EXPERT REVIEWS

Sleep disorders: impact on daytime functioning and quality of life

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This article provides an overview of the daytime symptoms associated with the most common sleep disorders, namely insomnia, restless legs syndrome, obstructive sleep apnea syndrome and shift wake–sleep disorder. Psychological and social dysfunction resulting from these sleep disturbances are explained and discussed in detail. Health-related quality of life is a concept that reflects the changes in diverse aspects of subjective wellbeing of the patients due to an illness. Therefore, studies reporting quality-of-life issues associated with the aforementioned sleep disorders will also be presented. Finally, we review the limited data regarding the effects of treatment on quality-of-life outcomes.

Keywords: daytime functioning • insomnia • mental health • obstructive sleep apnea • quality of life • restless legs syndrome • shiftwork • shiftwork-related sleep disorder • sleep disorder

Many patients with sleep disorders seek medical attention because of daytime symptoms or negative consequences of sleep disruption, which suggests that the night-time symptoms may be less bothersome than the daytime consequences of sleep problems. Increasing amounts of research data in sleep medicine suggest that sleep disorders impair the physical, psychological and social aspects of wellbeing. Despite the growing interest in sleep medicine and research, the relationship between sleep disorders and various daytime symptoms often remain unrecognized in everyday clinical practice.

Recently, patient-reported outcomes have become increasingly accepted as relevant end points in clinical trials and in the evaluation of healthcare services [1]. This has led to the development of several questionnaires that aim to quantify self-perceptions concerning general health, functional wellbeing and various dimensions of quality of life (QoL). Increasing amounts of evidence support the notion that sleep–wake disorders are associated with impaired daytime wellbeing and functioning.

This article examines the various daytime consequences, psychosocial burden and impairment in QoL caused by some of the most common chronic sleep disorders, namely insomnia, restless legs syndrome (RLS), obstructive sleep apnea syndrome (OSAS) and shiftwork-related sleep disorder.

Insomnia

Epidemiology & relevance of insomnia

Insomnia is defined as a persistent difficulty in initiating and/or maintaining sleep and is associated with distress and impaired daytime functioning [2,3]. Most classifications distinguish primary insomnia from secondary insomnia, which is caused by the presence of somatic or mental illnesses or other sleep disorders, such as OSAS or RLS. The 2005 NIH consensus conference introduced 'comorbid' insomnia as a new concept to replace the term secondary insomnia, as it was felt that the term 'secondary insomnia' may contribute to undertreatment. This new terminology also emphasizes a paradigm shift; in this new framework comorbid insomnia is not merely a symptom of other diseases but a distinct entity in itself [4].

Insomnia is the most common sleep disorder with negative daytime symptoms, and it is clearly associated with impaired wellbeing and QoL. Insomnia is also associated with a number of somatic and psychiatric disorders, and it has been demonstrated to augment the burden of the underlying or comorbid condition [5,6]. Although conflicting data have been published [7], several authors have proposed that insomnia is a risk factor for cardiovascular events, immune dysfunction and even mortality [7,8]. Several studies, including ours, pointed out that insomnia is

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associated with increased healthcare utilization, absenteeism and accidents; therefore, it presents a substantial financial burden to modern societies [9–12]. Insomnia remains, however, a frequently underdiagnosed and undertreated condition [13].

According to the standard criteria, the prevalence of chronic insomnia in the general population has been reported to be approximately 5–10% [14–17]. Our cross-sectional study, involving a large (n = 12,000), nationally representative sample of the Hungarian adult population, yielded similar results: nearly half of the sample mentioned at least one insomnia symptom and the prevalence of clinically relevant insomnia was 9.2% [11]. The prevalence of insomnia is 1.5- to twofold higher among women than men, and there is a tendency to report insomnia symptoms more often as age advances. The theory that increasing age, *per se*, is associated with impaired sleep has recently been challenged and additional factors (e.g., psychiatric and physical comorbidities, chronic pain and inactivity) are felt to be responsible for the increased prevalence of insomnia in the elderly [18].

Insomnia, daytime functioning & quality of life

The most frequently reported daytime consequences of chronic insomnia include daytime sleepiness, fatigue, depressed mood, lack of energy, impaired cognition, memory problems, irritability, psychomotor dysfunction, and decreased alertness and concentration (**Table 1**) [19–21]. The insomniac population is heterogeneous in terms of their symptom profiles. This is particularly true for daytime sleepiness, which is prominent in some patients with insomnia, but is absent in others. The most common objective measure of daytime sleepiness is sleep latency, which is assessed by the Multiple Sleep Latency Test [22] or the Maintenance of Wakefulness Test [23]. The most widely used questionnaire for the subjective quantification of daytime somnolence is the Epworth Sleepiness Scale [24]. Typically, insomnia that is associated with other conditions (e.g., OSAS or rheumatoid arthritis) may also lead to daytime sleepiness [25]. However, studies also suggest that middle-aged insomniac patients do not necessarily complain about daytime sleepiness and most studies failed to find a correlation between the severity of insomnia and objective measures of daytime sleepiness [26–28]. While impaired cognitive and psychomotor abilities are frequently reported by insomniacs [29], there were no significant differences between patients with and without chronic insomnia in most objective tests measuring cognitive function and psychomotor ability [29,30], except for difficulties in balance [26,31].

