Beyond Counting Sheep: Exploring the Link between Polycystic Ovary Syndrome and Sleep Health

Nur K. Abdul Jafar, BSc(Hons), MScPH[1] Christie J. Bennett, BachNutDiet(Hons), GradDipHPE, PhD[2]
Lisa J. Moran, GDipPublic Health, BSc(Hons), BND, PhD[1] Darren R. Mansfield, MBBS, FRACP, PhD[3,4]

[1] Monash Centre for Health Research and Implementation, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia
[2] Be Active Sleep and Eat (BASE) Facility, Department of Nutrition and Dietetics, School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria, Australia
[3] Monash Lung and Sleep, Monash Health, Clayton, Victoria, Australia
[4] Faculty of Medicine, Nursing and Health Sciences, School of Psychological Sciences, Monash University, Clayton, Victoria, Australia

Address for correspondence Darren R. Mansfield, MBBS, FRACP, PhD, Monash Lung and Sleep, Monash Health, 246 Clayton Road, Clayton, VIC 3168, Australia (e-mail: Darren.Mansfield@monashhealth.org).

Semin Reprod Med 2023;41:45–58

Abstract

Polycystic ovary syndrome (PCOS) is a common hormonal condition with reproductive, metabolic, and psychological sequelae that affects 8 to 13% of reproductive-aged women and 3 to 11% of adolescent girls. Sleep is often compromised in women with PCOS due to increased rates of sleep problems, with the most established problem being obstructive sleep apnea (OSA). OSA is highly prevalent in reproductive-aged adult women with PCOS, but not so in adolescence. The international evidence-based PCOS guideline to improve health outcomes in women with PCOS indicated routine screening to identify and alleviate symptoms of OSA. The guidelines, however, did not weigh other multidimensional constructs of sleep health such as sleep disturbances (e.g., sleep quality and quantity), beyond OSA. This is perhaps due to the lack of research and existing mixed findings in the area of PCOS and sleep health. This narrative review summarizes the current knowledge about OSA and expands further to include the limited knowledge about other sleep problems in PCOS among reproductive-aged women and adolescent girls. We broadly cover the prevalence, risk factors, and mechanisms of sleep problems in PCOS and their relationship with cardiometabolic and psychological health. A brief summary on treatment and intervention strategies for sleep problems in PCOS and future recommendations will be deliberated.

Keywords
- polycystic ovary syndrome
- sleep health
- sleep disorders
- sleep disturbance
- narrative review

Polycystic ovary syndrome (PCOS) is a chronic complex multisystem disorder, affecting 8 to 13% of reproductive-aged women and 3 to 11% of adolescent girls.[1,2] This varies depending on the type of population and diagnostic criteria used.[3] Current PCOS diagnostic criteria is based on the 2023 International Evidence-Based PCOS Guideline criteria,[3] which has evolved from the internationally endorsed European Society for Human Reproduction and Endocrinology/American Society for Reproductive Medicine (ESHRE/ASRM) consensus Rotterdam Criteria.[4–6] In adults, diagnosis of PCOS is based on the presence of two or three features of oligo/amenorrhea (OA), clinical/biochemical hyperandrogenism

Issue Theme Polycystic Ovary Syndrome; Guest Editors, Chau Thien Tay, BMedSc, MBBS (Hons), FRACP, PhD and Mahnaz Bahri Khomami, MD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0043-1777724.
ISSN 1526-8004.

(HA), and polycystic ovary morphology (PCOM) on ultrasound,[5] while in adolescence, PCOS diagnosis can be confirmed from both OA and HA diagnosis.[7,8] Serum anti-Müllerian hormone (AMH) could also be used as an alternative over PCOM for diagnosing PCOS in adults.[3] Affected women often experience significant metabolic, reproductive, psychological, and dermatological sequelae.[9–15] Insulin resistance (IR) is a key pathophysiological contributor to clinical features of PCOS that presents in a form mechanistically distinct from obesity-associated IR.[16] Excess adipose tissue further worsens the presentation of PCOS likely through the contribution of extrinsic IR associated with weight gain.[17,18] Another key pathophysiological driver of PCOS is hyperandrogenism, clinically manifested as hirsutism, acne, and alopecia.[19] Hormonal imbalances such as increased luteinizing hormone (LH) and decreased follicle-stimulating hormone (FSH) stimulate excess androgen production, contributing to hyperandrogenism in women with PCOS.[19] IR accompanied by compensatory hyperinsulinemia as well as hyperandrogenism drive the pathogenesis of PCOS, contributing to metabolic and reproductive complications in women with PCOS.[20]

Sleep health is a multidimensional pattern of sleep–wakefulness, adapted to individual, social, and environmental demands.[21] Sleep is a prerequisite for all physiological systems and is critical for optimal cognitive functioning, performance, and overall well-being.[22] Among the most well-studied sleep disorders in women with PCOS is obstructive sleep apnea (OSA). OSA is characterized by repetitive collapse of the upper airway during sleep.[23] Beyond OSA, knowledge about other sleep problems in PCOS is less studied. The few studies in this area have reported that women with PCOS tend to sleep lesser (<5–6 hours) than the recommended sleep duration of 7 to 9 hours of sleep per day for adults,[24] in addition to poor sleep quality and difficulty sleeping.[25–29] In a subset of women with PCOS, sleeping >9 hours may be indicative of a comorbid condition.[30]

The international evidence-based guidelines for the assessment and management of PCOS recommended lifestyle management interventions (defined as improving dietary or physical activity via behavioral modification) as the primary initial treatment strategy.[3] Although the PCOS guidelines mentioned routine screening to identify and alleviate symptoms of OSA,[3] other multidimensional constructs of sleep health are not fully considered. Improving sleep health by targeting sleep problems may promote adherence to healthy lifestyle behaviors in women with PCOS.[26,31] In this review, sleep problems encompass both sleep disorders and sleep disturbances. Here, we defined sleep disorders as clinical sleep conditions such as OSA, sleep-disordered breathing (SDB), insomnia, and circadian rhythm (sleep–wake) disorders. Sleep disturbances are defined as a spectrum of sleep conditions that encompass both clinical sleep symptoms or features of a sleep disorder (e.g., excessive daytime sleepiness [EDS] or hypersomnia, restless legs syndrome [RLS]) as well as other sleep measures that are not necessarily associated with clinical sleep symptoms that identify as poor sleep quality, disrupted sleep patterns, sleep difficulties, sleep loss, and abnormalities in sleep architecture (see ►**Table 1**). We narratively synthesized the literature for studies that examined the associations between OSA and other sleep problems in women with PCOS.

Role of Sleep in Health

Sleep plays an essential role in both body and mind recovery, by restoring and supporting various biological functions like memory consolidation, physiological and psychological development, modulation of immune response, and removal of brain waste.[22] Sleep is divided into two main categories: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep that occur in 45-minute stages and alternates between each other forming a 90-minute cycle. NREM sleep consists of stages N1, N2, and N3 (i.e., slow-wave sleep [SWS] or stages 3 and 4).[32] A higher proportion of REM sleep, important for memory consolidation, appears in the latter half of the sleep period at the expense of NREM sleep, where the body regenerates and immune system strengthened.[32] Unhealthy sleep such as reduced sleep duration can decrease sleep cycles and time spent in NREM sleep (see ►**Fig. 1**). Sleep problems can also occur in chronic conditions such as PCOS and vice versa.[33] From ►**Table 2**, beyond the presence of sleep deficiency, sleep health incorporates other dimensions of sleep[21] such as satisfaction/quality of sleep, sleep duration, sleep timing, alertness/sleepiness, and sleep continuity or efficiency. Taken together, healthy sleep is important for maintaining both body and psychological health.

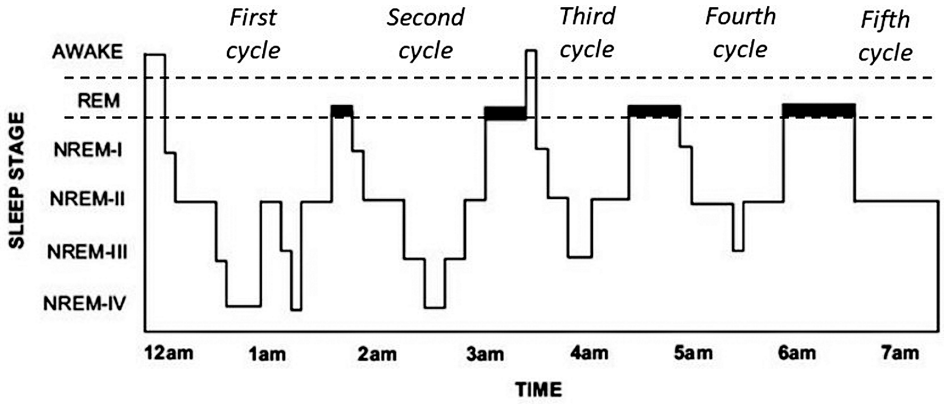
Measurement of Sleep in PCOS

The sleep measures that are commonly used to detect sleep problems in general populations, including reproductive-aged

Table 1 Categories of sleep problems in women with PCOS

Sleep problem categories	Definition
Sleep disorders	Clinical sleep conditions such as OSA, SDB, insomnia, and circadian rhythm (sleep–wake) disorder
Sleep disturbances	Spectrum of sleep conditions that encompass both clinical sleep symptoms or features of a sleep disorder (e.g., EDS or hypersomnia, RLS) as well as other sleep measures that are not necessarily associated with clinical sleep symptoms, such as poor sleep quality, disrupted sleep patterns, sleep difficulties, sleep loss, and abnormalities in sleep architecture

Abbreviations: EDS, excessive daytime sleepiness; OSA, obstructive sleep apnea; PCOS, polycystic ovary syndrome; RLS, restless legs syndrome; SDB, sleep-disordered breathing.



