

Luis San^{1,2,*}
Belén Arranz^{1,2}

The Night and Day Challenge of Sleep Disorders and Insomnia: A Narrative Review

¹Parc Sanitari Sant Joan de Déu, Camí Vell de la Colonia 25, E-08830 Sant Boi de Llobregat, Barcelona, Spain

²CIBERSAM, Centro de Investigación Biomédica en Salud Mental, Instituto de Salud Carlos III, Madrid, Spain

Abstract

This is a narrative review of sleep disorders, especially chronic insomnia, as a primary diagnosis or as a comorbid diagnosis associated with different psychiatric and organic diseases. The epidemiological evidence is reviewed, the diagnostic criteria most frequently used in clinical practice are examined, and a series of therapeutic recommendations for the correct treatment of this pathology is presented. Sleep disorders are very prevalent in the general population (one-third experiences difficulty with sleep initiation/maintenance at least once a week, and about 6–15% meet the criteria for insomnia disorders), but remain relatively poorly understood and frequently overlooked by healthcare professionals. Prevalence estimates of insomnia disorder vary between 5% and 20%. Sleep disorders co-exist with psychiatric and medical conditions with an interactive and bidirectional relationship. About 70–80% of psychiatric patients show some sleep disturbance and there is a correlation between the severity of the sleep disturbance and the severity of the psychopathology. Untreated sleep disorders increase the risk of cardiovascular events, cognitive impairment, motor vehicle accidents, obesity, diabetes, and efficiency and safety at work, leading to increased all-cause healthcare utilization and being a strong predictor of sick leave or disability pension and poor quality of life. Sleep disorders can cause drowsiness or excessive daytime sleepiness, which can lead to functional impairment in 15% of the general adult population. Sleep quality should be a routine target in the evaluation of patients with psychiatric and non-psychiatric diseases to ensure sleep health based on early diagnosis and adequate therapeutic approaches.

*Corresponding author details: Luis San, Parc Sanitari Sant Joan de Déu, Camí Vell de la Colonia 25, E-08830 Sant Boi de Llobregat, Barcelona, Spain; CIBERSAM, Centro de Investigación Biomédica en Salud Mental, Instituto de Salud Carlos III, Madrid, Spain. Email: 12636LSM@COMB.CAT

Keywords

sleep disorders; insomnia; mental illness; cardiovascular disease; obesity; daytime sleepiness; sleep health; cognitive decline; quality of life

Introduction

Sleep disturbance is a term that encompasses different conditions (e.g. insomnia, hypersomnia, parasomnia, sleep disorders, restless leg syndrome, sleep apnea, *etc.*) and is frequently used as a synonym for sleep deprivation, poor sleep quality, or sleep problems. Sleep disorder is an under-recognized public health challenge that affects millions of people and is strongly associated with morbidity and mortality [1]. Poor sleep health is currently considered a key indicator and risk factor for mental illness and other pathological conditions. Sleep problems have shown a shift as an epiphenomenon of diseases to play a causal role in the complex interrelationships with psychiatric disorders, cardiovascular events, obesity, or neurodegenerative diseases [1]. Although the precise function of sleeping has not been fully elucidated, there is robust evidence that sleep is vital for human health, having a crucial influence on central nervous system restoration, neuroplasticity, learning and memory consolidation, maintaining immune function, and affect/emotion regulation [2–4].

It is well known that the physiological and behavioral normal rhythms are characteristically aligned to the regular daily light/dark cycle. Sleep is one of the most outstanding examples of these rhythms, alternating sleep cycle stages of non-rapid eye movement (NREM) and rapid eye movement (REM) during the night. These cycles are also associated with remarkable changes in cardiovascular and metabolic regulation and neurological activity. With the raising importance of sleep, it is also obvious that sleep health involves duration as well as other dimensions, such as regularity, timing, efficiency, quality, and alertness. In addition to sleep duration, late sleep timing seems to increase the

risk of cardiovascular and metabolic disturbances, probably due to circadian misalignment associated with late-night light exposure. Indeed, some studies show that nearly any light at night heightens the relative risk for a cardiovascular or metabolic disorder [5]. Sleep fragmentation is associated with a higher incidence of cognitive decline and an increased risk of developing Alzheimer's disease [6].

On the other hand, in modern society, some people are trying to reduce the duration of sleep to enjoy more effective lives, avoiding sleep as a useless time. In many countries, a drop in sleep duration but also on sleep quality has been observed [7]. Moreover, it seems that insomnia is a long-term disorder. The course of insomnia is more probable to be persistent in subjects with more severe insomnia at baseline and in women and older adults [8]. Sleep disorders continue to affect a considerable number of individuals in the general population, their impact is even more pronounced in clinical practice and remains relatively poorly understood and overlooked by healthcare professionals.

This narrative review explores the existing state of knowledge of sleep disorders especially insomnia in adults, to provide contextualized information leading to a more comprehensive understanding of insomnia's effects over 24 hours (night and day) in patients with psychiatric and nonpsychiatric diseases.

Epidemiology of Sleep Disorders

Different studies show that the prevalence of sleep disorders is consistently high. An investigation of a representative sample of the general population has reported a prevalence of sleeping problems of 56% in the USA, 31% in Western Europe, and 23% in Japan [9]. Worldwide, between 30% and 35% of adults have some symptoms of insomnia, which may increase up to 75% in older people [10]. Roughly, one-third of adults in developed countries exhibit difficulty with sleep initiation or maintenance at least once a week, and about 6–15% meet the criteria for insomnia disorders [11].

One-year incidence rates are 30.7% for insomnia symptoms and 7.4% for insomnia syndrome [12]. In a recent epidemiological study of insomnia carried out in Spain and using the diagnostic criteria of the International Classification of Sleep Disorders, 3rd edition (ICSD-3), the authors reported a prevalence of insomnia symptoms of 43.4%, chronic insomnia disorder of 14%, and chronic insomnia syndrome of 13.7% [13]. These data imply that the prevalence of chronic insomnia disorder in Spain has more than doubled in 20 years, with an increase of almost 47% [13].

Physicians should be aware that sleep disorders continue to be an unmet public health problem [14], with major concerns due to its high prevalence, associated comorbidities, reduced quality of life, and adverse short- and long-term night and day consequences that require appropriate diagnosis and treatment, close monitoring, and effective preventive strategies.

