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Interventions to Improve Sleep and Their Impact on Work and Daytime Impairment

Thesis for the Degree of Philosophiae Doctor

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Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
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Norsk tittel: **Intervensjoner for å forbedre søvn og deres innvirkning på arbeids- og dagtidsfunksjon**

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Sammendrag

Mange mennesker sliter med dårlig søvn, noe som også påvirker hvordan de fungerer på jobb og på fritiden. Ulike behandlinger (eller intervensjoner) for søvnproblemer, for eksempel kognitiv atferdsterapi for insomni (KAT) eller lys- og mørketerapi (hvor eksponeringen for lys gjennom døgnet reguleres), kan være svært effektive og føre til bedre søvn. Det er imidlertid uvisst om slik behandling også fører til at man fungerer bedre på dagtid.

Målet med denne doktorgraden var å undersøke hvordan ulike intervensjoner påvirker både søvn og funksjonsnivået på dagtid. Dette ble gjort gjennom fire forskningsstudier. De to første studiene undersøkte sammenhengen mellom søvnvansker og arbeidsfunksjon hos personer med insomni og om bedre søvn også førte til bedre arbeidsfunksjon. Deltakerne ble enten gitt søvnbehandling (KAT) eller generell informasjon om gode søvnvaner. Den tredje studien undersøkte effekten av blåblokkert belysning (hvor de blå frekvensene som finnes i vanlig lys er fjernet) sammenlignet med standard sykehusbelysning på søvn, søvnighet og kognitiv prestasjon i en gruppe med friske voksne. Blåblokkert belysningen er installert i deler av den nye akuttpsykiatriske avdelingen på St. Olavs Hospital i Trondheim, og i den fjerde studien undersøkte vi hvordan slik belysning på arbeidsplassen påvirket søvnen og arbeidsfunksjonen til sykepleiere som jobbet kvelds- og/eller nattevakter.

Resultatene fra de to førte studiene viste at de som hadde mindre søvnproblemer etter behandlingen fungerte bedre på jobb og på fritiden seks måneder senere. Det å bli kvitt søvnproblemene var også det som førte til bedret funksjonsnivå på dagtid. Den tredje studien

viste at å oppholde seg i blåblokkert lys påvirket søvnmønsteret til deltakerne slik at de ble trøtte tidligere på kvelden og sov litt bedre. Den fjerde studien viste at det ikke var noen forskjeller i søvn og arbeidsfunksjon avhengig av om sykepleierne jobbet i blåblokkert belysning eller standard sykehusbelysning, bortsett fra at den blåblokkerte belysningen gjorde sykepleierne litt trøttere på kveldstid.

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Summary

Background and aims. Sleep problems are prevalent in modern society and have significant adverse effects on individual health and well-being. In the general population, insomnia disorder is the most reported sleep problem. In clinical settings, sleep problems often co-occur in patients with other health conditions; for example, disturbances in the sleep–wake cycle are common features of a wide range of mental health conditions. In recent decades, research has identified several different interventions that are efficacious for insomnia and other sleep disturbances, such as cognitive behavioral therapy for insomnia (face-to-face or digital CBT-I) and light and dark therapies (where light exposure is manipulated). However, there is a gap in our understanding of whether these different treatment strategies also improve daytime functioning. This issue is not only of theoretical importance but also likely to impact on the quality of life of the individual and their capacity to participate in work and other activities. Furthermore, the economic consequences of nighttime sleep disturbances are partly explained by the associated daytime impairment in daytime functioning. As such, the main aim of the thesis was to investigate the effect of different interventions on both sleep and daytime functioning. This was achieved through a sequence of four studies. Studies 1 and 2 explore the effect of CBT-I on work- and sleep-related outcomes in the general population and examine whether improvement in insomnia symptoms mediate improvement in work and activities outside of work. Study 3 explores the impact of exposure to a blue-depleted lighting environment compared with a standard lighting environment on biological markers of sleep, circadian rhythms, and neurocognitive functioning in healthy volunteers. These two lighting systems have been installed at the new acute psychiatric unit at St. Olavs Hospital (in Trondheim, Norway), and, as reported in study 4, this also allowed us to explore the impact of different lighting environments on the sleep patterns and work functioning of nurses engaged in shift work.