Sleep stage	Function	Unhealthy sleep
Non-rapid eye movement (NREM): Stage I Stage II Stage III } Slow-wave sleep Stage IV } (SWS) or deep sleep	Body regenerates and immune system strengthened	E.g., reduced sleep duration will decrease sleep cycles, and time spent in NREM (deep) sleep
Rapid eye movement (REM)	Memory consolidation	

Fig. 1 The sleep cycle and respective functions. Sleep is divided into two main categories: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep that occur in 45-minute stages, and alternates between each other forming a 90-minute cycle. NREM sleep consists of stages N1, N2, and N3 (i.e., slow-wave sleep [SWS] or stages 3 and 4). Unhealthy sleep such as reduced sleep duration can decrease sleep cycles and time spent in NREM sleep.

Table 2 Dimensions of sleep

Sleep dimensions	Definition
Satisfaction/quality of sleep	The subjective assessment of "good" or "poor" sleep
Sleep duration	The total amount of sleep obtained per 24 h
Sleep timing	The placement of sleep within the 24-h day
Alertness/sleepiness	The ability to maintain attentive wakefulness
Sleep continuity or efficiency	The ease of falling asleep and returning to sleep

Note: Dimensions of sleep adapted from Buysse.[21]

women and adolescent girls with PCOS, are summarized in ►**Supplementary Table S1** (available in the online version only). A gold standard of sleep measurement, overnight polysomnography (PSG) monitors sleep and respiration, including sleep–wake states and sleep stages (i.e., NREM and REM) as well as other parameters such as nasal air pressure, oxygen desaturation, and abdominal and thoracic respiratory efforts.[34] Previous studies used PSG to detect the presence and/or severity of OSA or SDB in women with PCOS based on derived index scores of apnea–hypopnea index (AHI), respiratory disturbance index (RDI), or oxygen desaturation index (ODI).[34–36] Some of these studies also used PSG to examine abnormalities in sleep architecture, referred to as atypical patterns of sleep stages across the night, sleep latency, or sleep efficiency.[37–45] However, the PSG is expensive, time-consuming, and first-night results may be biased to the new environment.[34] A simplified PSG testing using cardiorespiratory polygraphy (level 3 sleep testing) to diagnose OSA may be preferred given its utility, cost-effectiveness, and portability for home-based sleep monitoring.[46] Another time-saving and cost-effective proxy measure for sleep is actigraphy, usually worn on the wrist to record gross motor activity and heart rate.[47] In adult and pediatric populations, actigraphy may be used to diagnose people with insomnia as well as circadian rhythm disorders using a combination of actigraphic parameters such as total sleep time (total amount of time spent actually sleeping during a planned sleep episode), sleep onset latency (time taken to transit from wake to sleep), and number of wake episodes $>$ 5 minutes.[48] Both objective and subjective methods measure different aspects of sleep.[49] For example, self-perceived sleep problems in women with PCOS may differ from their biological sleep (objectively measured), considering that other biases and confounding factors may also influence sleep as a result of impaired daily functioning.[20] Performance of sleep questionnaires commonly used to detect sleep disorders or sleep disturbances tend to differ in adult women relative to adolescent girls with PCOS due to variations in epidemiology and pathophysiology of SDB as well as differential sleep–wake patterns between the two populations.[50] Some of these questionnaires include the Berlin Questionnaire (BQ) to assess risk for OSA in adults,[36] pediatric sleep questionnaire–sleep related disordered breathing scale (PSQ-SRDB),[51] and Pittsburgh Sleep Quality Index (PSQI).[52] The reliability and validity of screening questionnaires relies on their specificity and sensitivity

performance. Questionnaires can be effective negative screening tools. Positive results from screening questionnaires will render further diagnostic testing such as a follow-up PSG examination to confirm the diagnosis.[53] With good internal consistency and construct validity,[54] sleep questionnaires can be a feasible method to capture common sleep disorders or sleep disturbances in both reproductive-aged adult women and adolescent girls with PCOS.

Sleep Problems in Women with PCOS

Obstructive Sleep Apnea

Prevalence

OSA is characterized by a repetitive collapse (complete [apnea] or partial [hypopnea]) of the upper airway during sleep for at least 10 seconds and normally associated with oxygen desaturation and/or arousal from sleep.[23] Individuals with OSA symptoms tend to exhibit non-restorative sleep and daytime sleepiness, resulting in otherwise reduced performance, productivity, and higher rates of accidents.[23] It is possible that symptoms of OSA specific to women with PCOS differ in comparison to the general population. For example, in the clinical setting, women with PCOS and OSA often present with insomnia, fatigue, or mood disturbances, rather than snoring or daytime sleepiness.[23,36,55] In the general population, an OSA prevalence of 9 to 28% is reported in reproductive-aged women compared with 13 to 37% in older women and men.[23,36,56] In women with PCOS, OSA prevalence tends to increase significantly and ranges from 17 to 75%.[57–59] In adolescent with PCOS, OSA prevalence is generally variable (ranges from 0 to 57% as reviewed in the study by Helvaci et al[57]). Some literature also reported a lower OSA prevalence in adolescents compared with adults with PCOS (8 vs. 32% in one older meta-analysis).[57]

OSA is known to be more apparent in higher weight PCOS patients,[60] and more severe during REM sleep.[37,61] A meta-analysis of clinic-based studies ($n = 13$ studies) reported the risk of OSA was higher in adult patients with PCOS compared with those without PCOS (odds ratio [OR] = 9.74, 95% confidence interval [CI]: 2.76–34.41), but not in adolescents (OR = 4.54, 95% CI: 0.56–36.43).[57] In another meta-analysis, Kahal and colleagues (2020) reported 35.0% of women with PCOS had OSA (diagnosed using PSG and/or level 3 sleep testing) and this was markedly higher in obese (33.33–40.91%) than in lean (0%) women with PCOS ($n = 2$ studies) and in women with PCOS than in controls ($n = 8$ studies, OR = 3.83, 95% CI: 1.43–10.24).[59] While being of a higher weight may increase the risk of OSA in those with PCOS compared with healthy controls,[61,62] the correlation between having obesity and severity of OSA symptoms in PCOS is not usually apparent.[63] Several population-based studies have demonstrated increased risk of OSA in women with PCOS above and beyond potential risk factors such as age and body mass index (BMI).[64–67] For example, a population-based study from the United Kingdom reported significantly higher incidence rate for OSA in PCOS than controls, regardless of age and BMI.[67] Increased OSA prevalence in women with PCOS may still persist beyond the influence of weight. In a study using the Taiwan National Health Insurance Database, OSA prevalence increased significantly in women with PCOS ($n = 4{,}595$, 1.71 vs. 0.63 1,000 person-years) compared with age-matched controls ($n = 4{,}595$) and persisted even after adjustment for demographic data and medical comorbidities (i.e., hypertension, dyslipidemia, diabetes mellitus, and obesity).[65] Notably, the risks of OSA reported among women with PCOS compared with controls were relatively higher based on clinic-based studies (ORs = 3.83–11.24)[57,59,68,69] compared with population-based studies (HRs = 1.50–2.63).[64,65,67] One explanation for this finding is that clinic patients may result in a potential selection bias of more severe PCOS. Taken together, both clinic- and population-based studies showed elevated risk of OSA among women with PCOS. Excess adiposity and/or increasing age may have partly contributed to, but not solely explained, the relationship between PCOS and OSA.

To date, only $n = 19$ reported prevalence studies have included a PSG diagnosis.[37–45,61–63,70–76] Moreover, the seemingly lower prevalence of OSA (ranges from 0.4 to 2%) reported from population-based studies are likely to be underestimated given that these were based on diagnostic coding in the medical records.[64–67] In some studies, however, undiagnosed OSA syndrome as well as underestimation of true prevalence of OSA in women with PCOS may occur when ruling out the presence of OSA based on self-reported absence of snoring and daytime sleepiness.[42,53,77–79] Indeed, the wide variations in prevalence of OSA in previous studies were partly related to clinic-based participants with relatively small sample sizes, differences in study populations, and inclusion of mostly higher weight women with PCOS. Together, these limitations from prevalence studies affect the ability to establish cause–effect relationships between PCOS and OSA.

