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Review Article

A narrative review of interventions for improving sleep and reducing circadian disruption in medical inpatients

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ABSTRACT

Sleep and circadian disruptions are frequently observed in patients across hospital wards. This is alarming, since impaired nocturnal sleep and disruption of a normal circadian rhythm can compromise health and disturb processes involved in recovery from illness (eg, immune functions). With this in mind, the present narrative review discusses how patient characteristics (sleep disorders, anxiety, stress, chronotype, and disease), hospital routines (pain management, timing of medication, nocturnal vital sign monitoring, and physical inactivity), and hospital environment (light and noise) may all contribute to sleep disturbances and circadian misalignment in patients. We also propose hospital-based strategies that may help reduce sleep and circadian disruptions in patients admitted to the hospital.

1. Introduction

Poor sleep patterns and circadian rhythm disruption considerably impact health [1–4]. By utilizing data from more than 1.1 million men and women from 30 to 102 years of age from the Cancer Prevention Study II of the American Cancer Society it has been shown that short-duration sleepers experienced increased mortality hazard (15% for those reporting less than 3.5 or 4.5 h), compared with those reporting 7 h sleep per night [1]. In a separate study involving 185 healthy older adults, primarily in their 60s through 80s, sleep efficiency less than 80% (ie, less than 80% of the time in bed asleep) was associated with a ~2-fold greater mortality risk [2]. Finally, in a cohort of 28,731 female nurses (aged $\geq$ 44 years), night shift work – known to cause circadian disruption - increased all-cause mortality (HR: 1.26) [5]. Collectively, it is not surprising that proper sleep (for a brief description of sleep stages and sleep architecture, see Fig. 1) and maintenance of a robust circadian rhythm are widely seen as essential for a long healthy lifespan.

Although hospitalized patients represent a very heterogeneous population, in general they frequently suffer from sleep and circadian rhythm disruption. For example, 93 middle-aged general internal medicine inpatients (aged: 60.6 ± 20.3 years) reported about 1.5 h shorter nocturnal sleep duration in hospital than at home, accompanied with poorer subjective sleep quality [6]. The use of hypnotics to facilitate sleep is also much more prevalent among inpatients (>25%) compared to the general population (3%), although many patients do not suffer from sleep problems prior to hospital admission [7,8]. Moreover, 24-h constant bright light exposure, as is often found across hospital wards (eg, at intensive care units, ICUs), may considerably disrupt patients' normal circadian rhythm. Light suppresses the production of the pineal gland hormone melatonin [9] that advances the circadian timing of sleep, but also plays an important role in immunity and recovery. Disruptions to the sleep-wake cycle in hospitalized patients are of considerable concern, as they may alter diagnostic characteristics (eg, increased odds of having hyperglycemia during morning's blood testing), increase the risk of post-surgery complications, lower pain threshold, prolong the length of hospital stay, and

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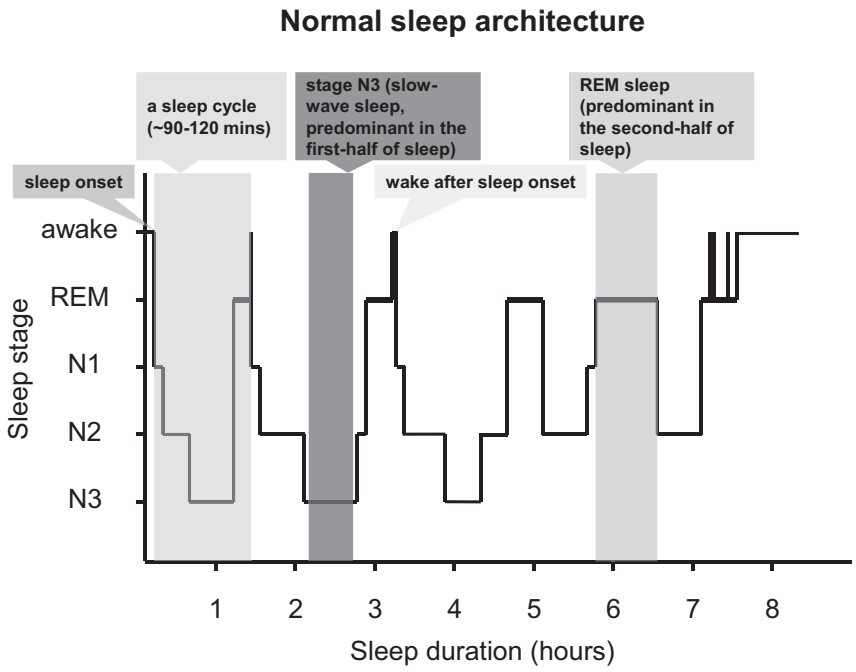