Sleep Disorders in DSM-5 and ICSD

Sleep disorder is a clinical diagnosis established by healthcare professionals based on patient symptoms, clinical observations, diagnostic criteria, and the use of rating scales and sleep diary reports, among other tools [8,15]. Diagnostic criteria of the American Psychiatric Association (APA) [16], the American Academy of Sleep Medicine (AASM) [17], the International Classification of Sleep Disorders (ICSD) [18], and the International Classification of Diseases (ICD-11) of the World Health Organization (WHO) [19] agree that insomnia is a subjective complaint of insufficient sleep quantity or quality, associated with difficulty initiating sleep, difficulty maintaining sleep, or early awakening, and clinically significant impairment of day functioning.

The discipline of sleep disorders medicine has progressed, and a good example is that the DSM-5 sleep-wake disorders are now more synchronized with other medical conditions. In the DSM-5, the etiological factors associated with sleep-wake disorders are considered, as is the increase in understanding and expertise acquired from sleep studies. The aim is to increase uniformity and consistency among healthcare professionals when evaluating and treating patients with various sleep disorders. Sleep-wake disorders include 11 diagnostic groups as shown in Table 1 [20]. The DSM-5 worked closely with other nosology systems, such as the ICSD-3 [18] (Table 2) and the ICD [19] to incorporate changes in diagnoses.

Increasing evidence shows that sleep disorders co-occur with other physical and psychiatric conditions [21] and may not be equally exacerbating. The DSM-5 criteria underscore the need for independent clinical attention to a sleep disorder regardless the presence of psychiatric or other medical problems. Also, the DSM-5 acknowledges that coexisting mental disorders, medical conditions, and sleep disorders are interactive and bidirectional.

Table 1. Sleep-wake disorders in DSM-5 (APA).

-	Insomnia disorder.
-	Hypersomnolence disorder.
-	Narcolepsy.
-	Obstructive sleep apnea hypopnea.
-	Central sleep apnea.
-	Sleep-related hypoventilation.
-	Circadian rhythm sleep-wake disorders.
-	Non-rapid eye movement (NREM) sleep arousal disorders.
-	Nightmare disorder.
-	Rapid eye movement (REM) sleep behavior disorder.
-	Restless legs syndrome and substance/medication-induced sleep disorder.

APA, American Psychiatric Association.

Insomnia Disorder

The DSM-5 defines insomnia disorder as a patient-reported complaint of sleep disturbance as difficulty falling asleep or staying asleep, frequent awakenings, and not being able to return to sleep, or early awakenings with daytime dysfunctions. For chronic insomnia, symptoms must be present for at least 3 months, occur at least 3 nights per week, and cause clinically significant distress or impairment. The most significant change in sleep-wake diagnostic criteria refers to the insomnia classification. That stresses the comorbid nature of insomnia and calls for treatment of both insomnia and the medical disorder. This change in insomnia diagnostic criteria in ICSD-3 and DSM-5 implies a paradigm shift (Table 3).

The evaluation of insomnia should include the nature, frequency, evolution, and duration of symptoms, as well as the response to treatment. The diagnosis of insomnia is established whether it occurs as an independent condition or is comorbid with another mental illness, medical condition, or another sleep disorder. Insomnia is a condition disorder that needs independent clinical attention. DSM-5 and ICSD-3 insomnia diagnostic criteria are similar due to collaborative efforts between the APA and the AASM classification task forces. Changes in insomnia diagnostic criteria give it more specificity and ensure greater consistency. Specifically in the DSM-5, the complaint of impaired daytime functioning or well-being is necessary to establish the diagnosis of insomnia disorder.

Many subjects may present insomnia symptoms (50% in the general population) without fulfilment of diagnostic criteria of insomnia disorder (prevalence estimates of insomnia disorder between 5% and 20%) [22]. Insomnia disorder and symptoms are associated with several medical diseases and injuries at work and non-workplaces. Also,

patients with insomnia accounted for greater healthcare utilization and cost than those without insomnia [23], but more importantly, insomnia may predict premature death. In a community-based cohort in Western Norway of 6236 participants aged 40–45 followed over 13–15 years, insomnia was related to a three-fold risk of mortality, being the risk higher in men or when insomnia was combined with short sleep duration [24].

Sleep Disorders and Psychiatric Conditions

Numerous studies confirm the high frequency of sleep disorders in psychiatric patients, about 70–80% of outpatients or hospitalized psychiatric patients show some sleep disturbance and there is a relationship between the severity of the sleep disturbance and that of the psychopathology [25]. In a cross-sectional study of outpatients aged 21–65 years with a primary diagnosis of either schizophrenia, mood or anxiety disorder, the overall prevalence of symptoms of sleep disorders was 40.8%, with symptoms of two sleep disorders co-existing in 23.6% of the patients and symptoms of three sleep disorders in 10.4% [26].

This high frequency of sleep disturbances in patients with mental illness compared to 25% of the general population, is because psychopathological pictures and sleep disturbances they reinforce each other, establishing a bidirectional relationship in which it is difficult to determine what is the cause and what is the consequence [27,28]. In this respect, sleep disturbances should not be viewed as one of the symptoms in the myriad manifestations of psychiatric conditions, rather than a complex and bidirectional interrelationship between psychiatric and sleep disorders [16,25]. Sleep disturbances are characteristically regarded as a core symptom of several psychiatric disorders and are included in their corresponding diagnostic criteria. Moreover, insomnia can herald a psychiatric disorder and may increase its risk of relapse [29].

Despite the frequent co-occurrence of sleep and psychiatric conditions, many sleep experts do not take psychiatric disorders into account when evaluating patients with sleep complaints and, conversely, many psychiatrists seem to ignore the role of sleep health among their psychiatric patients.

When addressing sleep disorders, there are three basic symptoms or groups of symptoms to consider: insomnia (difficulty initiating or maintaining sleep), hypersomnolence, including excessive and daytime sleepiness, and episodic sleep disturbances. The evaluation of sleep disorders can be carried out initially through the patient's

Table 2. International Classification of Sleep Disorders (ICSD).