Risk Factors and Mechanisms

Several potential risk factors have been identified in past studies that may contribute to the increased prevalence of OSA in women with PCOS. These include central adiposity, IR, hyperandrogenemia, low progesterone, and low oestradiol levels, which all have been implicated in OSA pathophysiology (►**Fig. 2**).[55,58,71,80,81] Central adiposity is the accumulation of excess adipose visceral fat that is common in PCOS, even among women without overweight or obesity. Fat accumulated in structures surrounding the upper airway increases the likelihood for airway collapse. Upper-body adiposity may also reduce lung volume and adversely impact respiratory control. Together, these physiological changes may contribute to OSA development.[55,58,71,81] Increased risk for OSA in women with PCOS may still persist even after adjustment for BMI,[37,61] suggesting that body fat distribution rather than total body fat (indicated by body size) may be more useful in determining actual OSA risk in PCOS. OSA is also strongly associated with IR,[37,82] another common risk factor in PCOS.[20,61,83,84] IR can be influenced by central adiposity through activation of inflammatory pathways, reduction in insulin-sensitizing adipokines, as well as

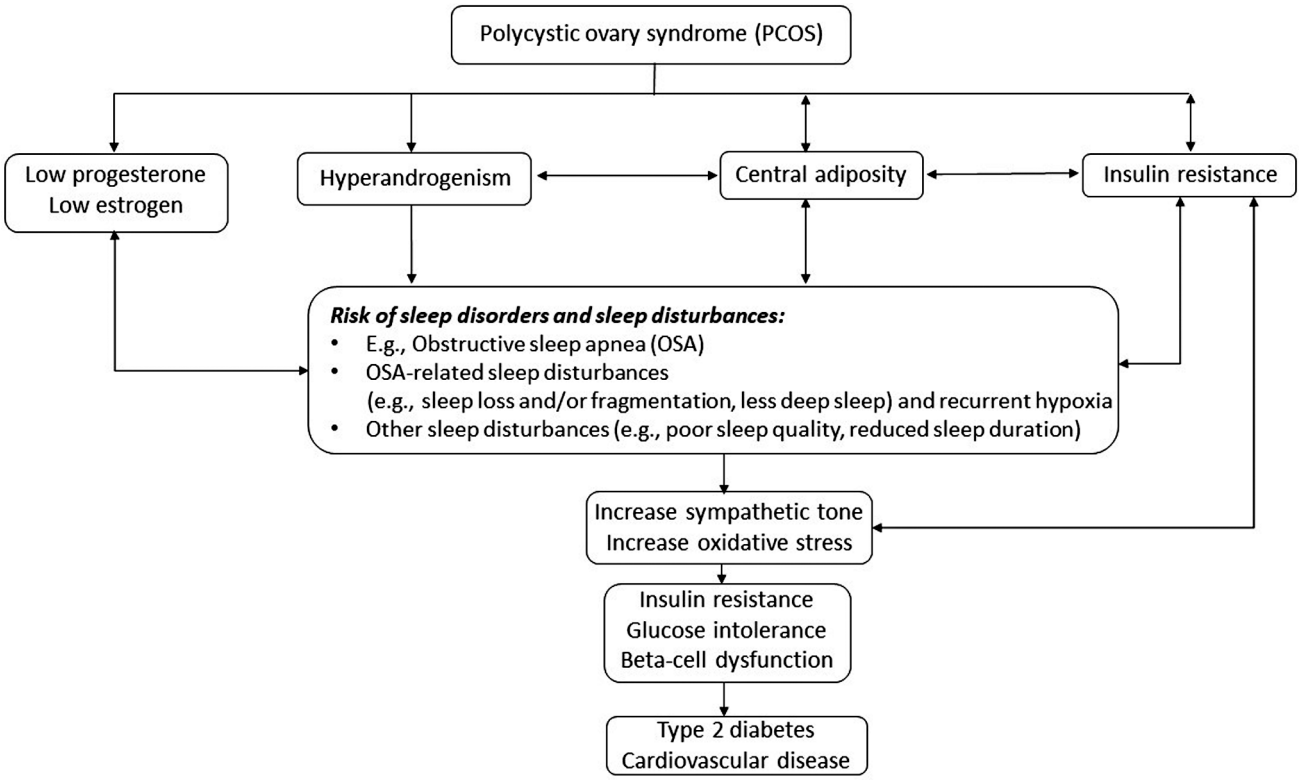


Fig. 2 Schematic pathways of the interrelating connections between polycystic ovary syndrome (PCOS), obstructive sleep apnea (OSA), sleep disturbances, and cardiometabolic risk. The hallmark characteristics of PCOS such as low progesterone and low estrogen levels (characterized by oligo-anovulation), hyperandrogenemia, central adiposity, and insulin resistance (IR) can promote the development of sleep disturbances and sleep disorders, especially OSA. Hyperandrogenemia and IR favor the development of excess adipose tissue. In turn, both excess adiposity and IR increase the severity of PCOS. OSA enhances sympathetic tone and oxidative stress, which also increases IR. In turn, sleep disturbances related to OSA and recurrent hypoxia can increase weight and contribute to IR, glucose intolerance, and β-cell dysfunction, leading to type 2 diabetes, and cardiovascular diseases.

directly between visceral depots and liver through portal circulation.[85] The increased amount of central adiposity accompanied with IR and insufficient sleep in PCOS may be a key factor related to the development of OSA.[61,84,86]

Other potential mechanisms that might increase the risk of OSA in PCOS include hyperandrogenemia, low progesterone, and low estrogen levels. Hyperandrogenemia or excess androgen levels have been associated with increased OSA risk in women with PCOS in some[38,62,70] but not all studies.[37,58,61] In PCOS patients, concentration of sex hormone-binding globulin (SHBG) is typically low since women with this condition tend to have elevated androgen levels and potentially compensated hyperandrogenemia and IR.[12,87] Higher dehydroepiandrosterone-sulfate (DHEAS) levels are also associated with overactive adrenal glands and PCOS symptoms. Hyperandrogenemia predisposes to OSA via effects on neural control of breathing[88] and upper airway mechanics.[89] Due to anovulation, both low progesterone and estrogen concentrations can potentially contribute to increase risk of OSA via alterations in upper airway muscle activity[90] as well as reduce clearance of norepinephrine, an adrenal hormone which impairs the body's ability to initiate and maintain sleep.

The severity of OSA attributed from other risk factors remains unclear and varies across studies depending on different cutoff points and methods to diagnose OSA. Furthermore, the temporality of PCOS and OSA remains equivocal. PCOS may either precede or succeed the development of OSA given that OSA may develop over time as features of PCOS worsen and that previous history of enlarged tonsils in adolescence with PCOS can also cause OSA during childhood.[42,91,92] Overall, previous findings suggest that IR was a stronger risk factor than age, weight, or hyperandrogenism for OSA,[37,61,73] and that the risk for sleep problems in PCOS is likely to be multifactorial, owing also to genetic and environmental determinants.[11,19] More research is needed to understand the interplay of risk factors and comorbidities that mediate the associations between PCOS and OSA.

Impact on Cardiometabolic Health

OSA is linked to detrimental metabolic derangements that lead to metabolic syndrome (MetS) (~60% MetS prevalence occurring in OSA patients) and IR,[93–96] as well as type 2 diabetes (T2DM) and cardiovascular disease development.[97] Sequentially, metabolic abnormalities associated with MetS and IR may exacerbate sleep disorders such as OSA,[98] although evidence demonstrating this latter association remains uncertain. In women with PCOS, greater OSA presence and severity have shown to precipitate or exacerbate IR, glucose intolerance, and hypertension.[55,80,81,83] OSA has also

been linked with non-alcoholic fatty liver disease in PCOS, independent of BMI.[99] Women with PCOS who had OSA or sleep disturbances are also susceptible to worsened cardiovascular risk factors (i.e., higher levels of BMI, systolic blood pressure, diastolic blood pressure, low-density lipoprotein cholesterol, fasting glucose, 2-hour glucose, waist circumference, and lower levels of high-density lipoprotein cholesterol), compared with controls.[69] From ►**Fig. 2**, OSA enhances sympathetic tone and oxidative stress, which also increases IR.[100,101] In turn, symptoms of OSA (e.g., sleep loss and/or fragmentation, less deep sleep) and recurrent hypoxia can increase central adiposity (e.g., by increasing energy intake and adipose tissue deposition) and contribute to IR, glucose intolerance, and β-cell dysfunction, leading to T2DM and cardiovascular diseases. These metabolic disturbances eventually culminate in a vicious cycle and worsen PCOS phenotypic presentation.[55,80,81,83] Regardless of weight, women with PCOS and OSA may still represent a higher metabolic risk population relative to those without OSA. Several studies have observed increased risk for metabolic disorders in those women with PCOS and OSA to persist, even after adjustment for BMI.[61,70] Conversely, Tasali and colleagues found this association to be insignificant after adjusting for BMI,[82] suggesting that adiposity could be a potential confounder.[42,45,102]

Among adolescents with PCOS and obesity, those with MetS had significantly worse symptoms of OSA or SDB compared with those without MetS.[45] This suggests that in addition to obesity, OSA could also be potentially driven by MetS, leading to increased risk of IR (by homeostatic model assessment [HOMA] index), hypertension, dyslipidemia, and triglycerides (TG).[42] Despite the presence of MetS, other studies have observed that the risk of OSA is not significantly increased in adolescent with PCOS due to the lower AHI levels that did not meet the OSA diagnostic criteria.[39,41,43,44] These authors concluded that the pathological mechanisms leading to OSA syndrome in adolescent patients with PCOS may develop in the later course of the disease.[41,43,44] Hence, studies in adolescent PCOS populations may provide insights into early identification of risk groups for the development of OSA as well as MetS. Taken together, sleep problems and metabolic abnormalities occur at increased frequency among higher weight women with PCOS and this could worsen cardiometabolic parameters.

Treatment and Intervention Strategies

The cardiometabolic benefits of treating OSA in both adults and adolescents with PCOS are unclear. A study conducted in reproductive-aged women with PCOS and obesity ($n = 19$) showed that 8 weeks of home continuous positive airway pressure (CPAP) treatment of OSA may exert beneficial effects on cardiometabolic function in PCOS such as decreased sympathetic output and improved insulin sensitivity.[103] In a case study of an adolescent patient with PCOS and obesity, nasal CPAP (nCPAP) treatment in combination with lifestyle intervention (caloric restriction and exercise program) and hormonal treatment resulted in the resolution of OSA, significant weight loss (from obese [BMI = 34.5 kg/m^2] to healthy BMI [BMI = 23.5 kg/m^2]), and significant improvements of clinical and biochemical hyperandrogenism.[104] However, it is not known whether CPAP treatment or lifestyle interventions mainly drove changes in OSA symptoms or weight. It is important that treatment of OSA should not be generalized across both adults and adolescents with PCOS as younger individuals could also report lower OSA symptom profiles.[105] Appliance-based treatments including CPAP or mandibular advancement splints may be efficacious,[106] but consideration must be given to adherence and tolerability. Taken together, a forward-looking focus of OSA treatment in PCOS patients should prioritize the management of symptoms,[31,60] with the benefits of longer-term health risk reduction remaining to be established.