According to several earlier prospective studies, the presence of insomnia is associated with an increased risk of depression, anxiety and suicide, with increased odds ratios (ORs), ranging from 2 to 5, compared with those without insomnia [32–34]. A cohort study involving 1053 male medical students with a median follow-up period of 34 years reported an increased multivariate relative risk (risk ratio: 2.0) of clinical depression in those who reported insomnia at baseline [35]. Several other studies also found that insomnia may precede the onset of depressive disorder among adults and adolescents [36–38]; however, negative findings have also been reported [39,40]. Childhood sleep problems were independently associated with increased odds of adult anxiety disorders (OR: 1.6) in a multivariate analysis of 943 participants [39]. Recently, in a population-based prospective study of 25,130 adults with 11 years of follow-up, chronic insomnia was significantly associated with the development of anxiety (OR: 1.6), after adjustment for several relevant factors [40]. Several reports from a large epidemiologic survey (the latest report had a median follow-up period of 12.6 years) indicated that insomnia at baseline was associated with a twofold higher risk of subsequent alcohol-related problems according to multivariate models [33,34,41]. People with insomnia are more likely to use alcohol as a sleeping aid than subjects without insomnia, and they perceive alcohol as emotionally reinforcing [42]. Individuals with insomnia were 2.4-times more likely to develop nicotine dependence and 7.2-times more likely to develop drug abuse or dependence in a longitudinal study of 979 participants [32]. Sleep problems in early childhood significantly predicted the use of alcohol, marihuana, illicit drugs and smoking during adolescence (aged 12–14 years) among 275 boys from a community-based sample [43]. Finally, in a recent survey of 3134 youths, chronic insomnia increased the subsequent risk of somatic health, interpersonal and psychological problems and disturbed daily activities in multivariate models during a 12-month follow-up period [44].

Although the question has not been completely settled, it seems that many individuals with insomnia are not simply sleep deprived and factors other than sleep disruption may be responsible for the daytime complaints of these patients [30]. Misperception of nocturnal sleep and dysfunctional beliefs regarding the daytime consequences of poor sleep may lead to an increased awareness and more frequent reporting of daytime consequences of poor sleep, even in the absence of objective (e.g., polysomnographic) markers of daytime sleepiness or sleep deprivation [45,46]. Furthermore, excessive worries regarding sleep may actually trigger and maintain sleep disruptions. Depressive symptoms and anxiety can also increase the psychological burden of the condition in insomniac patients. In these patients, the mental health issues may explain or contribute to daytime dysfunction. Another theory suggests that hyperarousal, which would also account for the lack of sleepiness, may be responsible for troubled sleep and daytime symptoms [30,47]. The presence of fatigue, which is the most frequently and consistently reported daytime symptom of insomnia, is compatible with all of these theories [48,49].

Patients with insomnia often seek professional help because of their perceived daytime symptoms rather than the amount or quality of sleep they get. Daytime dysfunction may seriously impair social, occupational and recreational life domains and overall QoL.

Earlier studies suggested an association between the presence of sleep problems and reduced work performance, but causality could not be determined owing to the cross-sectional design of the surveys [12,50]. In a recent cohort study, however, chronic insomnia was a significant, independent predictor of permanent work disability following adjustment for sociodemographic and shiftwork characteristics, comorbidities and health-related behaviors [51].

Table 1. The most commonly reported daytime symptoms of patients with various sleep disorders.

Symptom	Sleep disorder		
	Insomnia	*Restless legs syndrome*	*Obstructive sleep apnea syndrome*
Physical	Fatigue/anergia Sleepiness	Discomfort Inability to get comfortable Pain Inability to stay still Fatigue/exhaustion Sleepiness	Excessive daytime sleepiness Morning headache Dry mouth and/or throat Fatigue Erectile dysfunction
Psychological	Depression Anxiety Irritability Alcohol and substance abuse	Depressed mood	Irritability Depression
Cognitive performance	Decreased alertness and concentration Impaired memory consolidation Psychomotor dysfunction	Concentration difficulties Decreased work performance	Decreased attention and vigilance Impaired memory and learning Psychomotor and executive dysfunction

It should be noted that measures of daytime dysfunction that were originally developed for other disorders have been used to assess daytime impairment in patients with insomnia. This may hinder achieving the true understanding of the real nature of the daytime symptoms experienced by insomnia sufferers. Carey *et al.* conducted a qualitative study of daytime and social aspects of insomnia using focus groups [52]. The results shed light on the occult nature of the disorder; insomnia sufferers hid their symptoms because they thought that other people did not consider their condition debilitating or a 'real' illness. In this study, subjects made an effort to compensate for their impairments and to appear more functional at home or during work, which further fueled their feelings of isolation. Female participants were especially susceptible to the pervasive effects of insomnia on their social life. Patients with insomnia were also unable to develop a secure relationship with their physician in order to discuss their problems [52]. Further studies are needed to determine whether these results can be generalized. The aforementioned findings also indicate that more sophisticated methods are needed in order to capture the full range of the 'insomnia experience'.

Owing to its multidimensional, subjective approach, measurement of health-related QoL seems more feasible than, for example, objective measures of daytime sleepiness to capture the impact of insomnia on various dimensions of daytime functioning. The most widely used tool to measure health-related QoL in insomniac patients is the 36-item Short Form Health Survey (SF-36) of the Medical Outcomes Study, which includes eight dimensions (Table 2) [53]. Patients with insomnia reported significantly worse QoL scores in most dimensions of SF-36 compared with good sleepers (Table 3) [9,54–60]. Several authors suggested that none of the SF-36 dimensions is affected more severely by insomnia than others [58,61]. Léger *et al.* compared patients with severe and mild insomnia with good sleepers from the general population in a cross-sectional study. They found that insomniacs reported impaired QoL in all dimensions of the SF-36 scale, even if patients with anxiety and depression were excluded. Therefore, nocturnal sleep problems in this study seemed to be associated with worse QoL independent of psychiatric illness. An additional finding in this study suggested that the severity of insomnia correlated with the QoL scores, indicating that the SF-36 questionnaire is a sensitive tool for assessing the effects of insomnia on QoL [58]. Katz *et al.* found that patients with severe insomnia had more severely impaired QoL in nearly all domains than participants with congestive heart failure or clinical depression [56]. Similarly, adult hypnotic users with chronic insomnia demonstrated lower SF-36 scores in both mental and physical domains than the reference values from general practices, although the difference diminished with increasing age [62].