Major diagnostic sections	Cluster/disorder
Insomnia	- Chronic insomnia disorder.
	- Short-term insomnia disorder.
	- Other insomnia disorders.
Sleep-related breathing disorders	- Obstructive sleep apnea disorders.
	- Central sleep apnea syndromes.
	- Sleep-related hypoventilation disorders.
	- Sleep-related hypoxemia disorder.
Central disorders of hypersomnolence	- Narcolepsy type 1.
	- Narcolepsy type 2.
	- Idiopathic hypersomnia.
	- Kleine-Levin syndrome.
	- Hypersomnia due to a medical disorder.
	- Hypersomnia due to a medication or substance.
	- Hypersomnia associated with a psychiatric disorder.
Circadian rhythm sleep-wake disorders	- Insufficient sleep syndrome.
	- Delayed sleep-wake phase disorder.
	- Advanced sleep-wake phase disorder.
	- Irregular sleep-wake rhythm disorder.
	- Non 24-hour sleep-wake rhythm disorder.
	- Shift work disorder.
	- Jet lag disorder.
Parasomnias	- Circadian sleep-wake disorder not otherwise specified.
	- NREM-related parasomnias.
	- REM-related parasomnias.
Sleep-related movement disorder	- Other parasomnias.
	- Restless legs syndrome.
	- Periodic limb movement disorder.
	- Sleep-related leg cramps.
	- Sleep-related bruxism.
	- Sleep-related rhythmic movement disorder.
	- Benign sleep myoclonus of infancy.
	- Propriospinal myoclonus at sleep onset.
	- Sleep-related movement disorder due to a medical disorder
	- Sleep-related movement disorder due to a medication or substance.
- Sleep-related movement disorder, unspecified.	
Other sleep disorders	

NREM, non-rapid eye movement; REM, rapid eye movement.

interview and medical history followed by complementary work-up tests, including general psychological assessment to rule out the type of mental disorder (depression, anxiety, *etc.*), sleep studies (e.g., polysomnography), and any laboratory testing and radio imaging studies to exclude other non-psychiatric disorders that may be an etiological factor of insomnia. It is important to remember that sleep disturbances may be the first symptom of a mental illness. In a systematic review and meta-analysis of 36 studies, there was a significant link between any sleep disruption and an

increased risk of developing a mood or psychotic disorder during the peak age range for the onset of these conditions [30].

In a review of various psychiatric disorders and their associated sleep complaints [31], the authors reported sleep-onset insomnia, frequent awakenings, nocturnal restlessness, and early morning awakenings 2 to 4 hours earlier than desired, with difficulty returning to sleep in mood disorders. Common sleep disturbances associated with anxiety disorders are sleep-onset or sleep-maintenance insomnia.

Table 3. Diagnostic criteria of chronic insomnia disorder across DSM-5 and ICSD.

DSM-5 (2013)	ICSD-3 (2014)
<ul style="list-style-type: none"> ● A frequent sleep complaint with one or more of the following insomnia symptoms: <ol style="list-style-type: none"> 1. Increased sleep latency. 2. Unsatisfactory maintenance of sleep is evident by the frequent awakenings and eventual difficulty in returning to sleep. 3. Early morning awakenings accompanied by trouble in returning to sleep. ● The sleep complaints related to clinically significant daytime impairments in social, occupational, academic, behavioural, or other vital function areas. 	<ul style="list-style-type: none"> ● A predominantly sleep complaint accompanied by one or more of the following symptoms by the patient or parent/caregiver of the patient: <ol style="list-style-type: none"> 1. Difficulty initiating sleep. 2. Difficulty maintaining sleep. 3. Waking up earlier than desired. 4. Reluctance in going to bed to sleep on time. 5. Trouble in sleeping without parent/caregiver involvement. ● Sleep complaints coupled with one or more of the following consequences as a result of night-time sleep difficulty: <ol style="list-style-type: none"> 1. Tiredness/uneasiness/fatigue. 2. Memory impairment/attention or concentration deficiency. 3. Social, family, occupational, or academic impairment. 4. Irritability/mood disturbance. 5. Daytime somnolence or sleepiness. 6. Behavioural problems like hyperactivity, impulsivity, hostility, or aggression. 7. Lack of energy for new beginning/reduced motivation/initiative. 8. Error/accident-proneness. 9. Sleep difficulty-related nighttime ruminations.
<ul style="list-style-type: none"> ● The occurrence of symptoms with a weekly frequency of at least three nights. ● The persistence of sleep complaints with the same weekly frequency of at least three months. ● The events of sleep complain even in enough opportunity to sleep. 	<ul style="list-style-type: none"> ● The sleep-wake complaints despite adequate opportunity and environment for sleep. ● The weekly sleep disturbance and considerable impairments at least three times. ● The persistence of mentioned complaints with said weekly frequency for at least three months.
<ul style="list-style-type: none"> ● Insomnia is not better explained and does not exclusively occur during other sleep-wake disorders like narcolepsy, sleep-related breathing disorders, circadian rhythm sleep disorders, parasomnia, <i>etc.</i> ● The occurrence of insomnia is not due to the biological effects of substance abuse or the use of medications. ● The coexistence of medical and mental condition/s do not sufficiently explain the predominance of insomnia. 	<ul style="list-style-type: none"> ● The sleep-wake difficulty of insomnia cannot be explained better by the occurrence of other sleep disorders.

Typical findings in psychotic disorders comprise substantial sleep disturbance and serious difficulty initiating sleep, partial or complete inversion of the day-night cycle or reversion to a polyphasic sleep pattern, with reduced sleep efficiency occurring before psychotic decompensation. Sleep is also impaired in subjects with substance abuse as well as in subjects with eating disorders (e.g., nocturnal eating-drinking syndrome). Finally, left untreated sleep disturbances may exacerbate psychiatric disorders and complicate recovery [32].

In relation to suicide, most suicides worldwide are related to psychiatric diseases, with depression, psychosis, and substance use among the most relevant disorders [33]. Sleep disturbances have been identified as a risk factor for suicidal ideation and behaviour and should be an element of suicidal risk assessment in patients with psychiatric disorders.

In a systematic review and meta-analysis of 41 articles with samples drawn from 11 countries, the results across several manifestations of sleep disturbance (overall disturbance, insomnia, nightmares, *etc.*) were consistent in yielding a positive association with all subsequent suicidal thoughts and behaviours (suicidal ideation, suicidal attempts, and suicidal deaths) [34].