Methods. Studies 1 and 2 used data about (i) a subsample of currently employed adults who participated in a randomized controlled trial (RCT) of face-to-face versus digital CBT-I (n = 77) and (ii) a community-residing sample of participants in a large-scale RCT of online CBT-I versus psychoeducation (n = 1721). Analyses investigated the effects of CBT-I on presenteeism (reduced productivity while at work), activity impairment (in activities outside of work), absenteeism (scheduled work time missed), and employment status (binary measure) 6 months after treatment and whether the improvement in insomnia symptoms (from baseline to 9-week follow-up) mediates the improvements in work- and activity-related outcomes observed at 6-month follow-up. Study 3 recruited 12 healthy adults to a cross-over RCT, and data were collected on sleep (measured with actigraphy, polysomnography, and radar technology), circadian rhythms (estimated based on melatonin levels in saliva samples), neurocognitive functioning (measured with a performance test), subjective sleepiness (based on questionnaires), and side effects (based on questionnaires) to evaluate potential side effects of the lighting systems. In study 4, nurses working shifts in the hospital inpatient unit (n = 25) were recruited to a non-randomized 12-week cross-over trial of the effects of a blue-depleted work environment on performance at work (measured with work diaries), sleep (measured with sleep diaries and actigraphy), medical and mental health (based on questionnaires), and side effects (based on questionnaires).

Results. Study 1 showed that participants reported lower levels of presenteeism at work ($p = .001$; Cohen's $d = 0.46$) and impairment in activities outside of work ($p < .001$; Cohen's $d = 0.66$) at 6-month follow-up compared with baseline. Further, individuals who met the criteria for remission reported lower levels of presenteeism ($p = .002$; Cohen's $d = 0.45$) and activity impairment ($p = .006$; Cohen's $d = 0.69$) compared with those who did not meet the criteria for remission. In study 2, there was a significant total effect of dCBT-I compared with psychoeducation on activity impairment (estimated effect −5.6%) and an

indirect effect of improvement in insomnia symptoms on presenteeism and activity impairment (estimated effect −5.4% and −5.5%, respectively) at 6-month follow-up. However, there were no effects on absenteeism (studies 1 and 2) or employment status (study 2). In study 3, the healthy volunteers exhibited greater phase advancement of circadian sleep rhythms compared with baseline (1:20 hours in blue-depleted light environment vs. 0:46 hours in standard hospital lighting; $p < .001$). In addition, residing in a blue-depleted light environment was associated with an increase in total sleep time (by 8.1 min; $p = .032$) and time in rapid eye movement sleep (by 13.9 min; $p < .001$). There were no differences in the ratings of subjective sleepiness or side effects between conditions but some indication of differences in neurocognitive functioning. Study 4 demonstrated that nurses showed increased sleepiness (+17%) during evening shifts in the blue-depleted compared with the standard hospital light environment ($p = .034$; Cohen's $d = 0.49$) and a 0.2 increase in the number of cups of caffeinated beverages consumed during night shifts in the standard lighting condition compared with the blue-depleted light environment ($p = .027$; Cohen's $d = 0.37$). No other significant differences were reported between conditions on other subjective (diary) or objective (actigraphy) outcome variables.

Conclusions. While insomnia and poor sleep affect many individuals, available interventions (e.g., CBT-I or use of blue-depleted lighting) may be beneficial. Taken together, the findings from this thesis show that CBT-I not only improves insomnia symptoms but also demonstrate that it is the reduction in the severity of insomnia symptoms that led to positive effects on work and daily activities. Further, it was demonstrated that, compared with a standard lighting condition, a blue-depleted light environment was associated with improved sleep for healthy volunteers who resided in each environment for five days and did not have any significant adverse effects on nurses' sleep or work functioning when engaged in shift work under such conditions. The reported findings require replication and confirmation in

studies specifically designed to test the direct and indirect effects of sleep and altered light interventions on daytime functioning. However, the findings from this sequence of studies are encouraging, as they point toward the positive impact of sleep interventions on work and other activities in addition to the absence of negative effects on those exposed to different lighting environments.