Effect of treatment in insomnia

The effect of insomnia therapies on daytime symptoms remains unclear. Most intervention studies focus solely on sleep indices and, as pointed out in a recent review, only a few insomnia treatment studies had examined daytime functioning as an outcome [63].

As an example, zopiclone, a nonbenzodiazepine hypnotic, showed a significant beneficial effect on daytime symptoms, which included 'daytime wellbeing', 'morning freshness', 'daytime alertness' and 'ability to concentrate' [64–66] in both their social and professional life [67]. In a recent randomized, double-blind, placebo-controlled study involving 830 patients with insomnia, 6 months of eszopiclone treatment improved SF-36 scores in physical functioning, vitality and social functioning domains, as well as the results of the Work Limitations Questionnaire [68]. Conversely, several studies of zopiclone did not find any improvement in daytime deficits related to insomnia compared with placebo [69–71].

Cognitive–behavioral therapies have also been effective in alleviating daytime symptoms in patients with insomnia [72,73]. In a randomized, controlled trial comparing the treatment effects of cognitive–behavioral therapy, hypnotic treatment (zopiclone) and placebo, 46 older patients with primary insomnia were enrolled. In measures of worry, anxiety, depression, interpersonal relationships, subjective alertness, vigilance and QoL, both cognitive–behavioral

Table 2. The subscales of the SF-36 questionnaire.

Subscale	Definition
Physical functioning	Limitations on physical activities, such as walking, bathing and strenuous sports
Role physical	Problems with work or other daily activities as a result of physical health
Bodily pain	Intensity of bodily pain or limitations because of pain
General health	Perception of current health and health outlook
Vitality	Level of energy
Social functioning	Extent health interferes with normal social activities
Role emotional	Problems with daily activities as a result of emotional issues
Mental health	Mental health screening

SF-36: 36-item Short Form Health Survey.
Data from [53].

therapy and zopiclone resulted in moderate improvements in the outcomes; none of the treatments were clearly superior to the others [74]. Elderly patients with comorbid insomnia had a decreased number of naps and reported less interference of sleep with daily functioning after receiving cognitive–behavioral therapy compared with placebo treatment [75]. In an intervention study assessing the QoL of insomniacs, the physical functioning, emotional role limitation and mental health domains of the SF-36 questionnaire improved significantly following cognitive–behavioral therapy using primary-care reference values as a control [62].

In summary, patients with insomnia have worse QoL than good sleepers in several domains. Daytime functioning and QoL should be assessed more systematically as primary outcome measures in intervention studies of insomnia therapies. The SF-36 questionnaire seems to be a sensitive tool for assessing the QoL of patients with insomnia. Furthermore, prospective studies are needed in order to investigate the potential causal relationship between sleep problems, measures of daytime dysfunction and impaired QoL. Finally, treatment trials should always employ valid QoL instruments as outcome measures.

Restless legs syndrome

Epidemiology & relevance of RLS

Restless legs syndrome is a sensory–motor disorder characterized by unpleasant sensations, usually in the legs, accompanied by an urge to move the limbs. The symptoms are provoked by inactivity and are relieved by movement, and they usually occur or worsen during evening or night hours. The essential criteria for the diagnosis of RLS are shown in Box 1 [76]. RLS is often associated with periodic limb movement during sleep [77].

The prevalence of RLS is 5–10% in the general population [78–82], while the rate of patients with RLS in the primary-care population is approximately 25% [83,84]. Women and elderly patients report symptoms of the condition more frequently. RLS shows a chronic course and symptoms usually seem to worsen with advancing age. RLS may be primary (familiar RLS) or develop secondary to other conditions, most commonly iron deficiency [85], pregnancy [86,87], neuropathy [88] and chronic renal failure [89–91].

Several studies found that RLS and periodic limb movement in sleep are risk factors of mortality in patients with end-stage renal failure [89,92–94]. Despite these findings, RLS remains an under-recognized disease and only a small portion of patients receive appropriate diagnosis and treatment [95–97].

Night-time & daytime symptoms & consequences of RLS

Symptoms of RLS and sleep disruption lead to impaired daytime activity and worse QoL [91,95]. Affective disorders and anxiety develop more frequently among RLS sufferers than in the general population [98], and there are reports suggesting that RLS is associated with hypertension and cardiovascular problems [78,99–101].

Owing to the nature of the symptoms, patients with RLS find it difficult to fall asleep and/or to maintain sleep [77,95,102]. In epidemiological surveys, sleep disruptions and unpleasant (often painful) sensations were commonly reported as the most troublesome symptoms among RLS patients (Table 1) [95,96,99,103]. In the RLS Epidemiology, Symptoms, and Treatment study, almost 60% of participants with RLS stated that their symptoms were associated with pain and nearly half of the cohort experienced disruption of daily activities and personal relationships [95].

Five large epidemiological studies indicated an association between the presence of RLS and depression in a pooled sample of 9258 adults [99,104–107]. The adjusted ORs for depression were between 2.6 and 13.06 in patients with RLS compared with subjects without RLS. In one of the surveys, men suffering from RLS reported depressed mood (OR: 2.6) and reduced libido (OR: 2.2) more frequently and showed a tendency toward social isolation related to RLS, compared with individuals without RLS [99]. Compared with population-based controls, 130 respondents with RLS showed an elevated 12-month risk of panic disorder, generalized anxiety disorder and major depression (OR: 2.6–4.7) [98]. Complaints of not being refreshed when waking up and morning and daytime headache were also more common in patients affected by RLS than in control individuals [99].