Recently, some authors [35] published a systematic review and meta-analysis of objective sleep markers associated with suicidal ideation and behaviour. They screened 43 potential full texts, of which 11 studies were suitable for meta-analysis. Their publication included 939 patients with psychiatric disorders (major depressive disorder, bipolar disorder, and schizophrenia/schizoaffective) and 144 healthy controls. Most of the studies ($n = 10$) examined current suicidal ideation using the Beck scale for suicide

ideation. Seven studies used actigraphy, 6 studies used polysomnography (PSG), and 2 studies used sleep electroencephalography (EEG). Most of eligible studies had a low risk of bias. The study concluded that there is a decreased total sleep time in patients with versus without current suicidal ideation. These findings are consistent with associations between subjective sleep alterations and risk of suicide. Assessment of sleep disturbance and sleep duration is particularly recommended for patients with a diagnosis of psychiatric disorder which are high-risk clinical diagnoses for suicide.

Sleep Disorders and Non-Psychiatric Conditions

Sleep disorders can be present as comorbidities of different non-psychiatric diseases, but also can play a role in the cause of these conditions [14]. Untreated sleep disorders seem to increase the risk of cardiovascular conditions, cognitive impairment, motor vehicle accidents, obesity, type 2 diabetes, and efficiency and safety at work, leading to increased all-cause healthcare utilization and being a strong predictor of sick leave or disability pension and poor quality of life [36,37].

Cardiovascular Diseases

Sleep problems are common among subjects with cardiovascular disease (CVD) contributing to the morbimortality of total CVD, coronary heart disease (CHD), and stroke [1]. A systematic review and meta-analysis of 15 studies, including 474,684 male and female participants (follow-up 6.9–25 years) and 16,067 events showed that short duration of sleep (≤ 5 or 6 hours per night in most studies) was associated with a greater risk of developing or dying from CHD, stroke and total CVD [38]. It is concluded that people reporting consistently sleeping ≤ 5 hours per night should be regarded as a higher risk group for cardiovascular morbidity and mortality. However, it is important to consider multiple sleep health indicators, not only sleep duration, as risk factors for CVD outcomes.

Inadequate Sleep Health and Obesity

Sleep is a crucial modulator of neuroendocrine function and glucose metabolism, and sleep loss results in metabolic and endocrine alterations, including an alteration in glucose tolerance and appetite-regulating hormones [39]. The obesity epidemic has been paralleled in modern society by a trend of reduced sleep duration. Other dimensions

of sleep health have been associated with increased obesity. This association of sleep disorders and overweight is known as a cardio-metabolic disorder. Inadequate sleep is associated with hormonal changes, increased appetite and caloric intake, obesity, or high body mass index (BMI). Orexins (hypocretins) regulate feeding behavior and are key modulators of the sleep/wakefulness cycle [40]. Sleep quantity and quality play an important role in weight control given that sleep and obesity share a mutual relationship. Obesity may contribute to poor sleep especially obstructive sleep apnea syndrome (OSA), which may further impair sleep quality. Strong and consistent evidence exists for the bidirectional link between sleep health and obesity [41]. As we know, obesity, lifestyle, diet or physical exercise are closely related and may contribute to poor sleep health and sleep disorders.

Circadian misalignment is a phenomenon that can involve unsuitable timing of sleeping, eating, and other behaviors, and is a risk factor for lifelong obesity and metabolic syndrome [42]. The circadian system regulates glucose metabolism, and the presence of metabolic syndrome increases the risk of CVD, diabetes and insulin resistance, psychiatric disorders, and other severe chronic diseases.

Insomnia and Cognitive Impairment

Cognitive performance has been extensively investigated about sleep disturbances. A systematic review and meta-analysis of 48 studies with 4539 participants showed that insomnia was associated with impairments of cognitive domains, including subjective cognitive performance and objective measures of perceptual function, manipulation and retention/capacity in working memory, complex attention, alertness, episodic memory, and problem-solving in executive functions [43]. Moreover, longitudinal data indicate poor sleep is a risk factor for cognitive decline in later life [44]. In middle-aged and older adults of the Canadian Longitudinal Study on Aging (26,363 participants followed for 3 years), self-reported memory worsening was significantly more frequent for participants who developed probable insomnia disorder at follow-up than those who developed insomnia symptoms only or who remained without symptoms [45].

Different types of sleep disturbances, such as insomnia, fragmentation, day-time dysfunction, prolonged latency, rapid eye movement sleep behavior disorder and excessive time in bed have been associated with a higher risk of all-cause cognitive disorders [46,47]. In a recent study of an ongoing cohort of London-based civil servants, in-

creasing sleep difficulties over 5 years during the retirement transition were associated with a more pronounced decline in inductive reasoning [48]. The findings of all these studies support the need to treat insomnia as a potential factor for improving cognitive outcomes.

Sleep Disturbances and Daytime Sleepiness

Sleep disorders and insomnia syndrome can also cause drowsiness or excessive daytime sleepiness (EDS), which is associated with both physical and psychiatric comorbidities and functioning impairment [49]. The ICSD defines EDS as the inability to stay awake and alert during waking episodes, resulting in periods of irrepressible need for sleep or unintended lapses into drowsiness or sleep [50]. In the DSM-5 diagnostic classification, hypersomnia refers to a symptom criterion, whereas hypersomnolence disorder is a separate disorder with specific criteria [16]. This disorder is characterized by excessive night-time sleep, lapses into sleep during the day, and/or significant sleep inertia and is not related to narcolepsy, circadian rhythm sleep-wake disorders, or substance use. EDS with symptoms of functional impairment is present in 15% of the general adult population [51].

In a large sample of 7072 Chinese adolescents, with both baseline and 1-year follow-up data, insomnia and EDS were significantly associated with poor academic performance, particularly in mathematics [52]. In another study conducted to assess the effects of EDS and insomnia disorder on laboratory-based measures of cognitive performance, daytime performance deficits on simple tasks seemed most dependent on daytime sleepiness, while performance deficits on complex tasks appeared related to insomnia disorder [53].