Fig. 1. Normal sleep architecture. Sleep in humans consists of four distinct sleep stages: sleep stage N1, N2, slow-wave sleep (SWS; also known as N3), and rapid-eye movement (REM) sleep. Nocturnal sleep consists of 4–6 sleep cycles. In the first hours after sleep onset, SWS typically predominates, whereas REM sleep is more prevalent in later parts of sleep.

reduce graft survival [10–15]. Therefore, improving sleep and reducing circadian rhythm disruption in hospitalized patients need to become a high priority. With this in mind, the present narrative review discusses how patient characteristics, hospital routines, and hospital environment may all contribute to sleep and circadian disruptions in patients. We also propose hospital-based strategies that may help reduce sleep disturbances and circadian misalignment in patients admitted to the hospital.

2. Patient characteristics

2.1. Insomnia

Insomnia is defined as persistent difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep, and results in daytime impairment [16]. The symptoms of insomnia can be assessed using the Insomnia Severity Index (ISI) [17]. Primary chronic insomnia is prevalent among 6–11% of the general population [18,19]. In addition to the pre-existing chronic insomnia, new onset insomnia in the form of adjustment insomnia is common during hospital stay. Typical triggers for transient adjustment insomnia are stress, significant life changes, and external environmental causes (eg, noise). In this way, new onset transient insomnia at hospital can be regarded as a normal response. Accordingly, in a group of 205 general inpatients, 36% had newly onset of insomnia during hospitalization [20]. Consequently, hypnotics including benzodiazepine receptor agonists (Z drugs) and benzodiazepines are frequently used by hospital staff to alleviate insomnia symptoms among inpatients. A retrospective study found that 26% of hospital patients (n = 642) were treated with hypnotics, most frequently trazodone (30%), lorazepam (24%) and zolpidem tartrate (18%) [7]. A separate study found that 29% of the patients without pre-admission hypnotic use (n = 100) received sleep medication during admission, of which the majority were zopiclone and benzodiazepines [21].

Though Z drugs and benzodiazepines are beneficial in curtailing sleep onset latency and possibly promoting melatonin secretion [22], some (eg, estazolam, temazepam) have been shown to reduce slow-wave sleep [23]. This sleep stage plays an important role for immune functions, maintenance of brain health, and energy metabolism [24–26]. In addition to their effects on sleep, Z drugs and benzodiazepines exert various side effects, including drowsiness, cognitive impairment, and increased risk of delirium [27,28]. Among patients with impaired glucose metabolism (eg, type 2 diabetes mellitus), administration of Z drugs and benzodiazepines may further disrupt daytime glycemic control [29]. Despite these side effects, the use of hypnotics among inpatients is alarmingly high. For example, a recent investigation involving 1308 elderly patients showed that 15.9% received benzodiazepines or zopiclone to treat sleep problems [30]. Further arguing against the excessive hypnotic use in hospital, a systematic review did not find sufficient evidence that pharmacotherapy (including benzodiazepines, non-benzodiazepine sedatives, melatonin, propofol, and dexmedetomidine) improves the quality or quantity of sleep in hospitalized patients with sleep complaints [31].