List of Papers

Paper 1

Kjørstad, K., Sivertsen, B., Vedaa, Ø., Langsrud, K., Faaland, P. M., Vethe, D., Vestergaard, C. L., Scott, J., & Kallestad, H. (2021). The Effect of Reducing Insomnia Severity on Work- and Activity-Related Impairment. *Behavioral Sleep Medicine, 19*(4), 505–515. https://doi.org/10.1080/15402002.2020.1799792

Published: July 30, 2020

Paper 2

Kjørstad, K., Sivertsen, B., Vedaa, Ø., Langsrud, K., Vethe, D., Faaland, P.M., Vestergaard, C.L., Lydersen, S., Smith, O.R.F., Scott, J., & Kallestad, H. The effects of digital CBT-I on work productivity and activity levels and the mediational role of insomnia symptoms: Data from a randomized controlled trial with 6-month follow-up.

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Paper 3

Vethe, D., Scott, J., Engstrøm, M., Salvesen, Ø., Sand, T., Olsen, A., Morken, G., Heglum, H. S., Kjørstad, K., Faaland, P. M., Vestergaard, C. L., Langsrud, K., & Kallestad, H. (2020). The evening light environment in hospitals can be designed to produce less disruptive effects on the circadian system and improve sleep. *Sleep*. https://doi.org/10.1093/sleep/zsaa194

Published: September 21, 2020

Paper 4

Kjørstad, K., Faaland, P.M., Sivertsen, B., Kallestad, H., Langsrud, K., Vethe, D., Vestergaard, C.L., Harris, A., Pallesen, S., Scott, J., & Vedaa, Ø. Sleep and Work Functioning in Nurses Undertaking Inpatient Shifts in a Blue-Depleted Light Environment.

Submitted: January 26, 2022 (at review)

List of Abbreviations

BDLE	Blue-Depleted Light Environment
CBT-I	Cognitive Behavioral Therapy for Insomnia
dCBT-I	Digital Cognitive Behavioral Therapy for Insomnia
EMA	Early Morning Awakening
ISI	Insomnia Severity Index
RCT	Randomized Controlled Trial
SE	Sleep Efficiency
SHUTi	Sleep Healthy Using the Internet
SIBS	Number of sleep periods
SOL	Sleep Onset Latency
SPT	Sleep Period Time
STLE	Standard Hospital Light Environment
TIB	Time in Bed
TST	Total Sleep Time
WASO	Wake After Sleep Onset
WPAI	Work Productivity and Activity Impairment Questionnaire

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Introduction

Sleep is ubiquitous, yet it remains 'one of the last great biological mysteries' (Walker, 2017), and its function has been compared with the mythological phoenix:

> That there is one they all say, where it may be no one knows.
>
> (Wolfgang Amadeus Mozart, 1790, as cited in Cirelli & Tononi, 2008)

Sleep and dreaming have fascinated humans for thousands of years. For example, a story in the Old Testament describes that the king of Egypt once dreamt about seven fat, healthy cows and seven ugly, skinny cows. Joseph interpreted the king's dream as a warning from God about seven years of plenty to come, followed by seven years of famine – thus saving Egypt from destruction. After the Second World War, an example of dreaming as a temporary (yet terrible) escape from reality was described by Victor E. Frankl in his book *Man's Search for Meaning* through a recollection of an incident during his imprisonment in a concentration camp. He wrote that:

> I shall never forget how I was roused one night by the groans of a fellow prisoner, who threw himself about in his sleep, obviously having a horrible nightmare. (…) I wanted to wake the poor man. Suddenly I drew back the hand which was ready to shake him. (…) At that moment I became intensely conscious of the fact that no dream, no matter how horrible, could be as bad as the reality of the camp which surrounded us, and to which I was about to recall him.
>
> (Frankl, 1959)