Many drugs have the potential to disrupt sleep-wake regulation, and insomnia or EDS are common side effects of psychotropic and non-psychotropic drugs through different mechanisms of action. The drug classes involved are antidepressants (tricyclics, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, norepinephrine reuptake inhibitors, norepinephrine-dopamine reuptake inhibitors, monoamine oxidase, and 5-HT₂ antagonist); antipsychotics (first- and second-generation); antiepileptics; antiparkinsonians; analgesics; H₁ antihistamines; cardiovascular drugs; corticosteroids; and theophylline [54].

The most used and prescribed agent for insomnia are benzodiazepines (BZD), due to the wide range of clinical effects, such as sedation, anxiety reduction, seizure inhibi-

tion, and muscle relaxation, they have been used in multiple indications including insomnia, anxiety, and epilepsy. However, BZD is also associated with a broad range of dose-dependent side effects due to increased gamma-aminobutyric acid (GABA) signaling throughout the brain. In addition, sudden discontinuation of benzodiazepines can have undesirable effects, with rebound insomnia being a notable adverse event. That may be due to the downregulation of GABA receptors on neurons as a reaction to sustained use of these agents.

For years, BZD tolerance and dependence have also been thought to be associated with benzodiazepines. Physical dependence may manifest in the form of withdrawal effects that may include symptoms of anxiety, convulsions, and sensory hyperreactivity. Withdrawal effects may occur upon discontinuation or rapid dose reduction of BZD. Unlike rebound insomnia, which is the brief exacerbation of the original symptoms of sleep disturbance, withdrawal effects refer to the manifestation of new symptoms that were not present before starting treatment. Potential harm use may also occur in a small subgroup of the population, particularly in those people with a history of alcohol and drug abuse [11].

Insomnia and Work Performance, Accidents, Functioning and Quality of Life

Insomnia significantly impacts individual subjects' productivity. Lack of sleep can impair cognitive function, with difficulty concentrating and remembering information, and make decisions. That can lead to decreased work performance and academic achievement. Considering that many studies link insomnia with a range of adverse effects on functioning, it is unsurprising that insomnia has been associated with significant workplace deficits, including worse performance, reduced productivity, and injuries with substantial workplace costs [55]. On the other hand, subjects with sleep disturbances are at high risk for traffic crashes, accidents at work, and injuries at home [56].

Reduced efficiency at work (absenteeism, accidents, or low productivity) is an expensive burden on workers, healthcare and social programs, and companies/business. The association between efficiency at work and sleep quantity or quality is reciprocal. Insomnia and daytime sleepiness are associated with an increased risk of injuries, and with a two- to seven-fold increase in the risk of traffic accidents among professional and non-professional drivers [37].

Insomnia is the most common sleep-wake disorder with negative impacts on several personal spheres, including well-being, overall quality of life, and daily functioning at work or school. Chronic insomnia is related to impaired quality of life after adjusting for co-morbidities, and this effect is age-related [37]. In a study of differences in the experience and factors perpetuating insomnia severity, difficulty in maintaining sleep, and poorer daytime functioning were perceived by older adults, whereas pre sleep arousal contributed to insomnia in younger adults [57].

Another measure of burden is the annual number of quality-adjusted life-years (QALYS) that are lost due to insomnia. Data from 34,712 adults in the National Epidemiologic Survey on Alcohol and Related Conditions-III showed that 27.3% of adults reported insomnia in the last 12 months, and the US annual loss of QALYs associated with insomnia was significantly larger than that associated with any of the other 18 medical conditions assessed [58].

Management of Sleep Disorders

A therapeutic approach should be considered when a patient has difficulty falling or staying asleep, poor sleep quality, insufficient sleep duration, early waking, or regular next-day impairment. The goal of insomnia management is to improve qualitative and quantitative aspects of sleep and distress associated with poor sleep, including daytime function. The treatment of sleep disorders includes two broad categories: cognitive behavioural therapy and pharmacological treatment. Many patients prefer non-pharmacological approaches, but also many patients taking hypnotics refer to a moderate degree of satisfaction [59,60].

Cognitive behavioral therapy for insomnia (CBT-I) is the first-line treatment recommended by clinical practice guidelines as an effective option to improve sleep quality [61,62].

- CBT-I combines cognitive therapy and behavioral approaches that aim to alter sleep-disruptive beliefs and thoughts and educate patients on lifestyle changes conducive to better sleep.

- CBT-I is the first-line treatment for patients with insomnia disorder.

- It is safe and effective, exhibits long-term results, can be used in adults of all ages with or without comorbid conditions, and can be combined with pharmacotherapy.

Table 4. Good sleep hygiene.

Element
<ul style="list-style-type: none"> • Maintain a regular sleep/wake schedule 7 nights a week. • Removing electronic devices close to bedtime. • Avoiding daytime napping. • Avoiding alcohol, nicotine, and caffeine before sleeping. • Avoiding eating dinner late. • Maintain a regular daytime exercise but avoid during the 2–6 hours before bedtime. • Avoid naps. • Avoid bedtime clock watching. • Correct management of stress. • Avoid lying to bed without feeling sleepy. • Bedroom should be a quiet, comfortable space (noise, light) reserved for sleeping.

Some examples of CBT-I include the following:

- **Sleep hygiene education** can relieve excessive worries that can contribute to insomnia. While sleep hygiene is usually the first treatment offered, it is seldom sufficient for more severe insomnia and is recommended for use in with other, more robust behavioral approaches. Recommendations include promoting behaviours that help sleep, and discouraging those interfering with sleep (Table 4) [63,64].

- **Sleep restriction therapy** aims to strengthen homeostatic sleep drive through mild sleep deprivation and to alleviate the anxiety that stems from sleep anticipation. It can be effective since the tendency of patients with insomnia to spend excess time in bed to catch up on sleep leads to conditioned arousal and fragmented sleep. There is strong evidence that circadian and homeostatic processes regulate sleep.

- **Stimulus control** is based on operant and classical conditioning principles. It is designed to eliminate the negative association between bed and undesirable outcomes that may be conditioned in patients with insomnia. It includes instructions that address conditioned arousal, where the goal is strengthening the bed and bedroom's association with sleep.

- **Relaxation training** comprises various techniques to lower somatic and cognitive arousal that may prevent sleep. This therapy reduces both day and night physiological and cognitive arousal in insomnia. Muscular tension and cognitive arousal are incompatible with sleep.