An additional problem of hypnotic use, especially concerning benzodiazepines and Z drugs, is that patients may suffer from rebound insomnia as well as rebound anxiety after being discharged from the hospital; without having access to sleep medication [32,33]. The use of less addictive or habit-forming sleep aids may help avoid such adverse effects. Suvorexant, which antagonizes signaling of the wake-promoting hypothalamic neuropeptide orexin, has been shown to be effective at decreasing sleep onset latency and increasing total sleep time in patients with insomnia [34,35]. Discontinuation after one year administration of suvorexant (40 mg/day, aged<65 years; 30 mg/day, aged $\geq$ 65 years, n = 522) showed no significant withdrawal effect; however rebound insomnia was detected compared to the placebo group (n = 259) [35]. Ramelteon is a selective melatonin receptor agonist which shortens sleep onset latency in adults with symptoms of insomnia. Following the discontinuation of a six month ramelteon

administration (8 mg/night, 30 min before bedtime), patients with chronic insomnia (n = 227) showed no withdrawal symptoms or rebound insomnia [36]. Nevertheless, ramelteon does not improve difficulties in sleep maintenance (ie, the most common symptom of insomnia) [37]. Moreover, suvorexant and ramelteon still have side effects similar to other sleep agents, with daytime somnolence being the most common. Hence, whenever hypnotics are prescribed for inpatients, relevant guidelines regarding symptom evaluation and choice of medication must be strictly followed [38,39].

Cognitive behavioral therapy for insomnia (CBT-I is recognized as the first-line treatment for chronic insomnia [39]. A single 1-h session of CBT-I (n = 20) showed sufficient efficacy for alleviating acute insomnia, with a lower ISI score compared to non-intervention controls (n = 20) at one month follow-up (Cohen's d = 0.64) [40]. This suggests that CBT-I could be introduced in hospital settings to ease adjustment insomnia among inpatients. The treatment effects of CBT-I have also been studied among patients with severe diseases. A study in 111 cancer patients showed that a two month CBT-I induced a rapid and durable mitigation of insomnia severity (Cohen's d = 2.59, ISI score at two month compared to baseline; Cohen's d = 2.41, five month compared to baseline) [41]. A meta-analysis involving patients with secondary insomnia (including patients with chronic pain, cancer, and coronary artery disease) showed that CBT-I significantly improved sleep quality as measured by the ISI (weighted mean difference (WMD), CBT-I vs. no intervention or sleep hygiene education: −6.36, SE: 1.27, n = 566), sleep onset latency (WMD, CBT-I vs. comparators: −20.68 min, SE: 3.27, n = 824), and wake after sleep onset (WMD, CBT-I vs. comparators: −20.79 min, SE:3.60, n = 733) [42]. However, despite the promising effects of CBT-I on insomnia in outpatient populations, to date there is no trial regarding the effect of CBT-I on inpatients. Finally, training to improve the understanding of normal sleep, sleep pathology, and the factors that can precipitate sleep disturbances could provide a broader context for clinical staff to interpret the sleep complaints of their patients, evaluate outcomes of sleep-promoting interventions, and guide decision making regarding referrals.

2.2. Obstructive sleep apnea

Sleep-disordered breathing (SDB), most commonly obstructive sleep apnea (OSA), considerably influences patients' disease progression and recovery. OSA is hallmarked by full or partial cessation of breathing (namely apnea and hypopnea) during sleep due to the collapse of upper airway structures. The severity of OSA is classified by the apnea-hypopnea index (AHI) as mild: $5 \leq$ AHI<15 per hour, moderate: $15 \leq$ AHI<30 per hour, or severe: AHI$\geq$30 per hour.

Apneas or hypopneas lead to decreased oxygen saturation, elevated blood pressure, and fragmented or light sleep [43]. OSA and other SDB disorders affect 10–17% of men and 3–9% of women in the general population, of whom the majority are undiagnosed and untreated [44,45]. In a study involving 2877 surgical patients, 81% of the 661 patients screened with high-risk for OSA had not been diagnosed before [45]. Several populations have a significantly higher prevalence of OSA, including individuals with obesity (up to 55%) [44], type 2 diabetes (50–90%) [29], and cardiovascular diseases (>50%) [46]. In hospitalized patients, OSA has been associated with an increased risk for cardiopulmonary complications, unplanned reintubations, and postoperative myocardial infarction [47]. Moreover, a study involving 1022 patients found that those with OSA (68% of the population) had a doubled risk of stroke or death, independent of other risk factors [48].