In Greek mythology and the Iliad, Hypnos, the god of sleep and the son of the night, was praised as a bringer of peace and escape from horrors. Interestingly, Hypnos' twin brother was the god of death, possibly reflecting the instant likeness between the two states from an

observer's point of view, as, for example, portrayed in the classic fairytale of Snow White and the Seven Dwarfs. After Snow White had eaten a poisonous apple given to her by her disguised stepmother, the queen, the seven dwarfs, and the prince all mistook Snow White's state of cursed sleep for death. Of course, the fairytale narrative of Snow White does not accurately depict real-life events, though in a popular science book, *Why We Sleep*, Professor Matthew Walker also illustrates the similarities between the appearance of sleep and death:

> Perhaps you walked into your living room late one night while chatting with a friend. You saw a family member, let's call her Jessica, lying still on the couch not making a peep, body recumbent, and head lolling onto one side. Immediately you turned to your friend and said "shhh, Jessica is sleeping". But how did you know? It took a split second of time, yet there was little doubt in your mind about Jessica's state. Why, instead, did you not think Jessica was in a coma or, worse, dead?
>
> (Walker, 2017)

Considering how dangerous it appears from an evolutionary perspective to lay defenseless for hours at a time every night, there must be an important reason as to why this behavior is essential to human functioning and well-being. It is common knowledge that a good night's sleep has important health benefits, and that 'to sleep on it' before making important decisions might be wise (Walker, 2017). Although the purpose of sleep and dreaming are not yet fully understood, it is well established that disturbances in this essential part of life that is sleep impairs the human ability to properly function and tackle the challenges of everyday life. The American father of sleep medicine, William C. Dement, famously stated that:

> Sleep is an essential part of life – but more importantly, sleep is a gift.

Sleep Disorders

In essence, sleep disorders are conditions that prevent you from getting a good night's sleep and affect your ability to function and/or perform during the day. Although specific symptoms vary depending on the nature of the sleep problem, the underlying cause is often lifestyle and environmental factors, such as stress, trauma, major life events (e.g., marriage, divorce, having children), shift work, use of electronic devices before bedtime, or aging (e.g., going through puberty or menopause) (WHO, 2004). Further, behavioral and biological mechanisms may contribute to the maintenance of poor sleep (Spielman, 1986). For example, an individual who experiences trouble falling asleep might start going to bed early to at least get some rest, spending hours awake in bed trying to sleep, possibly worrying about how they will feel tomorrow and deciding not to get up in the morning to compensate for the hours spent awake in bed trying to sleep. By changing their behavior in this way, they might construct an association between their bed and a state of wakefulness, possibly learning (on an unconscious level) that this behavior (i.e., spending several extra hours in bed) is necessary if they want to get any sleep at all.

For an individual, the nighttime symptoms of a sleep problem might be more easily recognizable than the thoughts and behaviors that may contribute to the development and maintenance of the sleep problem itself. Similarly, the immediate daytime consequences of a poor night's sleep (e.g., being tired after sleepless night) are easier to keep track of than the influence of persistent sleep problems on long-term health problems or daytime functioning. To ameliorate the impact of sleep problems on health and daytime functioning, it is important to improve public awareness of how and when to seek professional help and the benefits associated with improving troublesome sleep.

Sleep Disorder Diagnoses. In research and clinical practice, different sleep disorders are diagnosed based on identifying characteristics (American Psychiatric Association, 2013; WHO, 2019), and the following sections will briefly elaborate on the main characteristics and population-based prevalence of different sleep disorders. An overview of sleep disorders currently included in diagnostic manuals used in research and clinical practice are shown in Table 1.

In the general population, insomnia is the most reported sleep disorder, affecting ~10% to ~15% of the population at any given time (Pallesen et al., 2001, 2014). The disorder is characterized by difficulties initiating or maintaining sleep despite adequate opportunity, and significant distress or impairment in important areas of daytime functioning (American Psychiatric Association, 2013; WHO, 2019). Although sleep inertia (i.e., a temporary period of sleepiness and reduced performance immediately after waking up) is considered normal, the symptoms experienced by individuals with insomnia are more severe and may last throughout the day. As a result of too little sleep or poor sleep quality, individuals with

Table 1. An overview of sleep disorders. Reproduced from the *Desk Reference to the Diagnostic Criteria from DSM-5* (American Psychiatric Association, 2013).