Although the number of studies is limited, impaired QoL has been found repeatedly in patients with RLS (Table 4) [103,104,108–110]. Abetz *et al.* found that RLS patients referred to a sleep disorder center had significantly reduced SF-36 scores compared with the general population [110]. The impairment was more profound in the physical subscales. RLS patients also had significantly lower scores across most QoL domains when compared with populations with various cardiovascular diseases (e.g., hypertension, angina and congestive heart failure). The role physical, bodily pain and vitality domains of the SF-36 were significantly worse in RLS patients than in populations with clinical depression, Type II diabetes, chronic obstructive pulmonary disease and

Table 3. Relationship between insomnia and quality of life, assessed with the SF-36 questionnaire.

Study	Sample size (n)	Sample	Assessment of insomnia	SF-36 domains associated with insomnia	Ref.
Byles *et al.* (2005)	1011	Elderly women	PSQI and NHP sleep subscale	In adjusted models: all domains except for PF, SF and PCS	[54]
LeBlanc *et al.* (2007)	953	Population based	DSM-IV criteria, questions based on ISI and PSQI, three severity categories	Insomnia was the outcome 'V' was a significant predictor in adjusted model RP was nearly significant	[57]
Leger *et al.* (2001)	1053	Population based	DSM-IV criteria, three severity categories	In unadjusted models: all domains, of which the most affected were V, GH, MH and BP	[58]
Katz *et al.* (2002)	3445	Patients with chronic illness	Questions on DIS, DMS, three severity categories	In unadjusted models: all domains In adjusted models: MH, V and GH	[56]
Schubert *et al.* (2002)	2800	Population based, elders	Three questions on DIS and DMS	In adjusted models: all domains, of which the most affected were V, RP, GH, PCS and MCS	[59]
Baldwin *et al.* (2001)	5816	Population based	DIS and DMS assessed with the SHHS SHQ	In adjusted models: all domains, of which the most affected were MH and V	[60]
Hajak (2002)	1913	Population based	Four questions based on DSM-III and -IV	In unadjusted models: V, SF, MH and RE	[55]

BP: Bodily pain; DIS: Difficulty initiating sleep; DMS: Difficulty maintaining sleep; DSM: Diagnostic and Statistical Manual of Mental Disorders; GH: General health; ISI: Insomnia Severity Index; MCS: Mental component score; MH: Mental health; NHP: Nottingham Health Profile; PCS: Physical component score; PF: Physical functioning; PSQI: Pittsburgh Sleep Quality Index; RE: Role emotional; RP: Role physical; SF: Social functioning; SF-36: 36-item Short Form Health Survey; SHHS SHQ: Sleep Heart Health Study Sleep Habit Questionnaire; V: Vitality.

osteoarthritis. It must be noted, however, that the studies did not control for the presence of comorbidities; thus, the potential influence of other chronic diseases was not accounted for. In this study, patients with RLS were recruited from a secondary sleep disorder center; therefore, these patients were more likely to suffer from more severe symptoms than the average RLS population. Phillips *et al.* reported increased prevalence of poor general and mental health in RLS patients compared with individuals without RLS in a general population survey [111]. Rotdach *et al.* also found diminished mental health and an increased risk of depressive symptoms among RLS patients in a study of elderly population [104]. In another study, representative samples of the general population of several European countries and the USA were screened for RLS [108]. Patients with RLS showed similar reductions in both the mental and physical SF-36 domains compared with the rest of general population, independently of other factors, such as age or comorbidity. Approximately two-thirds of the patients with RLS were at least moderately distressed by their RLS symptoms, and this group had significantly worse scores on the Social Functioning scale than those without distress. Other RLS-related factors, such as the severity and frequency of the symptoms, were also associated with impaired QoL. An important finding of this study was that many patients in the primary-care population had been prescribed inappropriate medications for RLS [96].

The studies employing instruments to assess QoL suggested that RLS has a profound impact on vitality, occupational performance and daily activities as a result of physical problems. To what degree severe sleep deprivation in patients with RLS is responsible for these impairments is not known. On the other hand, RLS sufferers have difficulty sitting quietly; therefore, activities such as traveling for long periods of time, resting or going to the cinema, theatre or a concert can be extremely challenging for them and they may have to alter their lifestyle substantially or refrain from certain activities. Patients with RLS frequently develop depressed moods and symptoms of anxiety [95]. Impaired sleep has been suggested to lead to the emotional distress seen in RLS patients [112], but we also found that RLS was strongly associated with depression independently of insomnia among patients with chronic kidney disease [Szentkirályi A *et al.*, Unpublished Data]. Fatigue, social isolation and chronic pain, as well as dopaminergic abnormalities of the brain, could explain such a relationship. Since RLS is frequently unrecognized, the lack of diagnosis can fuel feelings of anxiety, hopelessness and social isolation. RLS also has a greater, or at least equivalent, impact on QoL compared with other chronic diseases, such as diabetes, heart failure or depression [95].

Effect of treatment in RLS

There is some evidence that medications that are effective in reducing RLS symptoms may improve daytime function. Two consecutive 12-week, prospective, double-blind, randomized comparison studies investigated the effect of the dopamine agonist ropinirole on QoL, measured using disease-specific (RLS QoL Questionnaire) and generic (SF-36) tools [113,114]. Use of

Box 1. Essential diagnostic criteria of restless legs syndrome.

- Urge to move legs (occasionally arms) accompanied with unpleasant, sometimes painful, sensations
- Symptoms start/worsen during rest (e.g., sitting or lying down)
- Symptoms are completely or partially relieved by movements of legs (or arms)
- Symptoms show circadian rhythm with an evening/early night preference

Data from [76].

ropinirole was associated with significant improvements in disease-specific QoL and daytime somnolence according to both studies. In these studies, three domains of the generic SF-36 scales (mental health, social functioning and vitality) also improved after treatment with ropinirole [114].