Early screening and treatment of OSA are important for inpatients, and standard diagnostic guidelines are available [49]. Polysomnography (PSG) is the gold standard method for diagnosing OSA. However, this technique is rarely available in general clinical settings. Alternatively, several questionnaire-based screening tools are available, such as the STOP BANG questionnaire [50] and the Score for Preoperative Prediction of OSA for the surgical ward [51]. However, the sole use of questionnaires for screening OSA is not recommended in clinical practice due to their variations in accuracy and specificity across different patient populations [52–54]. Continuous pulse oximetry can help to confirm the presence of OSA (through dipping in oxygen saturation) [55,56]. Studies in children referred to a pediatric respiratory clinic have revealed a considerable night-to-night variability in overnight oximetry [57]. This suggests that while a positive result of pulse oximetry from one night can be used to make a diagnosis of OSA, a negative result cannot rule it out. Therefore, repeating the overnight oximetry may give more confidence in initially negative findings. An alternative screening method for OSA is cardiorespiratory polygraph recording. This method uses nasal/oronasal airflow, chest wall and abdominal movements, and oxygen saturation. Recent data obtained from 27 boys and 23 girls, with a mean age of 5.3 ± 2.5 years, suggest that cardiorespiratory polygraphy achieves adequate sensitivity (90.9%) and specificity (94.1%) for diagnosis of OSA, although it may fail to accurately recognize milder forms of condition [58].

Continuous positive airway pressure (CPAP) therapy is the first-line treatment for OSA and is applicable in hospital setting [59]. The adherence to CPAP treatment among inpatients diagnosed with moderate to severe OSA is of great clinical importance. Among 1973 inpatients with high OSA risk (defined as two or more yes responses to the four questions of the STOP questionnaire), adherence to the positive airway pressure treatment ($\geq$4 h/night) led to a lowering of rapid response system events rate, compared to patients with low treatment compliance or non-treatment (16.99 vs. 53.40 vs. 56.21/1000 admissions) [60]. Rapid response systems are commonly used safety protocols in hospitals throughout the United States to identify and quickly intervene to reverse serious and potentially fatal deterioration of patients in the general hospital population [61]. Another study among 345 inpatients revealed that adherence to CPAP ($\geq$4 h/night, $\geq$70% nights of a 30-day period) was associated with fewer hospital readmissions in general and due to cardiovascular events (ORs of non-adherent group: 3.52 and 2.31, respectively) [62]. A meta-analysis including 904 surgery patients with OSA showed that perioperative CPAP use was linked to a slightly shorter length of stay, compared to patients without CPAP treatment (4.0 ± 4 vs. 4.4 ± 8 days) [63]. Collectively, while these studies link CPAP adherence to improved clinical outcomes, another possible interpretation of these data could be that patients who are adherent to CPAP tend to be those who exhibit greater self-efficacy generally, and that it is the latter trait that mediates improved clinical outcomes, not CPAP per se.

In case of milder forms of OSA (ie, AHI<15), avoidance of supine posture (in which the airway is more likely to be obstructed among OSA patients) during sleep could help reduce the occurrence of apneas. This could be achieved by using the sleep position trainer, where a small vibration is generated whenever the patient is in the supine position [64].

2.3. Anxiety and stress

Hospitalization may cause anxiety and stress. Thus, transient (new onset) insomnia may be regarded as a normal response to anxiety in mentally healthy people. A meta-analysis of 2880 ICU survivors found that anxiety symptoms were present in one-third of the patients [65]. According to another study involving 166 general ward patients (aged 50 years), 18% perceived anxiety as a disruptor to their sleep [66]. Stress and anxiety result in sympathetic activation, increasing the risk of light and fragmented sleep

[67]. Various factors, including an unfamiliar environment, lack of control, uncertainty, and worries about disease progression could trigger stress and anxiety during hospital stay [68]. The Hospital Anxiety and Depression Scale is an easy and clinically effective screening tool for the assessment of psychological well-being among inpatients [69].

Cognitive behavioral therapy (CBT) has proven useful in treating anxiety. In a study in 40 patients with terminal cancer providing brief CBT tailored to the concerns of patients with terminal cancer (targeting skills for relaxation, coping with cancer worries, and activity pacing) led to significant improvements in anxiety [70]. As CBT is becoming better available via digital sources as a self-assistant tool [71], clinical trials in hospital patient groups are needed to examine the effect size of self-applied CBT to ease anxiety and promote sleep. Other low-key changes could also be favorable to lower anxiety during hospitalization. A study indicated that transparency of treatment and caretaking, feeling in control, being involved in decision making, and preserving integrity could decrease feelings of worry and improve sleep among inpatients [67]. But even nursing methods such as communicating information to patients and families, asking for and offering assistance, and being respectful and responsive to patient preferences could be hypothesized to further help reduce patients' anxiety and thereby improve their sleep.