Sleep–Wake Disorders	Insomnia Disorder
	Hypersomnolence Disorder
	Narcolepsy
Breathing-Related Sleep Disorders	Obstructive Sleep Apnea Hypopnea
	Central Sleep Apnea
	Sleep-Related Hypoventilation
	Circadian Rhythm Sleep–Wake Disorders
Parasomnias	Non-Rapid Eye Movement Sleep Arousal Disorders
	Nightmare Disorder
	Rapid Eye Movement Sleep Behavior Disorder
	Restless Legs Syndrome
	Substance/Medication-Induced Sleep Disorder

insomnia may complain that they wake up tired most days and that the feeling of being unrested impacts upon their level of daytime functioning. For details on the diagnostic criteria of insomnia, see Table 2.

Table 2. The diagnostic criteria for Insomnia Disorder (780.52/G47.00). Reproduced from the *Desk Reference to the Diagnostic Criteria from DSM-5* (American Psychiatric Association, 2013).

A.	A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms: 1. Difficulty initiating sleep. (In children, this may manifest as difficulty initiating sleep without caregiver intervention.) 2. Difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakenings. (In children, this may manifest as difficulty returning to sleep without caregiver intervention.) 3. Early morning awakening with inability to return to sleep.
B.	The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.
C.	The sleep difficulty occurs at least 3 nights per week.
D.	The sleep difficulty is present for at least 3 months.
E.	The sleep difficulty occurs despite adequate opportunity for sleep.
F.	The insomnia is not better explained by and does not occur exclusively during the course of another sleep–wake disorder (e.g., narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep–wake disorder, a parasomnia).
G.	The insomnia is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).
H.	Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia.
Specify if:	**With non-sleep disorder mental comorbidity**, including a substance use disorders **With other medical comorbidity** **With other sleep disorder**
	Episodic: Symptoms last at least 1 month but less than 3 months **Persistent:** Symptoms last 3 months or longer **Recurrent:** Two (or more) episodes within the space of 1 year
Note: Acute and short-term insomnia (i.e., the symptoms lasting less than 3 months but otherwise meeting all criteria with regard to frequency, intensity, distress, and/or impairment) should be coded as an other specified insomnia disorder.	

Hypersomnolence disorder and narcolepsy are characterized by excessive daytime sleepiness and a compulsion to take naps during the day or recurrent periods of an irrepressible need to sleep within the same day, despite adequate nighttime sleep (American Psychiatric Association, 2013). Cataplexy (i.e., sudden bilateral muscle weakness with maintained consciousness) can be a feature of narcolepsy, often brought on by a strong emotional trigger such as laughing or excitement. It is difficult to estimate the prevalence of these disorders due to the lack of a consistent definition of excessive sleepiness and the growing tendency to label a symptom of excessive sleepiness, by itself, as a disease or a disorder (without other accompanying symptoms of hypersomnolence or narcolepsy) (Ohayon, 2011).

Breathing-related sleep disorders, such as obstructive sleep apnea, are also associated with excessive daytime sleepiness due to poor sleep quality caused by the core symptom of the disorder, which is repeated respiratory arrests during sleep, often accompanied by loud and intense snoring. The prevalence of sleep apnea in Norway is estimated at between ~8% and ~16%, with the different estimated rates being partly explained by the different severity thresholds for identifying cases (Hrubos-Strøm, 2011).

Circadian rhythm sleep–wake disorders are problems that occur when there is a misalignment between the sleep–wake cycle and the environment that results in interference with daily activities, typically affecting adolescents and young adults or individual with severe mental health conditions. The most common type is delayed sleep–wake phase disorder, characterized by difficulties with falling asleep until late at night and waking up in time for morning responsibilities (caused by the delay in the phase of a major sleep episode). Differing from insomnia and other sleep disorders of excessive sleepiness, the architecture and maintenance of the sleep period itself is not usually disrupted (American Psychiatric Association, 2013; WHO, 2019).