Obstructive sleep apnea

Epidemiology & relevance of OSA

Obstructive sleep apnea is characterized by repeated episodes of pharyngeal collapse and airflow interruption during sleep followed by a reduction in arterial oxygen saturation and increase in inspiratory effort. These respiratory events are usually terminated by arousals, of which the patients are usually unaware. The severity of the disease is assessed by the apnea–hypopnea index (AHI), which is the total number of apneas (i.e., complete cessation of airflow) and hypopneas (i.e., partial reduction in airflow) per hour of sleep [115].

The shallow, fragmented sleep that is caused by arousals is not restorative and contributes to excessive daytime sleepiness, in which case the term OSAS is used (for diagnostic criteria see Box 2) [116].

It is estimated that the prevalence of OSAS is approximately 2–4% in women and 4–9% in men [117] and the frequency increases with age [115,117,118]. The major risk factors of the condition include obesity, positive family history and certain anatomical features [115].

Obstructive sleep apnea syndrome is a risk factor for hypertension [119–121], stroke [122] and various cardiovascular diseases [123–125]. Other somatic conditions, such as the metabolic syndrome, diabetes [126] and chronic renal disease, have also been associated with OSAS [94]. Despite these adverse chronic conditions and their additional impact on QoL, the majority of the subjects with sleep apnea still remain unrecognized in the general population.

Effect of OSA on daytime functioning & QoL

The most prevalent daytime symptoms seen in adults with sleep-disordered breathing are summarized in Table 1. Excessive daytime sleepiness is a frequent and major symptom in patients with sleep apnea, while lack of energy and fatigue are also common problems. However, none of these symptoms are universally present in all subjects with sleep apnea.

The features of cognitive deficit and impaired vigilance found in patients with OSAS are similar to the symptoms seen in patients with organic damage of the CNS; verbal performance, attention, memory, learning and logical skills, motor coordination and other executive functions are usually affected [127,128]. In a population-based study with 841 adults, AHI was independently associated with impaired psychomotor performance and this relationship was not fully explained by daytime sleepiness [129]. Individuals with OSAS are usually aware of their neuropsychological impairments, which may fuel feelings of depression and helplessness.

Excessive daytime sleepiness and cognitive deficits associated with OSAS are common causes of motor vehicle accidents [130]. Patients with severe OSAS exhibited a reduced driving performance as measured by 'Steer Clear', a commonly used driving simulation task [131]. In the USA, approximately 800,000 drivers were involved in OSAS-related collisions with an estimated total cost of 1400 lives and US$16 billion in 2000 [132].

Patients with OSAS also frequently complain of sexual dysfunction [133,134]. A prevalence study analyzing 1025 males with erectile dysfunction showed that 91% of these individuals had at least mild OSAS [133]. Sexual dysfunction may contribute to the emotional distress [135], problems in sexual relationship and impaired QoL experienced by some patients with OSAS [136].

A number of smaller studies found an elevated prevalence of depressive symptoms (24–58%) among patients with sleep-disordered breathing [137]. The largest epidemiologic survey to date, conducted on 18,980 subjects, indicated that 18% of individuals with a high risk of sleep apnea were diagnosed with major depression. This relationship remained significant even after controlling for obesity and hypertension [138]. In a 4-year longitudinal study, the risk for incident depression was twofold higher for participants with mild OSA (AHI: 5–15/h) than for subjects without OSA [139]. Several smaller studies indicated a significant association between anxiety and OSAS [140–143], while others did not find such a relationship [144]. In a large cohort of veterans, individuals with OSAS had a significantly greater prevalence of depression (22%), anxiety (17%), post-traumatic stress disorder (12%) and psychosis (5%) than subjects without sleep apnea [145]. Only one of these studies reported a direct correlation between AHI and anxiety, which suggests that other factors, such as fragmented sleep or daytime somnolence, may account for anxiety in the majority of these patients [140].

Several authors suggested that women are more likely to present with atypical symptoms of sleep apnea, such as irritability, tiredness, insomnia, use of sedatives and mood disturbances [146,147]. Witnessed apneic events are also less commonly reported in women than men, which may promote underdiagnosis of OSAS among women [148].

Reports assessing QoL in patients with OSAS used both generic (i.e., SF-36) and disease-specific tools (i.e., the Calgary Sleep Apnea QoL Instrument) [149]. This scale is specifically designed to measure changes after the initiation of therapies, such as continuous positive airway pressure (CPAP) therapy (discussed in detail later), and it is also sensitive for the side effects of the CPAP treatment.

In most studies, QoL was assessed in a cross-sectional design comparing OSAS patients with controls and/or population norms [150]. In one study, patients with OSAS were asked to

Table 4. Review of studies on the relationship between restless legs syndrome and quality of life, assessed with the SF-36 questionnaire.

Study	Patients with RLS (n)	Sample	Assessment of RLS	Domains of SF-36 associated with RLS	Ref.
McCrink *et al.* (2007)	489 (Europe) 315 (USA)	Population based	Four diagnostic questions based on standard criteria	In adjusted models: severity of RLS was negatively associated with PCS, physical domains and SF in Europe Severity of RLS was negatively associated with all dimensions and composit scores in the USA	[108]
Allen *et al.* (2005)	158	Population based	Four diagnostic questions based on standard criteria	In adjusted models: all domains, of which the most affected: BP, GH and V	[103]
Kushida *et al.* (2007)	375	Population based	Four diagnostic questions based on standard criteria	In adjusted models: all domains, of which the physical domains were most affected	[109]
Rothdach *et al.* (2000)	36	Elderly population	Three diagnostic questions based on standard criteria	In unadjusted model: MH (GH was near significant)	[104]
Abetz *et al.* (2004)	85	Patients referred to sleep clinic plus population-based normal control	RLS severity with IRLS-PV (validated questionnaire)	In unadjusted models: presence of RLS was associated with all domains, of which the physical domains were most affected RLS severity was associated with RP, BP, V, SF and MH	[110]