2.4. Chronotype

A study in 117 general ward patients (mean age 48 years) hospitalized for>72 h showed that 56% reported earlier bed and wake times as a disruptor of their sleep [72]. The chronotype of a patient can help to predict the resilience to the dictated early sleep-wake schedule in the hospital. Whereas larks (ie, early chronotype) are most alert earlier in the day and will be less affected by the early-timed routines, night-owls (ie, late chronotype) are most alert later during the day. Thus, it could be hypothesized that the greater the mismatch between circadian preference and hospital schedules, the higher the risk of impaired sleep and circadian disruption.

In addition, the night−time activity of night owls could disturb sleep onset of larks in shared patient rooms. The most apparent solution would be to cluster patients with a similar chronotype into the same patient room, to avoid evening/morning disturbances, and to allow later-timed controls or treatments in the night owl chronotype. Treating late chronotype patients with a 30-min morning bright light exposure followed by afternoon melatonin administration could represent an additional solution for advancing the sleep-wake rhythm of late chronotypes [73].

As discussed in the "Hospital Environment" section, patients, especially those who are bed-bound, are often exposed to unnatural light conditions when admitted to the hospital (eg, constant bright light; less pronounced differences in indoor light characteristics between the day and night). Daily changes in light intensity function as a timing cue to adjust circadian phases [4]. Therefore, unnatural light conditions in the hospital may further exacerbate circadian misalignment in patients.

2.5. Disease-related melatonin deficiency

Decreases in melatonin occur in many disease conditions, such as migraine and other forms of severe pain, type 2 diabetes and insulin resistance, as well as certain types of cancer [74]. Decreased levels of melatonin have also been described in Alzheimer's disease [75,76]. Reduced transparency of the lens for blue light (eg, due to yellowing of the lens or cataract) may be another factor resulting in lower amplitude of melatonin rhythms, especially in older patients [77,78]. Oral administration of melatonin in the evening to restore the normal endogenous day/night rhythm of melatonin may be a strategy to overcome disease-related melatonin deficiency. Additionally, increased light exposure during the day, especially during morning hours, may further help reduce circadian misalignment in patients.

3. Hospital routines

3.1. Pain relief and timing of medication

Patients' sleep quality might deteriorate due to illness symptoms like pain, shortness of breath, nocturia, nausea, vomiting, diarrhea, or itching. Pain and sleep interact in a bidirectional manner [79], and could therewith cause a vicious cycle. Additionally, the side effects of medication following intake of beta-blockers or opioids may also impede patients' sleep [80,81]. Chronotherapy, referring to the appropriate timing of medication to relieve illness symptoms at times when they are most disruptive (eg, by targeting pain during nocturnal sleep) should be considered [12]. Conversely, drugs that interfere with sleep should be either avoided or administered at reasonable times (eg, diuretics in the morning to prevent nocturia). Evidence suggests an inhibitory effect of beta-blockers on melatonin release in humans [82], and counter-acting this effect by evening melatonin administration improved sleep in patients taking atenolol or metoprolol [83]. In addition to its well-known effects on sleep propensity, melatonin also possesses analgesic properties. Exogenous administration of melatonin has for instance been successfully used in the treatment of fibromyalgia, migraine and during surgical operations [84]. However, controlled trials in hospitalized patients are needed to confirm these findings. Nonsteroidal anti-inflammatory drugs (NSAID) are also known to disrupt sleep by increasing the number of awakenings and decreasing sleep efficiency, possibly due to suppression of melatonin [85,86]. It could be suggested that NSAID usage during daytime, and melatonin supplementation during the evening, may result in pain relief while simultaneously preserving sleep, depending on the patient's disease and pain condition.

