy are significant. Review of past or evolving OSA should be part of pregnancy risk management. |
| Women may develop worsened or new onset OSA in peri- and post-menopausal periods; consider reassessment and retesting at times throughout the woman's life. |
| Although less effective, there are other treatments for OSA besides CPAP, such as oral appliances, surgery, and positional therapy. |

## Conclusion

Newer, more accurate studies clearly demonstrate that sleep apnea is more common in women than previously believed. It may present with a different symptom pattern than those reflected in traditional teachings on the topic. Women often present with insomnia, fatigue, and depression. During the female life span, the possibility of sleep apnea during pregnancy, and the peri- and post-menopausal periods must be considered. Repeat testing may be required at various phases in a woman's life.

Women are more likely to present with milder objective disease than men and traditional home sleep studies may miss or underestimate clinically significant cases. Full PSG should be considered when there is a high index of suspicion and aggressive symptomatic treatment should be initiated. Research and known data surrounding OSA diagnosis and treatments have been largely based on male populations and further attention and research into this condition in women will help guide best practices.

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