BP: Bodily pain; GH: General health; IRLS-PV: Patient version of the International Restless Legs Scale; MH: Mental health; PCS: Physical component score; RLS: Restless legs syndrome; RP: Role physical; SF: Social functioning; SF-36: 36-item Short Form Health Survey; V: Vitality.

grade the importance of several OSAS-related items that may be potentially influencing their QoL [151]. The items with the most important impact on QoL clustered into five domains:

- Daytime symptoms
- Nocturnal symptoms
- Limitation of activities
- Emotions
- Interpersonal relationships

In surveys assessing impaired QoL with the SF-36 questionnaire, patients with OSAS had the most pronounced reductions in the domains of vitality, role physical and social functioning (for a summary see **Table 5**) [60,152–157]. In the first population-based study examining subjects with OSAS, even mild sleep-disordered breathing was associated with lower QoL in all SF-36 domains, except for pain and limitations in usual role activities because of emotional problems, even after controlling for possible confounding factors such as age, sex, BMI and history of cardiovascular conditions [153]. The adverse changes associated with OSAS were most prominent in the domains of social functioning, vitality and limitations in usual role activities because of physical health problems. The magnitude of the reduction in QoL associated with OSAS was comparable to the magnitude of changes reported in conditions such as arthritis, hypertension or diabetes. The Sleep Heart Health Study, enrolling nearly 6000 subjects, indicated an independent, strong relationship between severe OSAS and worse QoL in the SF-36 scale domains of physical functioning, general health, social functioning and, especially, vitality, even after controlling for various potential confounding factors [60]. In summary, patients with OSAS consistently report worse QoL than those without sleep apnea, with the most pronounced effect in the vitality and the social functioning domains of the SF-36 questionnaire.

Multiple mechanisms could potentially contribute to the decline of QoL in patients with OSAS. Subjective daytime sleepiness was associated with worse QoL in OSAS patients in several studies [60,155,158,159]. These findings are supported by other results that show that increased sleepiness may have a negative impact on the general perception of emotional and physical health and the quality of social interactions [160,161]. On the other hand, the depression score was the strongest independent predictor of SF-36 scores in patients with severe OSAS, although the direction of the association has not been established [154]. One potential explanation is that the symptoms of OSAS lead to impaired QoL, which may also affect the functional and emotional wellbeing of the patients and may result in depression, anxiety and irritability [162]. This theory is supported by the finding that the magnitude of the association between OSAS and depression is reduced when comorbidities such as hypertension and obesity are included in multivariate models, thus suggesting that these comorbidities may mediate some of the effects of OSAS on mood [163]. Common somatic diseases, especially obesity, may also promote lower self-perceived health in OSAS,

Box 2. Essential diagnostic criteria of obstructive sleep apnea/hypopnea syndrome*.

Criterion A:

- Excessive daytime sleepiness that is not better explained by other factors

Criterion B:

- Two or more of the following that are not better explained by other factors:
  - Choking or gasping during sleep
  - Recurrent awakenings from sleep
  - Unrefreshing sleep
  - Daytime fatigue
  - Impaired concentration

Criterion C:

- Overnight monitoring demonstrates five or more obstructed breathing events per hour during sleep

*The subject must fulfil criterion A or B, plus criterion C.
Data from [116].

as found in a study of 49 snorers and 81 OSAS patients [155]. Interestingly, objective sleep parameters were only correlated with the physical domains of QoL, probably reflecting feelings of fatigue and tiredness due to nonrestorative sleep [155].

Effect of therapy in OSA

The standard therapy for moderate or severe OSAS is applying nasal CPAP through a mask. While using this device during sleep might seem challenging, patients enjoy substantial benefits of regular CPAP use in improved sleep and daytime symptoms (especially in terms of sleepiness, fatigue and cognitive function) and improved QoL [125]. A meta-analysis that included 12 randomized, controlled trials indicated that CPAP therapy significantly reduced both subjective and objective measures of daytime sleepiness, especially in patients with more severe apnea [164]. In a recent study, CPAP therapy significantly reduced depressive symptoms assessed with the Beck Depression Inventory after both short-term (4–6 weeks) and long-term (1 year) follow-up [165], while in another study, there was no improvement in the emotional status of 20 patients with severe OSAS following 1 year of treatment [140]. Kawahara *et al.* found that CPAP therapy significantly reduced daytime somnolence and depression, as assessed by the Epworth Sleepiness Scale and the Zung self-depression scale, respectively, and QoL was also improved in seven out of eight domains of the SF-36 questionnaire [166]. Alleviating depression seemed to be an important factor in achieving better QoL [166]. Several authors found that the severity of anxiety in OSAS patients significantly decreased following either CPAP treatment or surgery [141,143]. There are inconclusive results regarding whether the presence of depression and anxiety in OSAS patients would negatively affect treatment adherence with the CPAP device [167,168]. The number of car accidents was significantly reduced among drivers with OSAS following CPAP treatment [169]. Cognitive performance in attentive, visuospatial learning and motor tasks were normalized after 15 days of CPAP treatment, while executive functions and constructional abilities were not affected by either short- or long-term (4 months) treatment with CPAP [170]. Finally, CPAP therapy seems to be effective in improving QoL in most domains of SF-36 scale, especially in the vitality, social functioning, role physical and mental health scores [150].