Other Sleep Problems

Insomnia, Circadian Rhythm Disorders, and Sleep Disturbances

Prevalence

Another common sleep disorder in PCOS is clinical insomnia which is characterized by the impairment of the ability to initiate or maintain sleep for at least three nights per week and affects daytime functioning.[107,108] Insomnia is associated with daytime symptoms of fatigue without sleepiness[109] and is linked to long-term health outcomes, including increased cardiovascular risk and cognitive decline later in life.[110,111] Insomnia is also relatively more prevalent in women with PCOS compared with healthy controls.[77,112] For example, Franik et al reported clinically significant insomnia to occur more often in women with PCOS than in controls according to both Athens Insomnia Scale (AIS: 12.6 vs. 3.2%) and Insomnia Severity Index (ISI: 10.5 vs. 1.1%).[112]

Circadian rhythm disorders or circadian misalignment, where one's body's internal clock is misaligned with the environment, can manifest as an advanced, delayed, or non-24 hours (i.e., free running circadian phase).[113] Circadian misalignment impacts social functioning,[114] and is closely related to mental health conditions.[115] Up to 3% of adults in the general population have reported a form of circadian rhythm disorder[116]; however, the prevalence of circadian rhythm disorders in women with PCOS remains unknown. In women with PCOS, levels of melatonin concentrations (from saliva, urine, and follicles) have been used to detect abnormal circadian rhythms.[117–119] For example, Shreeve et al reported elevated night-time urinary levels of melatonin metabolite 6-sulfatoxymelatonin (aMT6s) and increased oxidative stress marker levels with reduced sleep quality in those with PCOS, compared with controls.[117] The presence of both poor sleep quality and high melatonin metabolite levels among PCOS group may seemed counterintuitive, since melatonin is a hormone that promotes sleep.[120] However, the authors discussed that elevated night-time melatonin levels could potentially act as a free radical scavenger[121] for the increased oxidative stress (oxidants and antioxidants imbalance) often seen in those with PCOS.[122] In another study, obese adolescent girls with PCOS showed later

clock-hour of melatonin offset, later melatonin offset relative to sleep timing, and longer duration of melatonin secretion than obese controls.[118] More studies using objective sleep measures together with comprehensive investigation of serum melatonin levels are needed to determine the prevalence of circadian rhythm disorders and understand the associations between sleep and melatonin alterations in PCOS populations.

In addition to sleep disorders, women with PCOS are also at higher risk of sleep disturbances such as poor sleep quality, disrupted sleep patterns, abnormalities in sleep architecture, sleep difficulties, sleep loss, and sleep-related impairment (►**Table 1**). Two recent meta-analyses ($n = 9$ studies and $n = 18$ studies, respectively) used data from Asian, Western, and/or Oceania countries and reported higher incidence of poor sleep quality (i.e., higher PSQI scores), shorter duration of sleep, lower sleep efficiency, and higher sleep-onset latency in women with PCOS compared with healthy controls (OR = 11.24, 95% CI: 2.00–63.10 and OR = 6.22; 95% CI: 2.77–13.97, respectively).[68,69] As early as the adolescent period, girls with PCOS and obesity are already experiencing sleep disturbances such as increased sleep-onset latency and reductions in REM sleep and sleep efficiency, compared with girls without PCOS and obesity.[39] In adult women with PCOS, sleep difficulties (i.e., difficulty initiating sleep, more restless sleep, more severe tiredness) and increased difficulty falling asleep have been reported in numerous epidemiological studies (up to 68%), even after adjustment for BMI and other comorbidities.[27,28] In some cases, despite similar duration of nocturnal sleep, women with PCOS still report more severe tiredness than healthy controls.[27] Women with PCOS are also prone to sleep disturbances such as EDS or hypersomnia in which an individual repeatedly feels excessively sleepy in the day or sleep longer than usual at night.[123] A recent meta-analysis reported significantly higher Epworth Sleepiness Scale (ESS) scores (i.e., greater daytime sleepiness) in women with PCOS compared with controls ($n = 4$ studies, mean difference [MD] = 2.49, 95% CI: 0.80–4.18).[68] Although only one case–control study examined EDS with PCOS in adolescence, this study similarly reported significantly higher prevalence for both SDB (45.6 vs. 27.8%) and EDS (54.4 vs. 35.6%) in adolescent girls with PCOS compared with age-, ethnicity-, and BMI-matched controls.[118] However, women with PCOS may experience EDS even without OSA syndrome.[61] RLS is both a sleep and movement disorder characterized by an irresistible urge to move the legs, typically in the evenings and can severely disrupt sleep.[124] Only one study reported higher RLS prevalence in women with PCOS (23.3% out of $n = 73$) in conjunction with higher PSQI, ESS, ISI, and BQ scores, compared with controls.[77]

Knowledge gaps exist with regard to other types of sleep problems related to PCOS risk. Over the last two decades, the majority of observational studies that investigated the prevalence of sleep problems in reproductive-aged women with PCOS were from cohort or case–control studies and only two were longitudinal studies. Out of these studies, $n = 10$ examined the presence of OSA, SDB, or sleep apnea only,[63,65–67,72,73,78,79,82,125] while others ($n = 13$) have included sleep disorders such as insomnia, circadian rhythm disorders, and/or sleep disturbances like EDS.[37,38,61,62,64,70,74–77,112,117,119] Eight studies focused on examining sleep disturbances (i.e., sleep difficulties, short sleep, and/or poor sleep quality), but not clinical sleep disorders in PCOS.[25–29,126–128] To date, nine studies based on three study cohorts have investigated PCOS with sleep problems specific to adolescent girls.[39–45,102,118] There remains a paucity of objective research that examine the prevalence of sleep disturbances in PCOS without clinically diagnosed sleep disorders. This is further compounded with the overlapping terminology of sleep disturbances and sleep disorders in the PCOS literature. It should be acknowledged that sleep instruments such as PSQI not only measures sleep quality but also other sleep disturbances, incorporating features identical to that reported in insomnia.[52] Lastly, the accuracy of sleep instruments to detect sleep problems may vary across the type of study populations, depending on the PCOS diagnostic criteria.[3,5,7]

Risk Factors and Mechanisms

Similar to OSA above, studies that reported the link between hyperandrogenism and the risk of disrupted sleep patterns are equally mixed.[74,77,117,126,127] Melatonin is a neuroendocrine hormone that entrains our 24-hour internal clock and sleep patterns.[129] Alterations in melatonin secretion (i.e., lower overall melatonin and delayed melatonin onset) may influence sleep patterns and/or circadian rhythm in women with PCOS,[130] but studies are limited.[117–119] For some of these studies, IR and hyperandrogenism were also linked to changes in melatonin secretions.[118,119] Certain single-nucleotide polymorphisms (SNPs) in the melatonin receptor gene have been associated with PCOS risk and its metabolic complications such as IR.[131] This speculates that genetic predisposition to PCOS may play a role in influencing sleep problems related to the condition. Emerging evidence suggests that women with PCOS are more likely to have evening chronotypes (i.e., circadian preference in behavioral and biological rhythms toward eveningness) than those without the condition.[126,132] Individuals with evening chronotypes have circadian rhythms that are phase delayed in the 24-hour cycle which may affect the performance of morning activities including work and family life (i.e., social jet-lag).[133] Few studies that examined chronotype in women with PCOS (using questionnaires) reported associations between evening chronotype with increased testosterone levels,[126,132] poor subjective sleep quality,[126] and worse hormonal and metabolic profile in PCOS.[132]

Impact on Cardiometabolic Health

Sleep disturbances such as poor sleep quality, short sleep (<5–6 hours), or long sleep (>9–10 hours) can negatively influence diet, stress, and other lifestyle factors that can contribute to weight gain, hypertension, and obesity, which are risk factors for T2DM and cardiovascular disease.[97] For example, inadequate sleep can affect levels of ghrelin and leptin,[134] lowering adherence to a healthy diet and regular

meal patterns,[135] which contributes to weight gain.[136] Insufficient sleep and circadian misalignment also predispose individuals to poor metabolic health and promote weight gain.[137] Poor sleep patterns were also observed in adolescence with PCOS and obesity and were more likely to correlate with metabolic dysfunction and a greater number of MetS symptoms.[45] For example, poorer sleep efficiency measured by actigraphy correlated with higher percentage of liver fat, waist circumference, and higher TG in adolescent girls with PCOS and obesity.[45] Contrary to these findings, studies from another group reported PCOS status, parameters of body weight/body composition, and MetS did not seem to impact significantly on respiratory PSG variables in obese adolescent girls with PCOS.[41,43,44] In a cross-sectional study, for example, the authors investigated the differences in PSG variables between adolescents with PCOS and obesity with and without MetS. The authors found no differences among the study groups concerning respiratory PSG variables (i.e., apnea index, hypopnea index, number of obstructive apnea, AHI, and stages 3 and 4), but instead found differences in sleep architecture (i.e., sleep-onset latency and sleep efficiency).[41] Hence, more research is needed to understand the impact of sleep problems on cardiometabolic health in specific PCOS populations.