Pharmacotherapy should only be considered in patients unable to participate in CBT-I, in those who still have

symptoms despite CBT-I, or as a temporary adjunct to CBT-I, and should be used in combination with CBT-I whenever possible [61,62]. Medication approaches are considered second-line treatment for insomnia disorder, and often are used without an endpoint, for that reason when prescribed, they should be used on a time-limited basis. Current consensus indicates that adults should sleep at least 7 hours per night, nevertheless, about 35% do not follow this recommendation. Appropriate medical attention to insomnia disorder is warranted because of the adverse effects of the condition on patients' long-term health, functioning, and productivity [8,65].

In line with the recommendations to improve the quantity and quality of sleep and daytime functioning, preservation of sleep architecture (i.e. the percentage of time spent in each sleep stage during the night) is key to defining the quality of sleep [66] and some drugs commonly used for insomnia fail to maintain them appropriately. Moreover, the efficacy and safety are partly determined by the pharmacokinetic profile of therapeutic agents. Half-life is an important determinant of the duration of drug action, which to some extent, also affects the tendency for patients to experience residual effects. Drugs with longer half-lives tend to have residual effects (undesirable daytime effects). On the other hand, a very short half-life limits a drug's duration of action, which in turn makes the drug less effective at maintaining sleep [65,67].

In health promotion and prevention, morbidity, and mortality, evaluation and treatment of sleep disorders are of utmost importance. DSM-5 attempts to bring homogeneity and precision in sleep disorder diagnoses have achieved more synchrony between the of sleep disorders classification systems and other medical disorders, and consequently better clinical attention to and treatment of sleep disorders. DSM-5 stresses the need for independent clinical attention to sleep disorders regardless of psychiatric or other medical problems that may be present.

Clinicians should not assume that all sleep-related symptoms are consequences of psychiatric illness or medication but should instead be aware of the potential for co-existing sleep disorders that require treatment. Recognizing and managing sleep disorders in patients with psychiatric disorders are critical to improving early diagnosis, treatment response, quality of life, and overall health.

There is increasing evidence supporting the beneficial impacts of physical activity on mental health, with studies examining the effects of both brief bouts or more extended periods of exercise. Systematic evaluations of mental diseases have indicated better outcomes for those patients with

physical activity, specifically in sleep disorder outcomes. These reports have also included evaluation of psychological aspects, such as self-esteem, cognitive function, mood, anxiety, depression, and quality of life. According to general results, exercise enhances mood and self-esteem while decreasing stress tendencies, a factor known to aggravate mental and physical diseases. People who exercise regularly have a better frame of mind and experience a favorable effect on sleep quality [68].

A recent systematic review and network meta-analysis included studies comparing pharmacological treatments that can be effective for the acute and long-term treatment of insomnia in adults [69]. The findings of this analysis epitomize the best existing evidence to guide the selection of pharmacological medication for insomnia disorder in adults and supports shared decision-making between patients, carers, and their clinicians, as well as policymakers. All statements comparing the merits of one drug with another should be tempered by the potential limitations of the current analysis, the quality of the available evidence, the characteristics of the patient populations, and the uncertainties that might result from the choice of dose or treatment setting [69].

Insomnia is a well-established health problem associated with several important deleterious effects. General routine screening in at-risk populations is mandatory; when indicated, an evidence-based treatment plan should be established. An important challenge for the future is integrating non-pharmacologic therapy into the standard pharmacological treatment in patients with sleep disorders managed in daily practice. Patients diagnosed with almost all psychiatric disorders experience sleep disturbances among their symptoms. Therefore, insomnia-related components should be included in the overall therapeutic approach to mental diseases, which undoubtedly will contribute to improving the diagnostic and therapeutic processes and, more remarkably, the outcome of psychiatric patients [36].

Conclusions

This review highlights the high prevalence of sleep disorders in the general population especially insomnia, particularly in patients with mental illness and with short- and long-term consequences in the night and the day of people who suffer it. Psychiatric disorders and sleep disorders present complex and bidirectional relationships, which supports the importance of ruling out psychiatric disorders in patients with sleep disorders and appropriately treating sleep and insomnia disorders in psychiatric patients. Sleep disturbances are also highly relevant due to their association

with cardiovascular diseases, obesity, metabolic syndrome, cognitive impairments, daytime sleepiness, and decreased quality of life. Sleep disturbances and insomnia often remain undertreated and are frequently overlooked by health-care professionals. Sleep duration and quality should be a routine target in assessing psychiatric and non-psychiatric diseases to ensure sleep health based on early diagnosis and adequate therapeutic approaches.

Author Contributions

LS and BA have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data. Both authors have been involved in drafting the manuscript or revising it critically for important intellectual content. Both authors have given final approval of the version to be published. Both authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