Spouses of heavy snorers also often experience disrupted sleep, worse self-reported health and lower marital satisfaction. Based on questionnaire data collected from 1032 women, those living with heavy snorers were more frequently affected by insomnia symptoms, morning headache, daytime sleepiness and fatigue than women sleeping with nonsnorers [171]. Parish *et al.* studied 54 patients with OSAS and their bed partners; treatment with CPAP significantly improved excessive daytime sleepiness and QoL domains role-physical, vitality , social functioning and mental health for both the patients and their bed partners [172].

In summary, OSAS is associated with a number of daytime symptoms and significant deficits in physical, mental and social wellbeing. Treatment with CPAP is not only beneficial for cardiovascular outcomes but also usually dramatically improves daytime functioning and QoL.

Shiftwork

Epidemiology & relevance of shiftwork

Shiftwork can be defined as "a way of organizing daily working hours in which different persons or teams work in succession to cover more than the usual 8-h workday, up to and including the whole 24 h" [173]. In practical terms, any work schedule is considered shiftwork if they are not within the 09:00–17:00 or 08:00–16:00 time range. In recent years, as a response to social and economic demands, the so-called '24-h society' has dramatically evolved and expanded. According to surveys in European countries, the USA and also in developing countries, approximately 20% of employees are working in alternating shifts [301]. However, the number of people working alternating shifts in social, communication, leisure, transportation, medical services and in factories is probably rapidly rising [174].

Several headline catastrophes such as the Challenger explosion, the Bhopal disaster, the Exxon Valdez oil spill, the Three Mile Island and the Chernobyl reactor meltdown have been, at least in part, attributed to human errors secondary to fatigue and sleepiness, which might have been related to the effects of shiftwork [175].

Exposure to shiftwork is associated with increased sick leave [176] and increased prevalence of various somatic conditions, including coronary heart disease and peptic ulcer [177]. Disruption of the circadian rhythm leads to hormonal changes; therefore, women working night shifts are more prone to developing menstrual irregularities, infertility and adverse pregnancy outcomes [178,179].

Daytime consequences & QoL in shiftwork

There are large differences among individual shiftworkers in terms of the adaptation to disrupted sleep–wake cycle and sleep deprivation. Some of the individuals concerned will chronically

Table 5. Relationship between obstructive sleep apnea syndrome and quality of life assessed with the SF-36 questionnaire.

Sample size (n)	Sample	Domains of SF-36 associated with OSAS	Ref.
737	Population based	In adjusted models: AHI was negatively associated with all domains except for BP and RE	[153]
5816	Population based	In adjusted models: severe OSAS was associated with PF, GH, V and SF; compared with normative data all physical domains and V were impaired in those with severe OSAS	[60]
94	Patients referred to sleep center	Lower scores in all domains compared with normal population, especially in V, RE and SF. In adjusted models: the amount of deep sleep predicted PF, BP and V	[157]
135 (male)	Patients referred to sleep clinic	AHI correlated negatively with PF and GH. Arousal index correlated with PF and RP	[152]
94	Patients referred to sleep clinic	Lower values in all domains except for PF and BP	[154]
77	Patients referred to sleep clinic and primary care controls	In adjusted models: AHI was significantly associated with PF and RP, and was marginal with V	[156]
130	Snorers and OSAS patients referred to sleep clinic	Lower scores in all domains compared with normal population, especially in V, RP, SF, MH and RE. EDS and BMI negatively correlated with all domains and these parameters predicted worse QoL in PF, RP, GH, V, SF, RE and MH in adjusted models	[155]

AHI: Apnea–hypopnea index; BP: Bodily pain; EDS: Excessive daytime sleepiness; GH: General health; MH: Mental health; OSAS: Obstructive sleep apnea syndrome; PF: Physical functioning; QoL: Quality of life; RE: Role emotional; RP: Role physical; SF: Social functioning; SF-36: 36-item Short Form Health Survey; V: Vitality.

experience excessive sleepiness during shifts and symptoms of insomnia in recuperation periods, a condition that is called 'shift wake–sleep disorder' (SWSD) [2,180]. Approximately 10% of night-shift workers suffer from SWSD, a condition associated with an increased risk of adverse health outcomes, depression, increased absenteeism and employee turnover compared with night-shift workers without SWSD [181]. It seems that those working in backward-rotating systems and night shifts have the most pronounced risk of developing SWSD [182].

The sleep–wake pattern is disturbed in shiftworkers, and sleep problems are commonly reported and have also been verified by objective measures [183]. The most troublesome sleep-related symptoms include difficulties of initiating sleep, shortened sleep, impaired sleep quality between shifts and somnolence during working hours [176,181,183]. In a study of healthcare professionals from five nations, night-time workers reported feeling more tense and tired, both physically and mentally, compared with daytime workers [184,185]. High levels of fatigue leads to deficits in sustained attention and psychomotor performance, which has been confirmed in shiftworkers as the hours of the night shift progress [186]. Although it had been previously suggested that domestic responsibilities for women contributed to work-related fatigue, a recent study of full-time shiftworker nurses found that having dependents was protective against the development of maladaptive fatigue [185]. Disruption of the circadian rhythm may lead to impaired cognitive performance in the long term, as suggested by a study on jet lag [187]. Rouch *et al.* found that employees carrying out shiftwork for a long period of time had worse performance on speed and memory tasks compared with non-shiftworkers [188]. A particular relevance of these symptoms is that they may hamper job performance, productivity and safety [189].

Working shifts interferes with family life and imposes restrictions on the workers' community and leisure activities, leading to social isolation in a day-tuned society [175,190,191]. Spouses of shiftworkers also complain of significant disturbances in social and domestic life [192–194]. In a study of 2570 individuals, working in night or rotating shifts was associated with a significantly higher rate of missed family or social occasions [181]. Irregular hours also impose a major challenge for emergency practitioners, impacting their wellbeing and longevity [195]. Alternating shifts have been suggested to contribute to the high divorce rate, burnout and high attrition rate among healthcare providers [175,194,196].