Treatment and Intervention Strategies

Several studies have explored using other lifestyle-related approaches to improve the sleep quality and/or quantity of women with PCOS, including physical activity,[138] behavioral modification,[139] dietary intake,[140] and psychosocial well-being.[141] Other studies have also explored pharmacological approaches such as magnesium,[142] melatonin,[143] and metformin supplementation.[144] Recently, Oberg and colleagues in a randomized controlled trial compared sleep health variables assessed by actigraphy in women with PCOS (-overweight/obese) with controls and also assessed sleep variables after a 4-month behavioral modification intervention (using goal setting, problem solving, stress management, stimulus control, and techniques for avoiding instant gratification to target diet and physical activity and achieve long-term weight control) in comparison with minimal intervention. The authors reported that women with PCOS had normal total sleep duration (7.2 hours), but poorer sleep efficiency than controls (87 vs. 93%) and behavioral modification intervention seemed to reduce the amount of daytime sleep compared with the minimal intervention group, suggesting improved sleep behavior.[139] However, the reduction in daytime napping following behavioral intervention in the PCOS group could also be attributed to the fact that participants were told not to nap during the day. Moreover, collection of sleep data for the control group was partly completed during the COVID-19 pandemic where working from home was encouraged, enabling a wider window of sleep. Given that daytime napping is associated with increased risk of T2DM[145] and death of all causes,[146] behavioral modification interventions that target diet and physical activity could be a feasible strategy to improve the sleep health and cardiometabolic outcomes in women with PCOS.

In non-PCOS adult populations, cognitive behavioral therapy (CBT) for sleep interventions has shown to improve both sleep quality and quantity.[147,148] CBT for insomnia (CBT-I) is a well-recognized non-pharmacological intervention for individuals with insomnia.[149] CBT-I involves techniques such as stimulus control (e.g., modulating cues for wakefulness), relaxation techniques, sleep restriction, sleep hygiene education (e.g., patient education about healthy sleep habits), and cognitive restructuring (e.g., altering dysfunctional attitudes and beliefs about sleep).[149,150] However, no studies so far have implemented CBT for sleep disturbance or CBT-I interventions in women with PCOS.

In the general population, non-pharmacological sleep health interventions like behavior change methods, mind–body exercise, sleep education, or relaxation techniques have shown promising evidence in improving both sleep quantity and/or sleep quality.[151] As mentioned above, only few studies in PCOS have used sleep health strategies (involving lifestyle-related approaches).[138–140] When optimizing sleep health, one should consider other multi-dimensions of sleep[21] (►**Table 2**) and factors that shape health, such as genetic, social, environmental, behavioral, and medical care domains.[152] Therefore, more research in PCOS populations is needed to understand the effectiveness of sleep health strategies in enabling better engagement to lifestyle interventions, further supporting their symptoms management efforts.

Sleep and Psychological Health in PCOS

Stress-related mood disorders such as depression and anxiety are prevalent in women with PCOS.[153] Women with PCOS who mostly live in higher weight bodies[13,154,155] may experience weight stigma and perceived weight bias that can lead to stress.[156,157] Furthermore, hyperandrogenemia in women with PCOS can clinically manifest as hirsutism, acne, and androgenic alopecia that impacts body image satisfaction, self-esteem status, leading to psychological symptoms in women with PCOS.[87,158] Mood disorders have been associated bidirectionally with sleep disruption and reduced sleep.[159] Poor psychological health can influence sleep in women with PCOS as evidenced in a cross-sectional study that reported obesity and depressive symptoms together mediated the increased occurrence of difficulty maintaining sleep in women with PCOS (OR = 1.92, 95% CI: 1.12–3.31).[28] Sleep health, when compromised, can influence individual's adherence to lifestyle management (such as diet). This is shown in a study in which the association between PCOS and improved diet quality may be maintained only if women can obtain enough good quality sleep.[26] Taken together, the assessment and management of both sleep and psychological health problems are integral in the management of PCOS symptoms.

Summary of Findings and Research Gaps

This review narratively summarizes the current knowledge on the prevalence, risk factors, and mechanisms of sleep

problems and its potential contribution to cardiometabolic health, as well as the link between sleep and psychological health in PCOS. We identified key gaps and challenges that need to be addressed to gain further clarifications on the true prevalence of sleep problems in PCOS and better understand the psycho-cardiometabolic benefits of OSA and sleep problems treatment in PCOS. First, future research in PCOS and sleep problems should include more high-quality studies (e.g., objective sleep measures) to detect sleep disturbances beyond clinical sleep disorders such as OSA. Second, future studies in PCOS should consider defining the terminology of sleep disturbances as a spectrum of sleep conditions that encompass both clinical sleep symptoms as well as findings from objective sleep measures (►**Table 1**). Third, the majority of past studies were conducted in Western populations and results may differ depending on the PCOS diagnostic criteria used; therefore, there is a need for more representation of studies across various racial or ethnic groups that may allow for inclusion of broader PCOS phenotypes. Similarly, more research in the pediatric (young person: 13 to <22 years) or adolescent population is warranted,[160] especially since adolescents are more susceptible to living in larger bodies due to poor lifestyle and sleep habits.[161] Adolescence is also a sensitive period where diagnosing PCOS is challenging, for example, due to menstrual irregularity and multifollicular ovaries.[7] Understanding the role of sleep and how sleep interacts with symptoms of PCOS in the early development of the syndrome may help clinicians identify PCOS tendencies and intervene early to improve metabolic and reproductive outcomes. It will be useful perhaps if the development of sleep behaviors is mirrored together with the life-course approach to PCOS to elucidate causal effects.

Although not mentioned in this review, we also acknowledge the importance of investigating sleep problems during the perinatal life-stage in women with PCOS since physiological and anatomical changes during pregnancy may be conducive to the development of SDB (especially snoring) typically in the last trimester.[162] While key features of PCOS are often no longer present in postmenopausal women, some research suggest that underlying metabolic and hormonal changes due to PCOS may persist into the later years,[163] thus highlighting important research in this area. Finally, investigating the effects of sleep disorders on reproductive health in women with PCOS[164] will provide valuable insights into future treatment options, especially for those women with PCOS who experience fertility issues.

Conclusion

In conclusion, the 2023 International Evidence-Based Guideline for the Assessment and Management of PCOS mentioned routine screening to identify and alleviate symptoms of OSA. This represents a big step to acknowledge the association of sleep health disturbances in PCOS, but other multidimensional constructs of sleep health should be explored further. When clarifying the link between PCOS and sleep health, we should also look beyond just alleviating the presence of sleep disorders, but to also understand how sleep plays a role holistically with other lifestyle aspects to better manage the symptoms of PCOS.

Conflict of Interest

All authors declared no conflict of interests.

Acknowledgments

This work was supported by a Veski Fellowship to L.J.M. and the NHMRC Centres of Research Excellence (CRE) (grant number 1171592). Veski and the NHMRC had no role in the design, analysis, or writing of this article. This research was supported by an Australian Government Research Training Program (RTP) Scholarship.

References

1 Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 2016;31(12):2841–2855
2 Naz MSG, Tehrani FR, Majd HA, et al. The prevalence of polycystic ovary syndrome in adolescents: a systematic review and meta-analysis. Int J Reprod Biomed (Yazd) 2019;17(08):533–542
3 Teede HJ, Tay CT, Laven JJE, et al. Recommendations from the 2023 International Evidence-based Guideline for the assessment and management of polycystic ovary syndrome. Eur J Endocrinol 2023;189(02):G43–G64
4 Azziz R, Carmina E, Dewailly D, et al; Task Force on the Phenotype of the Polycystic Ovary Syndrome of the Androgen Excess and PCOS Society. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril 2009;91(02):456–488
5 Eshre RRotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19(01):41–47
6 Zawadri J. Diagnostic criteria for polycystic ovary syndrome: towards a rational approach. Polycystic ovary syndrome. Curr I Endocrinol Metab 1992
7 Tay CT, Hart RJ, Hickey M, et al. Updated adolescent diagnostic criteria for polycystic ovary syndrome: impact on prevalence and longitudinal body mass index trajectories from birth to adulthood. BMC Med 2020;18(01):389
8 Teede HJ, Misso ML, Costello MF, et al; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Hum Reprod 2018;33(09):1602–1618
9 Dokras A, Stener-Victorin E, Yildiz BO, et al. Androgen Excess-Polycystic Ovary Syndrome Society: position statement on depression, anxiety, quality of life, and eating disorders in polycystic ovary syndrome. Fertil Steril 2018;109(05):888–899
10 Joham AE, Boyle JA, Zoungas S, Teede HJ. Hypertension in reproductive-aged women with polycystic ovary syndrome and association with obesity. Am J Hypertens 2015;28(07): 847–851
11 Kakoly NS, Khomami MB, Joham AE, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update 2018;24(04):455–467
12 Lim SS, Kakoly NS, Tan JWJ, et al. Metabolic syndrome in polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. Obes Rev 2019;20(02):339–352
13 Lim SS, Davies MJ, Norman RJ, Moran LJ. Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod Update 2012; 18(06):618–637