3.2. Vital sign monitoring

Vital sign monitoring is an essential part of hospital routines. Yet, nocturnal measurements (normally repeated 2-3times overnight) could impair inpatients' sleep quality. A study in 166 inpatients found that 34% reported nocturnal monitoring procedure as a major sleep disrupter [66]. Another study (n = 54,096) identified that patients with significantly fewer adverse events (evaluated by the Modified Early Warning Score) had overnight vital signs taken at a similar rate as high-risk patients, which suggested the institutions to properly reduce the nocturnal vital sign monitoring for low-risk medical inpatients [87]. Moreover, an intervention study demonstrated that avoiding waking of patients for vital sign monitoring and medication administration between 10pm and 6am reduced the sedative use from 32% to 16% [88]. Currently, it is challenging to determine to what extent the frequency of nocturnal vital sign collection could be reduced without affecting inpatients' safety, and limited efforts have been made to address the issue. Another intervention is to introduce wireless technologies that transmit patient vital signs information to a central location (eg, heart rate, body temperature, and blood pressure). Some portable, continuous vital sign monitoring system have already been piloted in the clinical setting and might be promising for promoting sleep while safeguarding early recognition of possible deterioration [89].

3.3. Bed rest and physical activity

Daytime physical activity improves nighttime sleep [90] and supports the maintenance of a healthy circadian rhythm [91].

Conversely, good sleep has been associated with increased engagement in physical activity [92]. Therefore, reduced physical activity due to limited opportunities to engage in exercise or outdoor activities might result in impaired sleep and circadian disruption during hospitalization. This in turn may decrease daytime physical activity due to a lack of motivation. Multiple ways exist to break this vicious cycle, such as encouraging patients to take a walk outside, serving meals in a separate room, or offering bed exercises, all of which are likely to aid sleep and support the maintenance of a normal circadian rhythm. Additionally, such interventions increase exposure to natural light with additional direct positive effects on sleep and circadian rhythm [15]. Another common behavior among inpatients is napping. A daytime nap may compensate in part for less sleep at night, and promote recovery from acute illness. However, possible obstacles to the practice of napping exist (reviewed in Ref. [93]). For example, a long daytime nap can interfere with the following night's (main) sleep. Excessive napping might be a marker of other pathology, including undiagnosed sleep disorders, such as OSA (see section "Patient characteristics"). Therefore, naps should be purposeful and clinicians should encourage patient vigilance and activity outside of these times; otherwise patients may drift in and out of sleep all day and night.

Table 1
Possible interventions to aid sleep and strengthen circadian rhythm in medical inpatients.

	Sleep/Circadian rhythm disruptor(s)	Main characteristic(s)	Intervention
Patient characteristics	Insomnia	• Complaint of at least one of the following symptoms: difficulty initiating sleep, difficulty maintaining sleep, early morning awakenings	• CBT for insomnia (CBT-I), single session for acute cases
		• Pre-existing insomnia might be even more pronounced in the hospital setting due to stress, anxiety, and disease-related worries	• Hypnotics (must strictly follow the treatment guidance to reduce inappropriate use)
	OSA	• Recurrent episodes of full or partial cessation of breathing during sleep	• Initiation of CPAP for AHI $\geq$ 15
		• The severity of OSA is classified by AHI	• Patient should avoid supine position to improve airflow
		• Sleepiness and frequent napping during the day	
	Anxiety and stress	• Particularly common in psychiatry ward, ICU, and surgery ward	• CBT
		• May cause acute insomnia, short sleep, and poor sleep quality	• Transparency of treatment and caretaking
			• Communicate information to patients and families
	Chronotype	• Mismatch between individual's circadian preference and timing of hospital schedules can interfere with patients' normal sleep patterns	• High luminance in morning hours and dimmed light in evening hours to entrain patients' circadian rhythm to the timing of hospital schedules
		• Inter-individual differences in circadian preferences can cause sleep problems among patients sharing the same patient room	• Grouping of patients with a similar chronotype (larks, owls)
	Melatonin deficiency	• Prevalent among older patients and certain neurological disorders (eg, AD)	• Administration of melatonin in the evening to restore the normal day/night rhythm of melatonin
		• Causes circadian disruption	• Increased light exposure during the day, especially in the morning after awakening
Hospital routine	Pain and timing of medication	• Poor sleep quality can be caused by acute and (eg, after surgery) chronic pain (eg, fibromyalgia)	• Sleep-oriented pain relief
		• Medicine taken prior to nocturnal sleep can alter melatonin production and impair sleep (eg, nonsteroidal anti-inflammatory drugs; diuretics)	• Appropriate timing of medication to reduce side effects on sleep and melatonin
			• Administration of melatonin in the evening
	Nocturnal vital sign monitoring	• Disrupts sleep of inpatient and fellow roommates	• Distance technologies for patient monitoring
			• Reduced frequency of vital sign check-ups in patients at sufficiently low risk of clinical deterioration
	Physical inactivity	• Low engagement in physical activity can impair sleep and cause circadian disruption (eg, due to reduced light exposure)	• Encourage mild-level physical activity in patients
			• Encourage outdoor activities
			• Dining area and other indoor design which promote patients' engagement in physical activity
Hospital environment	Noise	• Night-time noise levels can reach up to 70 dB in general wards	• Earplugs (especially in ICU patients)
		• Even higher noise levels are found in ICU	• Limiting the volume of alarms of medical devices to $\leq$ 40 dB
		• A noise level below 30–45 dB is required to facilitate a good sleep environment	• White noise used to mask background sounds
			• Melatonin at bedtime
			• Architectural arrangements
	Light	• Low-luminance light exposure during morning hours and/or excessive evening light exposure can delay melatonin phase	• Bright light exposure during morning hours and reduced artificial evening light exposure
		• Evening light stimulus increases alertness	• Architectural arrangements, such as larger window in patient room
		• Less pronounced differences in indoor light characteristics between the day and night	• Smart light bulb systems to mimic natural light variations