In a large epidemiological study, SWSD was associated with depression and neuroticism, as assessed by the Diagnostic Interview Schedule and Eysenck Neuroticism Scale, respectively [181].

Adjustments to disruption of the sleep–activity cycle are not uniform; biological factors [197], family, social environment, work load, shift type [198], health-related behaviors [199] and personality traits [200] may all contribute to interindividual differences in susceptibility to the negative effects of shiftwork. In a cross-sectional study, Kaliterna *et al.* compared shiftworkers with a schedule that included night shifts, shiftworkers without night shifts and non-shiftworkers using the QoL Profile Questionnaire [201]. Both groups of shiftworkers reported that more physical effort was required to complete their work and felt that the same work was more physically tiring. Shiftworkers with night shifts also perceived fewer opportunities to improve their fitness and to participate in leisure activities or hobbies than the two other groups. However, there were no differences regarding overall happiness, life satisfaction or overall QoL between groups. Night shiftworkers reported lower QoL in spirituality than non-shiftworkers, that is, they experienced less enjoyment in pursuing their personal values and standards.

This cohort also reported disruptions to their community life, including the availability of health and social services, recreational and educational activities, as well as to family and other social events.

Effect of treatment in shiftworkers

A number of treatment strategies are available for sleep–wake disturbances resulting from shiftwork. Nonpharmacological interventions include taking naps [202], improving sleep hygiene, taking exercise and using light therapy [180]. Caffeine may have the potential to improve alertness and performance, but it may also have adverse effects such as insomnia and anxiety [203]; therefore, it should be used with caution. Sleeping pills and stimulants might not be able to fully prevent symptoms of maladjustment and may induce unwanted effects, including hangover, tolerance and withdrawal; consequently, these should be avoided or used cautiously in SWSD [204]. In a double-blind, randomized trial, taking 200 mg modafinil before each shift compared with placebo reduced, but did not eliminate, excessive sleepiness and impairment in performance among patients with SWSD [205]. Conversely, in a recent study with a similar design, modafinil significantly improved patient functioning (measured by the Functional Outcomes of Sleep Questionnaire) and also improved scores on the mental components of the SF-36 QoL questionnaire [206].

Preventive or countermeasures can also be applied at the organizational level; both allowing employees to be involved in shift scheduling and implementing shiftwork lifestyle-training programs can significantly improve health and fatigue indices and reduce turnover and absenteeism [207].

Conclusion

Sleep disorders are not restricted to night hours but they have a profound effect on our everyday daytime functioning, productivity, home, travel and workplace safety, mental and physical wellbeing and QoL. This review only covered the most common sleep disorders (i.e., insomnia, RLS, OSAS and shiftwork-related sleep disorder), but we must acknowledge that there is a large variety of less common sleep disorders that also have deleterious effects on the overall wellbeing and QoL of the individuals affected.

Expert commentary

Sleep disorders are not readily recognized; consequently, they are frequently undiagnosed and undertreated in the general population. The full spectrum of pervasive effects of impaired sleep on daytime functioning and wellbeing is still not understood. As an example, more qualitative research would be required in areas such as the dysfunctional cognition and social problems associated with sleep problems.

Differentiating between patients with primary versus comorbid insomnia would help to identify clinical subgroups more accurately. More stringent classification would be essential to improving the design of therapeutic clinical trials. Several assumptions regarding dysfunction in chronic insomnia are based on studies with sleep-deprived but otherwise healthy patients, while a growing number of studies indicate that chronic insomnia is completely different from sleep deprivation.

Female gender is a risk factor for developing insomnia and RLS, although the reason for this is unclear. On the other hand, women seem to be more susceptible to the direct health consequences of shiftwork, and growing evidence suggests that females are as afflicted by OSAS as males, only they are characterized by a different set of daytime symptoms. Exploring gender differences in the etiology, prevalence, clinical manifestation and consequences of sleep disorders is an important research objective. The same holds true regarding investigating sleep problems in different age groups and specific clinical subpopulations.

The complex inter-relationships of excessive daytime sleepiness, fatigue, daytime cognitive functioning and QoL in patients with chronic sleep disorders are unclear, and prospective studies carefully designed to focus on these issues are desirable.

Currently, the effects of treatment on QoL and daytime functioning are not well understood and there is a need to develop disease-specific instruments to assess patient-reported outcomes.

Five-year view

A greater number of longitudinal studies will address the temporal relationship between sleep disorders, chronic sleep deprivation and measures of QoL. Furthermore, as patient-reported outcomes become more widely accepted in clinical trials, the development of tools assessing disease-specific QoL issues can also be expected.

Advancements in genetics and neuropsychology may provide further insights into the individual differences in susceptibility to developing sleep disorders and allow us to better characterize individual sensitivity to the development of daytime symptoms. The accumulated knowledge should also help to design more individualized therapeutic strategies.

Policy makers will become more aware of the global consequences of sleep problems. Hopefully, intervention strategies will be encouraged in order to reduce the cost of sleep disorders to occupational performance and safety, accidents, absenteeism and healthcare utilization.

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Key issues

- Sleep disorders such as insomnia, restless legs syndrome, sleep apnea and shiftwork sleep disorder occur frequently in the general population.
- The prevalence of sleep disorders is higher in patients with acute or chronic medical or mental health disorders.
- Sleep disorders are under-recognized problems.
- Sleep disorders are associated with impaired mental health and physical health, as well as a reduced quality of life.
- Various negative daytime consequences include sleepiness, depressed mood, social isolation and decreased productivity.
- Patients usually seek professional help because of daytime symptoms and/or dysfunction.
- Treatment potentially alleviates or reduces negative daytime symptoms and improves quality of life, although more research is clearly desirable in this area.
- Specific clinical subpopulations suffering from sleep disorders should be identified for more targeted interventions.

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