14 Tay CT, Teede HJ, Hill B, Loxton D, Joham AE. Increased prevalence of eating disorders, low self-esteem, and psychological distress in women with polycystic ovary syndrome: a community-based cohort study. Fertil Steril 2019;112(02):353–361
15 Tay CT, Teede HJ, Loxton D, Kulkarni J, Joham AE. Psychiatric comorbidities and adverse childhood experiences in women with self-reported polycystic ovary syndrome: an Australian population-based study. Psychoneuroendocrinology 2020; 116:104678
16 Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev 2012;33(06):981–1030
17 Lim SS, Norman RJ, Davies MJ, Moran LJ. The effect of obesity on polycystic ovary syndrome: a systematic review and meta-analysis. Obes Rev 2013;14(02):95–109
18 Teede HJ, Joham AE, Paul E, et al. Longitudinal weight gain in women identified with polycystic ovary syndrome: results of an observational study in young women. Obesity (Silver Spring) 2013;21(08):1526–1532
19 Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. Endocr Rev 2015;36(05):487–525
20 Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med 2010;8(01):41
21 Buysse DJ. Sleep health: can we define it? Does it matter?. Sleep 2014;37(01):9–17
22 Zielinski MR, McKenna JT, McCarley RW. Functions and mechanisms of sleep. AIMS Neurosci 2016;3(01):67–104
23 Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165(09):1217–1239
24 Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health 2015;1(04):233–243
25 Azizi Kutenaee M, Amirjani S, Asemi Z, et al. The impact of depression, self-esteem, and body image on sleep quality in patients with PCOS: a cross-sectional study. Sleep Breath 2020; 24(03):1027–1034
26 Bennett CJ, Mansfield DR, Mo L, et al. Sleep disturbances may influence lifestyle behaviours in women with self-reported polycystic ovary syndrome. Br J Nutr 2021;127(09):1–9
27 Mo L, Mansfield DR, Joham A, et al. Sleep disturbances in women with and without polycystic ovary syndrome in an Australian National Cohort. Clin Endocrinol (Oxf) 2019;90(04):570–578
28 Moran LJ, March WA, Whitrow MJ, Giles LC, Davies MJ, Moore VM. Sleep disturbances in a community-based sample of women with polycystic ovary syndrome. Hum Reprod 2015;30(02): 466–472
29 Shao S-Y, Zhao HQ, Lu ZY, Lei XH, Zhang Y. Association of sleep characteristics and night shift work with self-reported diagnosis of polycystic ovary syndrome: a questionnaire-based cross-sectional study. Reprod Dev Med 2023;7(01):50–55
30 Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. Sleep 2010;33(05):585–592
31 Cowan S, Lim S, Alycia C, et al. Lifestyle management in polycystic ovary syndrome - beyond diet and physical activity. BMC Endocr Disord 2023;23(01):14
32 Lockley SW. Principles of Sleep-Wake Regulation. Sleep, Health and Society: from Aetiology to Public Health. Oxford University Press, USA;; 2010:9–34
33 Teo P, Henry BA, Moran LJ, Cowan S, Bennett C. The role of sleep in PCOS: what we know and what to consider in the future. Expert Rev Endocrinol Metab 2022;17(04):305–318
34 Douglas JA, Chai-Coetzer CL, McEvoy D, et al. Guidelines for sleep studies in adults - a position statement of the Australasian Sleep Association. Sleep Med 2017;36(Suppl 1):S2–S22
35 Chung F, Liao P, Elsaid H, Islam S, Shapiro CM, Sun Y. Oxygen desaturation index from nocturnal oximetry: a sensitive and specific tool to detect sleep-disordered breathing in surgical patients. Anesth Analg 2012;114(05):993–1000
36 Jonas D, Amick H, Feltner C, et al. Screening for obstructive sleep apnea in adults: an evidence review for the US preventive services task force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017. Jan Report. (14–05216)
37 Tasali E, Van Cauter E, Ehrmann DA. Relationships between sleep disordered breathing and glucose metabolism in polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91(01):36–42
38 Yang H-P, Kang J-H, Su H-Y, Tzeng C-R, Liu W-M, Huang S-Y. Apnea-hypopnea index in nonobese women with polycystic ovary syndrome. Int J Gynaecol Obstet 2009;105(03):226–229
39 de Sousa G, Schlüter B, Buschatz D, et al. A comparison of polysomnographic variables between obese adolescents with polycystic ovarian syndrome and healthy, normal-weight and obese adolescents. Sleep Breath 2010;14(01):33–38
40 de Sousa G, Schlüter B, Menke T, Trowitzsch E, Andler W, Reinehr T. Relationships between polysomnographic variables, parameters of glucose metabolism, and serum androgens in obese adolescents with polycystic ovarian syndrome. J Sleep Res 2011; 20(03):472–478
41 de Sousa G, Schlüter B, Menke T, Trowitzsch E, Andler W, Reinehr T. A comparison of polysomnographic variables between adolescents with polycystic ovarian syndrome with and without the metabolic syndrome. Metab Syndr Relat Disord 2011;9(03): 191–196
42 Nandalike K, Agarwal C, Strauss T, et al. Sleep and cardiometabolic function in obese adolescent girls with polycystic ovary syndrome. Sleep Med 2012;13(10):1307–1312
43 de Sousa G, Schlüter B, Buschatz D, et al. The impact of insulin resistance and hyperandrogenemia on polysomnographic variables in obese adolescents with polycystic ovarian syndrome. Sleep Breath 2012;16(01):169–175
44 de Sousa G, Schlüter B, Menke T, Trowitzsch E, Andler W, Reinehr T. Longitudinal analyses of polysomnographic variables, serum androgens, and parameters of glucose metabolism in obese adolescents with polycystic ovarian syndrome. Sleep Breath 2012;16(04):1139–1146
45 Simon S, Rahat H, Carreau A-M, et al. Poor sleep is related to metabolic syndrome severity in adolescents with PCOS and obesity. J Clin Endocrinol Metab 2020;105(04):e1827–e1834
46 Nigro CA, Serrano F, Aimaretti S, González S, Codinardo C, Rhodius E. Utility of ApneaLink for the diagnosis of sleep apnea-hypopnea syndrome. Medicina (B Aires) 2010;70(01): 53–59
47 Ancoli-Israel S, Martin JL, Blackwell T, et al. The SBSM guide to actigraphy monitoring: clinical and research applications. Behav Sleep Med 2015;13(1, Suppl 1):S4–S38
48 Smith MT, McCrae CS, Cheung J, et al. Use of actigraphy for the evaluation of sleep disorders and circadian rhythm sleep-wake disorders: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med 2018;14(07):1231–1237
49 Bianchi MT, Williams KL, McKinney S, Ellenbogen JM. The subjective-objective mismatch in sleep perception among those with insomnia and sleep apnea. J Sleep Res 2013;22(05): 557–568
50 Marcus CL. Obstructive sleep apnea syndrome: differences between children and adults. Sleep 2000;23(Suppl 4):S140–S141
51 Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. Sleep Med 2000;1(01):21–32

52 Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28 (02):193–213

53 Ng SS, Tam W, Chan T-O, et al. Use of Berlin questionnaire in comparison to polysomnography and home sleep study in patients with obstructive sleep apnea. Respir Res 2019;20(01): 40

54 Nascimento-Ferreira MV, Collese TS, de Moraes ACF, Rendo-Urteaga T, Moreno LA, Carvalho HB. Validity and reliability of sleep time questionnaires in children and adolescents: a systematic review and meta-analysis. Sleep Med Rev 2016; 30:85–96

55 Sam S, Tasali E. Role of obstructive sleep apnea in metabolic risk in PCOS. Curr Opin Endocr Metab Res 2021;17:46–51

56 Ghavami T, Kazeminia M, Ahmadi N, Rajati F. Global prevalence of obstructive sleep apnea in the elderly and related factors: a systematic review and meta-analysis study. J Perianesth Nurs 2023:S1089-9472(23)00060-6

57 Helvaci N, Karabulut E, Demir AU, Yildiz BO. Polycystic ovary syndrome and the risk of obstructive sleep apnea: a meta-analysis and review of the literature. Endocr Connect 2017;6 (07):437–445

58 Kahal H, Kyrou I, Uthman O, et al. The association between obstructive sleep apnea and metabolic abnormalities in women with polycystic ovary syndrome: a systematic review and meta-analysis. Sleep 2018;41(07):zsy085

59 Kahal H, Kyrou I, Uthman OA, et al. The prevalence of obstructive sleep apnoea in women with polycystic ovary syndrome: a systematic review and meta-analysis. Sleep Breath 2020;24 (01):339–350

60 Fernandez RC, Moore VM, Van Ryswyk EM, et al. Sleep disturbances in women with polycystic ovary syndrome: prevalence, pathophysiology, impact and management strategies. Nat Sci Sleep 2018;10:45–64

61 Vgontzas AN, Legro RS, Bixler EO, Grayev A, Kales A, Chrousos GP. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. J Clin Endocrinol Metab 2001;86(02):517–520

62 Fogel RB, Malhotra A, Pillar G, Pittman SD, Dunaif A, White DP. Increased prevalence of obstructive sleep apnea syndrome in obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 2001;86(03):1175–1180

63 Gopal M, Duntley S, Uhles M, Attarian H. The role of obesity in the increased prevalence of obstructive sleep apnea syndrome in patients with polycystic ovarian syndrome. Sleep Med 2002;3 (05):401–404

64 Hung J-H, Hu L-Y, Tsai S-J, et al. Risk of psychiatric disorders following polycystic ovary syndrome: a nationwide population-based cohort study. PLoS One 2014;9(05):e97041

65 Lin T-Y, Lin P-Y, Su T-P, et al. Risk of developing obstructive sleep apnea among women with polycystic ovarian syndrome: a nationwide longitudinal follow-up study. Sleep Med 2017; 36:165–169

66 Sirmans SM, Parish RC, Blake S, Wang X. Epidemiology and comorbidities of polycystic ovary syndrome in an indigent population. J Investig Med 2014;62(06):868–874