Abbreviations: AD, Alzheimer's disease; OSA, Obstructive sleep apnea; CBT, cognitive behavioral therapy; CPAP, continuous positive airway pressure therapy; AHI, apnea-hypopnea index; ICU, intensive care unit.

4. Hospital environment

4.1. Noise

Typical hospital noise, such as talking, alarms, phones, and outside traffic triggers arousal and increases heart rate during rapid eye movement (REM) sleep in healthy adults [94]. Furthermore, noise can attenuate the magnitude of overnight melatonin release in healthy humans [95]. Thus, it could be speculated that noise in the hospital may lead to the development of sleep disturbances and circadian disruption in patients. Supporting this hypothesis, two studies in the general medicine and oncology wards (n = 92 and 166, respectively) found that 27–43% of patients identified noise as a major cause of poor sleep [66,96]. Acoustic measurements further revealed that the average noise level in the patient rooms was roughly 38 dB between 11pm and 7am, with a mean peak noise level of about 70 dB [96]. The latter is comparable to noise levels of a vacuum cleaner. In a separate hospital study, nocturnal noise levels were between 35 and 55 dB in patient rooms [97]. Even more harmful sound conditions were found in the ICU, where the average 24-hr noise level was over 45 dB, with a peak noise over 85 dB occurring 4–16 times per hour between 10pm and 5am [98]. To avoid possible negative effects on sleep, the sound pressure level should not exceed 30 dB (max peak noise: 45 dB), according to recommendations of the World Health Organization.

Using polysomnography, it has been shown in healthy adults that wearing earplugs ameliorated the noise effect on sleep under a four night mock ICU environment. Subjects (n = 10) fell asleep 24 min faster and the number of awakenings was reduced by 30%, compared with counterparts receiving no soundproofing equipment (n = 10) [95]. Another intervention arm (n = 10) in the same study with 1-mg melatonin administration at 9pm led to even better sleep quality [95]. Strategies such as limiting the volume of alarms of medical devices to 40 dB, using white noise [99], and changing patient room acoustics may further support inpatients' sleep [100]. However, further high-quality research is needed to strengthen the evidence base [101].

4.2. Light

Bright, preferably short wavelength light (ie, blue-enriched light) during morning hours supports the maintenance of a stable sleep-wake pattern and has been linked to increased nocturnal sleep quality [15,102]. Conversely, artificial blue-enriched light during evening hours delays the production of melatonin and impairs sleep quality [103]. Therefore, it is not surprising that unnatural light characteristics often found in the hospital may contribute to impaired sleep and circadian disruption. Advocating this hypothesis, a study involving 40 acute care inpatients (length of stay 72 h) observed that the mean luminance in the patient room was about 100 lux between 6am and 10pm, opposed to luminance typically found in normal living environments (office: 500 lux) [104]. The sleep duration of these inpatients was less than 4 h per day [104]. In addition to dim-light conditions during daytime, medical inpatients are often subjected to light during evening and night hours. For example, the maximal nocturnal luminance in ICU can reach as high as 1000–3000 lux [105]. This could explain why ICU patients lack the typical nocturnal peak of melatonin secretion and show a delayed circadian rhythm [106,107].