This research received unrestricted support by Idorsia, with no involvement in the development of the manuscript. The authors thank Marta Pulido, MD, for editing the manuscript and editorial assistance.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Hale L, Troxel W, Buysse DJ. Sleep Health: An Opportunity for Public Health to Address Health Equity. *Annual Review of Public Health*. 2020; 41: 81–99.
- [2] Dang-Vu TT, Desseilles M, Peigneux P, Maquet P. A role for sleep in brain plasticity. *Pediatric Rehabilitation*. 2006; 9: 98–118.
- [3] Garbarino S, Lanteri P, Bragazzi NL, Magnavita N, Scoditti E. Role of sleep deprivation in immune-related disease risk and outcomes. *Communications Biology*. 2021; 4: 1304.
- [4] Gruber R, Cassoff J. The interplay between sleep and emotion regulation: conceptual framework empirical evidence and future directions. *Current Psychiatry Reports*. 2014; 16: 500.
- [5] Kim M, Vu TH, Maas MB, Braun RI, Wolf MS, Roenneberg T, *et al.* Light at night in older age is associated with obesity, diabetes, and hypertension. *Sleep*. 2023; 46: zsac130.
- [6] Lim ASP, Kowgier M, Yu L, Buchman AS, Bennett DA. Sleep Fragmentation and the Risk of Incident Alzheimer's Disease and Cognitive Decline in Older Persons. *Sleep*. 2013; 36: 1027–1032.
- [7] Kohyama J. Which Is More Important for Health: Sleep Quantity or Sleep Quality? *Children (Basel, Switzerland)*. 2021; 8: 542.
- [8] Wilson S, Anderson K, Baldwin D, Dijk DJ, Espie A, Espie C, *et al.* British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: An update. *Journal of Psychopharmacology (Oxford, England)*. 2019; 33: 923–947.
- [9] Léger D, Poursain B, Neubauer D, Uchiyama M. An international survey of sleeping problems in the general population. *Current Medical Research and Opinion*. 2008; 24: 307–317.
- [10] Nguyen V, George T, Brewster GS. Insomnia in Older Adults. *Current Geriatrics Reports*. 2019; 8: 271–290.
- [11] Krystal AD, Prather AA, Ashbrook LH. The assessment and management of insomnia: an update. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*. 2019; 18: 337–352.
- [12] LeBlanc M, Mérette C, Savard J, Ivers H, Baillargeon L, Morin CM. Incidence and risk factors of insomnia in a population-based sample. *Sleep*. 2009; 32: 1027–1037.
- [13] de Entrambasaguas M, Romero O, Guevara JAC, de Larrinaga AÁR, Cañellas F, Salud JP, *et al.* The prevalence of insomnia in Spain: A stepwise addition of ICSD-3 diagnostic criteria and notes. *Sleep Epidemiology*. 2023; 3: 100053.
- [14] Roach M, Juday T, Tuly R, Chou JW, Jena AB, Doghranji PP. Challenges and opportunities in insomnia disorder. *The International Journal of Neuroscience*. 2021; 131: 1058–1065.
- [15] Patel D, Steinberg J, Patel P. Insomnia in the Elderly: A Review. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*. 2018; 14: 1017–1024.
- [16] American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th edn. (DSM-5). American Psychiatric Association: Arlington, VA. 2013.
- [17] Endee LM. Sleep Disorders. In Sprigg WH (ed.) *Essentials of Polysomnography: A Training Guide and Reference for Sleep Technicians* (pp. 13–38). 3rd edition. Jones and Bartlett Publishers Inc: Burlington, Massachusetts. 2020.
- [18] Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014; 146: 1387–1394.
- [19] ICD-11 for Mortality and Morbidity Statistics. Version 04. 2019. Available at: <https://icd.who.int/browse/11/2022-02/mms/en> (Accessed: 24 May 2023).
- [20] Khurshid KA. A review of changes in DSM-5 sleep-wake disorders. *Psychiatric Times*. 2015; 32: 16.
- [21] Freeman D, Sheaves B, Waite F, Harvey AG, Harrison PJ. Sleep dis-

- turbance and psychiatric disorders. *The Lancet. Psychiatry.* 2020; 7: 628–637.
- [22] Yamamoto M, Lim CT, Huang H, Spottswood M, Huang H. Insomnia in primary care: Considerations for screening, assessment, and management. *The Journal of Medicine Access.* 2023; 7: 27550834231156727.
- [23] Wickwire EM, Shaya FT, Scharf SM. Health economics of insomnia treatments: The return on investment for a good night's sleep. *Sleep Medicine Reviews.* 2016; 30: 72–82.
- [24] Sivertsen B, Pallesen S, Glozier N, Bjorvatn B, Salo P, Tell GS, *et al.* Midlife insomnia and subsequent mortality: the Hordaland health study. *BMC Public Health.* 2014; 14: 720.
- [25] Krystal AD. Psychiatric disorders and sleep. *Neurologic Clinics.* 2012; 30: 1389–1413.
- [26] Hombali A, Seow E, Yuan Q, Chang SHS, Satghare P, Kumar S, *et al.* Prevalence and correlates of sleep disorder symptoms in psychiatric disorders. *Psychiatry Research.* 2019; 279: 116–122.
- [27] Alvaro PK, Roberts RM, Harris JK. A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. *Sleep.* 2013; 36: 1059–1068.
- [28] Chokroverty S. Overview of sleep & sleep disorders. *The Indian Journal of Medical Research.* 2010; 131: 126–140.
- [29] Khurshid KA. Bi-directional relationship between sleep problems and psychiatric disorders. *Psychiatric Annals.* 2016; 46: 385–387.
- [30] Scott J, Kallestad H, Vedaa O, Sivertsen B, Etain B. Sleep disturbances and first onset of major mental disorders in adolescence and early adulthood: A systematic review and meta-analysis. *Sleep Medicine Reviews.* 2021; 57: 101429.
- [31] Abad VC, Guilleminault C. Sleep and psychiatry. *Dialogues in Clinical Neuroscience.* 2005; 7: 291–303.
- [32] Koffel E, Thuras P, Chakravorty S, Germain A, Khawaja IS. Poor Sleep Quality at Discharge as a Predictor of Readmission to a Psychiatry Partial Hospitalization Program. *The Primary Care Companion for CNS Disorders.* 2015; 17: 10.4088/PCC.15101826.
- [33] Bachmann S. Epidemiology of Suicide and the Psychiatric Perspective. *International Journal of Environmental Research and Public Health.* 2018; 15: 1425.
- [34] Liu RT, Steele SJ, Hamilton JL, Do QBP, Furbish K, Burke TA, *et al.* Sleep and suicide: A systematic review and meta-analysis of longitudinal studies. *Clinical Psychology Review.* 2020; 81: 101895.
- [35] Romier A, Maruani J, Lopez-Castroman J, Palagini L, Serafini G, Lejoyeux M, *et al.* Objective sleep markers of suicidal behaviors in patients with psychiatric disorders: A systematic review and meta-analysis. *Sleep Medicine Reviews.* 2023; 68: 101760.
- [36] Riemann D, Benz F, Dressle RJ, Espie CA, Johann AF, Blanken TF, *et al.* Insomnia disorder: State of the science and challenges for the future. *Journal of Sleep Research.* 2022; 31: e13604.
- [37] Garbarino S, Lanteri P, Durando P, Magnavita N, Sannita WG. Co-Morbidity, Mortality, Quality of Life and the Healthcare/Welfare/Social Costs of Disordered Sleep: A Rapid Review. *International Journal of Environmental Research and Public Health.* 2016; 13: 831.
- [38] Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *European Heart Journal.* 2011; 32: 1484–1492.
- [39] Beccuti G, Pannain S. Sleep and obesity. *Current Opinion in Clinical Nutrition and Metabolic Care.* 2011; 14: 402–412.
- [40] Inutsuka A, Yamanaka A. The physiological role of orexin/hypocretin neurons in the regulation of sleep/wakefulness and neuroendocrine functions. *Frontiers in Endocrinology.* 2013; 4: 18.
- [41] Lee JH, Cho J. Sleep and Obesity. *Sleep Medicine Clinics.* 2022; 17: 111–116.
- [42] Noh J. The Effect of Circadian and Sleep Disruptions on Obesity Risk. *Journal of Obesity & Metabolic Syndrome.* 2018; 27: 78–83.
- [43] Wardle-Pinkston S, Slavish DC, Taylor DJ. Insomnia and cognitive performance: A systematic review and meta-analysis. *Sleep Medicine Reviews.* 2019; 48: 101205.
- [44] Behrens A, Anderberg P, Berglund JS. Sleep disturbance predicts worse cognitive performance in subsequent years: A longitudinal population-based cohort study. *Archives of Gerontology and Geriatrics.* 2023; 106: 104899.
- [45] Zhao JL, Cross N, Yao CW, Carrier J, Postuma RB, Gosselin N, *et al.* Insomnia disorder increases the risk of subjective memory decline in middle-aged and older adults: a longitudinal analysis of the Canadian Longitudinal Study on Aging. *Sleep.* 2022; 45: zsac176.
- [46] 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. *Journal of Neurology, Neurosurgery, and Psychiatry.* 2020; 91: 236–244.
- [47] Chen K, Lv Y, Long X, Liu W, Zhou J. The Association between Insomnia-Like Sleep Pattern Changes and Cognitive Dysfunction: Possible Mechanism and Therapeutic Strategy. *Current Alzheimer Research.* 2021; 18: 858–875.
- [48] Teräs T, Rovio S, Pentti J, Head J, Kivimäki M, Stenholm S. Association of sleep with cognitive function during retirement transition: the Whitehall II study. *Sleep.* 2023; 46: zsac237.
- [49] Gandhi KD, Mansukhani MP, Silber MH, Kolla BP. Excessive Daytime Sleepiness: A Clinical Review. *Mayo Clinic Proceedings.* 2021; 96: 1288–1301.
- [50] American Academy of Sleep Medicine. *The International Classification of Sleep Disorders.* 3rd edn. American Academy of Sleep Medicine: Darien, IL. 2014.
- [51] Kolla BP, He JP, Mansukhani MP, Frye MA, Merikangas K. Excessive sleepiness and associated symptoms in the U.S. adult population: prevalence, correlates, and comorbidity. *Sleep Health.* 2020; 6: 79–87.
- [52] Zhang L, Yang Y, Luo Y, Liu ZZ, Jia CX, Liu X. A Longitudinal Study of Insomnia, Daytime Sleepiness, and Academic Performance in Chinese Adolescents. *Behavioral Sleep Medicine.* 2022; 20: 798–808.
- [53] Edinger JD, Bathgate CJ, Tsai S, Khassawneh B. Impact of daytime sleepiness and insomnia on simple and complex cognitive task performances. *Sleep Medicine.* 2021; 87: 46–55.
- [54] Van Gastel A. Drug-Induced Insomnia and Excessive Sleepiness. *Sleep Medicine Clinics.* 2022; 17: 471–484.
- [55] Kessler RC, Berglund PA, Coulouvrat C, Hajak G, Roth T, Shahly V, *et al.* Insomnia and the performance of US workers: results from