67 Kumarendran B, Sumilo D, O'Reilly MW, et al. Increased risk of obstructive sleep apnoea in women with polycystic ovary syndrome: a population-based cohort study. Eur J Endocrinol 2019; 180(04):265–272

68 Wang C, Huang T, Song W, et al. A meta-analysis of the relationship between polycystic ovary syndrome and sleep disturbances risk. Front Physiol 2022;13:957112

69 Zhang J, Ye J, Tao X, Lu W, Chen X, Liu C. Sleep disturbances, sleep quality, and cardiovascular risk factors in women with polycystic ovary syndrome: systematic review and meta-analysis. Front Endocr 2022:2187

70 Chatterjee B, Suri J, Suri JC, Mittal P, Adhikari T. Impact of sleep-disordered breathing on metabolic dysfunctions in patients with polycystic ovary syndrome. Sleep Med 2014;15(12):1547–1553

71 Tasali E, Van Cauter E, Ehrmann DA. Polycystic ovary syndrome and obstructive sleep apnea. Sleep Med Clin 2008;3(01):37–46

72 Tock L, Carneiro G, Togeiro SM, et al. Obstructive sleep apnea predisposes to nonalcoholic fatty liver disease in patients with polycystic ovary syndrome. Endocr Pract 2014;20(03):244–251

73 Vgontzas AN, Trakada G, Bixler EO, et al. Plasma interleukin 6 levels are elevated in polycystic ovary syndrome independently of obesity or sleep apnea. Metabolism 2006;55(08):1076–1082

74 Hachul H, Polesel DN, Tock L, et al. Sleep disorders in polycystic ovary syndrome: influence of obesity and hyperandrogenism. Rev Assoc Med Bras 2019;65(03):375–383

75 Kahal H, Tahrani AA, Kyrou I, et al. The relationship between obstructive sleep apnoea and quality of life in women with polycystic ovary syndrome: a cross-sectional study. Ther Adv Endocrinol Metab 2020;11:2042018820906689

76 Suri J, Suri JC, Chatterjee B, Mittal P, Adhikari T. Obesity may be the common pathway for sleep-disordered breathing in women with polycystic ovary syndrome. Sleep Med 2016;24:32–39

77 Caltekin M, Hamamci M, Onat T, Kirmizi D, Başer E, Yalvaç E Evaluation of sleep quality, restless legs syndrome, anxiety and depression in polycystic ovary syndrome. J Turk Sleep Med-Turk Uyku Tibbi Dergisi 2021;8(03):

78 Mokhlesi B, Scoccia B, Mazzone T, Sam S. Risk of obstructive sleep apnea in obese and nonobese women with polycystic ovary syndrome and healthy reproductively normal women. Fertil Steril 2012;97(03):786–791

79 Zhou X, Jaswa E, Pasch L, Shinkai K, Cedars MI, Huddleston HG. Association of obstructive sleep apnea risk with depression and anxiety symptoms in women with polycystic ovary syndrome. J Clin Sleep Med 2021;17(10):2041–2047

80 Copinschi G, Caufriez A. Sleep and the ovarian axis. Curr Opin Endocr Metab Res 2021;17:38–45

81 Sam S, Ehrmann DA. Pathogenesis and consequences of disordered sleep in PCOS. Clin Med Insights Reprod Health 2019; 13:1179558119871269

82 Tasali E, Van Cauter E, Hoffman L, Ehrmann DA. Impact of obstructive sleep apnea on insulin resistance and glucose tolerance in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2008;93(10):3878–3884

83 Bambhroliya Z, Sandrugu J, Lowe M, et al. Diabetes, polycystic ovarian syndrome, obstructive sleep apnea, and obesity: a systematic review and important emerging themes. Cureus 2022;14(06):e26325

84 Vgontzas AN, Bixler EO, Chrousos GP. Metabolic disturbances in obesity versus sleep apnoea: the importance of visceral obesity and insulin resistance. J Intern Med 2003;254(01):32–44

85 Mathieu P, Poirier P, Pibarot P, Lemieux I, Després J-P. Visceral obesity: the link among inflammation, hypertension, and cardiovascular disease. Hypertension 2009;53(04):577–584

86 Reutrakul S, Van Cauter E. Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes. Metabolism 2018; 84:56–66

87 Xing C, Zhang J, Zhao H, He B. Effect of sex hormone-binding globulin on polycystic ovary syndrome: mechanisms, manifestations, genetics, and treatment. Int J Womens Health 2022; 14:91–105

88 White DP, Schneider BK, Santen RJ, et al. Influence of testosterone on ventilation and chemosensitivity in male subjects. J Appl Physiol 1985;59(05):1452–1457

89 Cistulli PA, Grunstein RR, Sullivan CE. Effect of testosterone administration on upper airway collapsibility during sleep. Am J Respir Crit Care Med 1994;149(2, Pt 1):530–532

90 Popovic RM, White DP. Upper airway muscle activity in normal women: influence of hormonal status. J Appl Physiol 1998;84 (03):1055–1062

91 Kahal H, Kyrou I, Tahrani AA, Randeva HS. Obstructive sleep apnoea and polycystic ovary syndrome: a comprehensive review of clinical interactions and underlying pathophysiology. Clin Endocrinol (Oxf) 2017;87(04):313–319

92 Kang K-T, Chou C-H, Weng W-C, Lee P-L, Hsu W-C. Associations between adenotonsillar hypertrophy, age, and obesity in children with obstructive sleep apnea. PLoS One 2013;8(10):e78666

93 Lian Y, Yuan Q, Wang G, Tang F. Association between sleep quality and metabolic syndrome: a systematic review and meta-analysis. Psychiatry Res 2019;274:66–74

94 Parish JM, Adam T, Facchiano L. Relationship of metabolic syndrome and obstructive sleep apnea. J Clin Sleep Med 2007; 3(05):467–472

95 Wolk R, Somers VK. Sleep and the metabolic syndrome. Exp Physiol 2007;92(01):67–78

96 Xie J, Li Y, Zhang Y, et al. Sleep duration and metabolic syndrome: an updated systematic review and meta-analysis. Sleep Med Rev 2021;59:101451

97 Cappuccio FP, Miller MA. Sleep and cardio-metabolic disease. Curr Cardiol Rep 2017;19(11):110

98 Framnes SN, Arble DM. The bidirectional relationship between obstructive sleep apnea and metabolic disease. Front Endocrinol (Lausanne) 2018;9:440

99 Doycheva I, Ehrmann DA. Nonalcoholic fatty liver disease and obstructive sleep apnea in women with polycystic ovary syndrome. Fertil Steril 2022;117(05):897–911

100 Murri M, Luque-Ramírez M, Insenser M, Ojeda-Ojeda M, Escobar-Morreale HF. Circulating markers of oxidative stress and polycystic ovary syndrome (PCOS): a systematic review and meta-analysis. Hum Reprod Update 2013;19(03):268–288

101 Sverrisdóttir YB, Mogren T, Kataoka J, Janson PO, Stener-Victorin E. Is polycystic ovary syndrome associated with high sympathetic nerve activity and size at birth? Am J Physiol Endocrinol Metab 2008;294(03):E576–E581

102 Nandalike K, Strauss T, Agarwal C, et al. Screening for sleep-disordered breathing and excessive daytime sleepiness in adolescent girls with polycystic ovarian syndrome. J Pediatr 2011; 159(04):591–596

103 Tasali E, Chapotot F, Leproult R, Whitmore H, Ehrmann DA. Treatment of obstructive sleep apnea improves cardiometabolic function in young obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 2011;96(02):365–374

104 Pavone M, Salerno T, Cambiaso P, Verrillo E, Rossi FP, Cutrera R. Continuous positive pressure non-invasive ventilation for the management of obstructive sleep apnoea in a 15-year-old girl with polycystic ovary syndrome. J Paediatr Child Health 2012;48 (10):E194–E195

105 Trivedi M, ElMallah M, Bailey E, Kremer T, Rhein LM. Pediatric obstructive sleep apnea and asthma: clinical implications. Pediatr Ann 2017;46(09):e332–e335

106 Pattipati M, Gudavalli G, Zin M, et al. Continuous positive airway pressure vs mandibular advancement devices in the treatment of obstructive sleep apnea: an updated systematic review and meta-analysis. Cureus 2022;14(01):e21759

107 Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2(04):297–307

108 Fornal-Pawłowska M, Wołyńczyk-Gmaj D, Szelenberger W. [Validation of the Polish version of the Athens Insomnia Scale]. Psychiatr Pol 2011;45(02):211–221

109 Singareddy R, Bixler EO, Vgontzas AN. Fatigue or daytime sleepiness? J Clin Sleep Med 2010;6(04):405

110 Javaheri S, Redline S. Insomnia and risk of cardiovascular disease. Chest 2017;152(02):435–444

111 Xu W, Tan CC, Zou JJ, Cao XP, Tan L. Sleep problems and risk of all-cause cognitive decline or dementia: an updated systematic review and meta-analysis. J Neurol Neurosurg Psychiatry 2020; 91(03):236–244

112 Franik G, Krysta K, Madej P, et al. Sleep disturbances in women with polycystic ovary syndrome. Gynecol Endocrinol 2016;32 (12):1014–1017

113 Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest 2014;146(05): 1387–1394

114 Hood S, Amir S. Biological clocks and rhythms of anger and aggression. Front Behav Neurosci 2018;12:4

115 Walker WH II, Walton JC, DeVries AC, Nelson RJ. Circadian rhythm disruption and mental health. Transl Psychiatry 2020; 10(01):28