Either mimicking 24-h natural light variations in patient rooms, or exposing patients to natural light conditions during morning hours may aid their sleep and help entrain their circadian rhythms. A recent study investigated the effects of a dynamic lighting system on sleep among 196 cardiology ward patients. The system mimicked a natural light pattern, generating 300 lux, 4000 K light between 8am and 6pm, together with an enhanced luminance (blue-enriched light of 1750 lux, 6500 K) between 10:30am–12:30pm and a reduced luminance (100 lux, 3000 K) between 1:00pm and 2:00pm. During evening hours, reading lights with adjustable luminance (max 300 lux) were used by patients to restrict the light exposure when room light was dimmed. Patients of the intervention group slept around 30 min longer compared to patients under conventional light conditions [108]. A different study implementing enhanced light exposure during morning hours (from 9:00am to noon) in ICU patients (n = 11) found that the bright light exposure resulted in improved circadian synchronization and earlier timed rhythms [107]. In summary, construction measures and smart applications of ambient light could considerably aid sleep and strengthen circadian rhythm in medical inpatients.

Another condition frequently found in the hospital is that natural light is not evenly distributed within and between patient rooms. This may hamper the ability of patients laying further from the window to be in sync with the natural light/dark cycle, with possible undesirable implications for sleep and health. A study involving 99 inpatients showed that those whose beds were located closer to the window (distance<1 m) in the patients' room slept better, compared to those laying further from the window (distance >3 m; 7.3 ± 1.8 vs. 5.8 ± 2.4, 1–10 scale) [109]. Moreover, a study involving 1057 patients from internal, otolaryngology, surgery, and gynecology wards pointed to a role of natural daylight exposure on patients' length of stay. Patients located in southwest facing rooms (200–300 lux; mean 220 lux between 8am and 6pm) had a 29% shorter average length of stay, compared to patients in the northwest facing rooms (70–230 lux; mean 101 lux) [110]. Furthermore, sunnier compared to darker hospital rooms were associated with shorter length of stay and lower mortality in patients with myocardial infarction (n = 628) [111]. These studies implicate that circadian disruption due to weak light exposure may adversely affect patients' health and recovery.

5. Conclusions

Sleep disturbances and a disrupted circadian rhythm are prevalent among patients across hospital wards. Multiple causes exist (summarized in Table 1), including but not restricted to constant bright light conditions, low 24-h light amplitudes, noise due to staff activities or medical devices, hospital routines such as nocturnal vital sign monitoring, reduced physical activity, anxiety related to hospitalization, existence of specific sleep disorders, and a mismatch between the patient's chronotype and timing of the hospital schedule. At first glance, the complexity of factors contributing to sleep problems and circadian disruption might discourage hospital staff to tackle this problem. Moreover, there is limited evidence from randomized clinical trials testing to what extent strategies targeting these factors may improve sleep and stabilize circadian rhythm in patients of various wards and age. Conversely, any effort is likely to pay off as sleep and factors under circadian control (eg, melatonin supporting immunity and reducing pain sensitivity) lower the risk of post-surgery side effects, and decrease the risk of delirium [112–116].

Contributors

X.T., L.v.E., M.P., T.L., and C.B. did the literature search; X.T. and C.B. drafted the figure; X.T., L.v.E., M.P., T.L., and C.B. discussed and wrote the review. All authors equally contributed to this manuscript.

Declaration of interests

M.P. reports other from Bioprojet, other from Jazz Pharmaceuticals, personal fees from UCB- Pharma, personal fees from GSK, personal fees from Takeda, personal fees from MSD, other from Idorsia, other from Avadel, personal fees from Pfizer, other from Umecrine, outside the submitted work. The other authors have nothing to disclose and no conflicts of interest to report. The authors are unaware of any affiliation, funding, or financial holdings that might be perceived as affecting the objectivity of this review article.

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Conflicts of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.08.007.

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