the America insomnia survey. *Sleep*. 2011; 34: 1161–1171.

- [56] Léger D, Bayon V, Ohayon MM, Philip P, Ement P, Metlaine A, *et al.* Insomnia and accidents: cross-sectional study (EQUINOX) on sleep-related home, work and car accidents in 5293 subjects with insomnia from 10 countries. *Journal of Sleep Research*. 2014; 23: 143–152.
- [57] Sidani S, Ibrahim S, Lok J, O'Rourke H, Collins L, Fox M. Comparing the Experience of and Factors Perpetuating Chronic Insomnia Severity Among Young, Middle-Aged, and Older Adults. *Clinical Nursing Research*. 2021; 30: 12–22.
- [58] Olfson M, Wall M, Liu SM, Morin CM, Blanco C. Insomnia and Impaired Quality of Life in the United States. *The Journal of Clinical Psychiatry*. 2018; 79: 17m12020.
- [59] Buysse DJ. Insomnia. *JAMA*. 2013; 309: 706–716.
- [60] Krystal AD, Ashbrook LH, Prather AA. What Is Insomnia? *JAMA*. 2021; 326: 2444.
- [61] Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical Practice Guideline for the Pharmacologic Treatment of Chronic Insomnia in Adults: An American Academy of Sleep Medicine Clinical Practice Guideline. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*. 2017; 13: 307–349.
- [62] Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*. 2008; 4: 487–504.
- [63] Rosenberg R, Citrome L, Drake CL. Advances in the Treatment of Chronic Insomnia: A Narrative Review of New Nonpharmacologic and Pharmacologic Therapies. *Neuropsychiatric Disease and Treatment*. 2021; 17: 2549–2566.
- [64] Rémi J, Pollmächer T, Spiegelhalter K, Trenkwalder C, Young P. Sleep-Related Disorders in Neurology and Psychiatry. *Deutsches Arzteblatt International*. 2019; 116: 681–688.
- [65] Kryger M, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 6th edn. Elsevier: Amsterdam, The Netherlands. 2015.
- [66] Westerlund A, Lagerros YT, Kecklund G, Axelsson J, Åkerstedt T. Relationships Between Questionnaire Ratings of Sleep Quality and Polysomnography in Healthy Adults. *Behavioral Sleep Medicine*. 2016; 14: 185–199.
- [67] Sun SY, Chen GH. Treatment of circadian rhythm sleep-wake disorders. *Current Neuropharmacology*. 2022; 20: 1022–1034.
- [68] Mahindru A, Patil P, Agrawal V. Role of Physical Activity on Mental Health and Well-Being: A Review. *Cureus*. 2023; 15: e33475.
- [69] De Crescenzo F, D'Alò GL, Ostinelli EG, Ciabattini M, Di Franco V, Watanabe N, *et al.* Comparative effects of pharmacological interventions for the acute and long-term management of insomnia disorder in adults: a systematic review and network meta-analysis. *Lancet (London, England)*. 2022; 400: 170–184.