116 Kim MJ, Lee JH, Duffy JF. Circadian rhythm sleep disorders. J Clin Outcomes Manag 2013;20(11):513–528

117 Shreeve N, Cagampang F, Sadek K, et al. Poor sleep in PCOS; is melatonin the culprit? Hum Reprod 2013;28(05):1348–1353

118 Simon SL, McWhirter L, Diniz Behn C, et al. Morning circadian misalignment is associated with insulin resistance in girls with obesity and polycystic ovarian syndrome. J Clin Endocrinol Metab 2019;104(08):3525–3534

119 Li H, Liu M, Zhang C. Women with polycystic ovary syndrome (PCOS) have reduced melatonin concentrations in their follicles and have mild sleep disturbances. BMC Womens Health 2022;22 (01):79

120 Shochat T, Haimov I, Lavie P. Melatonin – the key to the gate of sleep. Ann Med 1998;30(01):109–114

121 Tamura H, Nakamura Y, Korkmaz A, et al. Melatonin and the ovary: physiological and pathophysiological implications. Fertil Steril 2009;92(01):328–343

122 Kuşçu NK, Var A. Oxidative stress but not endothelial dysfunction exists in non-obese, young group of patients with polycystic ovary syndrome. Acta Obstet Gynecol Scand 2009;88(05): 612–617

123 Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14(06):540–545

124 Allen RP, Picchietti DL, Garcia-Borreguero D, et al; International Restless Legs Syndrome Study Group. Restless legs syndrome/ Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria – history, rationale, description, and significance. Sleep Med 2014;15(08):860–873

125 Yang R, Gao C, Yan Y, et al. Analysis of the proportion and clinical characteristics of obstructive sleep apnea in women with polycystic ovary syndrome. Sleep Breath 2022;26(01):497–503

126 Gökmen Karasu AF, Şahbaz CD, Eren Doğu ZF, Takmaz T, Çalı H, Tanoğlu B. Chronotype and sleep quality assessment of patients with polycystic ovary syndrome. Med Bull Haseki 2021; 59:53–57

127 Lim AJ, Huang Z, Chua SE, Kramer MS, Yong E-L. Sleep duration, exercise, shift work and polycystic ovarian syndrome-related outcomes in a healthy population: a cross-sectional study. PLoS One 2016;11(11):e0167048

128 Yang Y, Deng H, Li T, et al. The mental health of Chinese women with polycystic ovary syndrome is related to sleep disorders, not disease status. J Affect Disord 2021;282:51–57

129 Lim AJR, Indran IR, Kramer MS, Yong EL. Phenotypic spectrum of polycystic ovary syndrome and their relationship to the circadian biomarkers, melatonin and cortisol. Endocrinol Diabetes Metab 2019;2(03):e00047

130 Macchi MM, Bruce JN. Human pineal physiology and functional significance of melatonin. Front Neuroendocrinol 2004;25(3-4):177–195

131 Yi S, Xu J, Shi H, Li W, Li Q, Sun YP. Association between melatonin receptor gene polymorphisms and polycystic ovarian syndrome: a systematic review and meta-analysis. Biosci Rep 2020;40(06): BSR20200824

132 Barrea L, Verde L, Vetrani C, et al. Evening chronotype is associated with hormonal and metabolic disorders in polycystic ovary syndrome. J Pineal Res 2023;74(02):e12844

133 Wittmann M, Dinich J, Merrow M, Roenneberg T. Social jetlag: misalignment of biological and social time. Chronobiol Int 2006; 23(1-2):497–509
134 van Egmond LT, Meth EMS, Engström J, et al. Effects of acute sleep loss on leptin, ghrelin, and adiponectin in adults with healthy weight and obesity: a laboratory study. Obesity (Silver Spring) 2023;31(03):635–641
135 Theorell-Haglöw J, Lemming EW, Michaëlsson K, Elmståhl S, Lind L, Lindberg E. Sleep duration is associated with healthy diet scores and meal patterns: results from the population-based EpiHealth study. J Clin Sleep Med 2020;16(01):9–18
136 Greer SM, Goldstein AN, Walker MP. The impact of sleep deprivation on food desire in the human brain. Nat Commun 2013;4 (01):2259
137 Chaput J-P, McHill AW, Cox RC, et al. The role of insufficient sleep and circadian misalignment in obesity. Nat Rev Endocrinol 2023; 19(02):82–97
138 Benham JL, Booth JE, Goldfield G, Friedenreich CM Rabi DM, Sigal RJ. Self-reported sleep quality and exercise in polycystic ovary syndrome: a secondary analysis of a pilot randomized controlled trial. Clin Endocrinol (Oxf) 2023;98 (05):700–708
139 Oberg E, Blomberg L, Åkerstedt T, Hirschberg AL. Different sleep pattern in over-weight/obese women with polycystic ovary syndrome. Front Endocrinol 2023:141068045
140 Missel AL, O'Brien AV, Maser H, et al. Impact of an online multicomponent very-low-carbohydrate program in women with polycystic ovary syndrome: a pilot study. F S Rep 2021;2 (04):386–395
141 Phimphasone-Brady P, Palmer B, Vela A, et al. Psychosocial interventions for women with polycystic ovary syndrome: a systematic review of randomized controlled trials. F S Rev 2022; 3(01):42–56
142 Gholizadeh-Moghaddam M, Ghasemi-Tehrani H, Askari G, Jaripur M, Clark CCT, Rouhani MH. Effect of magnesium supplementation in improving hyperandrogenism, hirsutism, and sleep quality in women with polycystic ovary syndrome: a randomized, placebo-controlled clinical trial. Health Sci Rep 2022;6(01):e1013
143 Shabani A, Foroozanfard F, Kavossian E, et al. Effects of melatonin administration on mental health parameters, metabolic and genetic profiles in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. J Affect Disord 2019;250:51–56
144 El-Sharkawy AA, Abdelmotaleb GS, Aly MK, Kabel AM. Effect of metformin on sleep disorders in adolescent girls with polycystic ovarian syndrome. J Pediatr Adolesc Gynecol 2014;27(06): 347–352
145 Chen G-C, Liu M-M, Chen L-H, et al. Daytime napping and risk of type 2 diabetes: a meta-analysis of prospective studies. Sleep Breath 2018;22(03):815–824
146 Zhong G, Wang Y, Tao T, Ying J, Zhao Y. Daytime napping and mortality from all causes, cardiovascular disease, and cancer: a meta-analysis of prospective cohort studies. Sleep Med 2015;16 (07):811–819
147 Murawski B, Wade L, Plotnikoff RC, Lubans DR, Duncan MJ. A systematic review and meta-analysis of cognitive and behavioral interventions to improve sleep health in adults without sleep disorders. Sleep Med Rev 2018;40:160–169
148 Kakinuma M, Takahashi M, Kato N, et al. Effect of brief sleep hygiene education for workers of an information technology company. Ind Health 2010;48(06):758–765
149 Sharma MP, Andrade C. Behavioral interventions for insomnia: theory and practice. Indian J Psychiatry 2012;54(04):359–366
150 Ham OK, Lee BG, Choi E, Choi SJ. Efficacy of cognitive behavioral treatment for insomnia: a randomized controlled trial. West J Nurs Res 2020;42(12):1104–1112
151 Albakri U, Drotos E, Meertens R. Sleep health promotion interventions and their effectiveness: an umbrella review. Int J Environ Res Public Health 2021;18(11):5533
152 McGinnis JM, Williams-Russo P, Knickman JR. The case for more active policy attention to health promotion. Health Aff (Millwood) 2002;21(02):78–93
153 Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 2017;32(05):1075–1091
154 Cohen R, Shikora S. Fighting weight bias and obesity stigma: a call for action. Obes Surg 2020;30(05):1623–1624
155 Wang FF, Wu Y, Zhu YH, et al. Pharmacologic therapy to induce weight loss in women who have obesity/overweight with polycystic ovary syndrome: a systematic review and network meta-analysis. Obes Rev 2018;19(10):1424–1445
156 Himmelstein MS, Incollingo Belsky AC, Tomiyama AJ. The weight of stigma: cortisol reactivity to manipulated weight stigma. Obesity (Silver Spring) 2015;23(02):368–374
157 Tomiyama AJ, Carr D, Granberg EM, et al. How and why weight stigma drives the obesity 'epidemic' and harms health. BMC Med 2018;16(01):123
158 Bazarganipour F, Ziaei S, Montazeri A, Foroozanfard F, Kazemnejad A, Faghihzadeh S. Body image satisfaction and self-esteem status among the patients with polycystic ovary syndrome. Iran J Reprod Med 2013;11(10):829–836
159 Alvaro PK, Roberts RM, Harris JK. A systematic review assessing bidirectionality between sleep disturbances, anxiety, and depression. Sleep 2013;36(07):1059–1068
160 Clark R, Locke M, Bialocerkowski A. Paediatric terminology in the Australian health and health-education context: a systematic review. Dev Med Child Neurol 2015;57(11):1011–1018
161 Australian Institute of Health and Welfare. Overweight and obesity among Australian children and adolescents. Cat. no. PHE 274. Canberra: AIHW; 2020
162 Morong S, Hermsen B, de Vries N. Sleep-disordered breathing in pregnancy: a review of the physiology and potential role for positional therapy. Sleep Breath 2014;18(01):31–37
163 Sharma S, Mahajan N. Polycystic ovarian syndrome and menopause in forty plus women. J Midlife Health 2021;12(01):3–7
164 Zhang Q, Wang Z, Ding J, et al. Effect of obstructive sleep apnea on *in vitro* fertilization outcomes in women with polycystic ovary syndrome. J Clin Sleep Med 2023