Shift work disorder is a circadian rhythm disorder that commonly affects individuals who work non-traditional hours. Approximately 20% of the workforce in the European Union are engaged in shift or nighttime work, and the estimated prevalence of shift work disorder in this population is 1 in 3 to 1 in 5 (Pallesen et al., 2021). This disorder is characterized by insomnia when attempting to sleep and/or excessive sleepiness while at work. To be diagnosed with shift work disorder, the symptoms must be associated with a shift work schedule that cause misalignment in the timing of sleep and wakefulness that often results in short sleep duration. Further, the symptoms should not be better explained by another sleep disorder, a medical or mental health condition, medication use, or a substance use disorder (American Psychiatric Association, 2013).

A parasomnia is a sleep disorder that involves unusual and undesirable physical events or experiences that disrupt sleep, including abnormal bodily movements, complex behaviors, or sleep talking during sleep (American Psychiatric Association, 2013). The most common parasomnia is restless legs syndrome, a neurological condition causing unpleasant or uncomfortable sensations in the legs and an irresistible urge to move the legs, affecting up to 19% of the population in Northern European countries (Ohayon, 2011).

In addition to the nature and prevalence of different sleep disorders, it is important to keep in mind that the severity of symptoms varies between individuals. The importance of symptom severity is reflected in diagnostic manuals, as professionals are required to categorize sleep disorders as either mild, moderate, or severe. For example, experiencing insomnia symptoms 3 nights per week (thus qualifying for an insomnia diagnosis) may be associated with significant impairment, but if the severity of symptoms increases (e.g., to experiencing symptoms 6–7 nights per week), the associated impairment might also become more prominent. Similarly, it is important to recognize that even subclinical symptoms of a sleep

disorder might impact on an individual's health or well-being. Further, subclinical symptoms might be a precursor to the development of a more serious sleep problem. In summary, the characteristics of the sleep disorders described in the preceding paragraphs reflect that there are many ways in which sleep can be disrupted, and the overall high estimates of prevalence indicate that insufficient sleep is a global problem with serious public health implications (Chattu et al., 2018).

Assessing Sleep Disorders. To correctly assess and diagnose a sleep problem, it is necessary to investigate the sleep history, the nature of the sleep problems, and the presence of any comorbid conditions (Spielman, 1986). Standardized instruments have been developed to assess sleep problems in clinical practice. Standardized assessments also facilitate comparisons between, e.g., different research studies and advance the state of knowledge about the effectiveness of treatments (Buysse et al., 2006).

The Insomnia Interview Schedule is an 86-item semi-structured interview that covers the following topics: the nature of the sleep–wake problem, the current sleep–wake schedule, the use of sleeping aids (e.g., sleep medications or other remedies believed to improve sleep) or other substances, the history of the sleep problem, the sleep environment, eating, exercise, and comorbidity (e.g., the presence of comorbid sleep disorders or medical and/or mental health conditions) (Morin, 1993). In addition to diagnostic interviews, it is important to collect concrete information about an individual's sleep. As a result of collaboration between insomnia experts and potential users, the consensus sleep diary was proposed as a tool to standardize the assessment of important dimensions of day-to-day variations in sleep, e.g., bedtimes and rise times, when sleep occurs, nightly awakenings, medication use, and sleep quality, thus guiding the choice of treatment to be provided and facilitating comparisons of sleep problems across individuals and populations (Carney et al., 2012).

Although the nature of, e.g., insomnia symptoms are subjective in their very nature, there are some advantages of objective measures of sleep, e.g., through use of actigraphy or polysomnography. Actigraphy data (i.e., motor activity data) can easily be assessed by use of a hand-worn device with little to no inconvenience to the individual. The motor activity data can then be used to estimate various sleep measures (e.g., sleep length and nightly awakenings), which could provide an overview of the individual's sleep–wake schedule even if the individual, for some reason, fails to fill out daily sleep diaries. The use of polysomnography is a comprehensive assessment of sleep that records brain activity (e.g., to quantify time spent in different sleep stages), bodily movements, and breathing throughout the night. It is a medical procedure required in diagnosing, e.g., breathing-related sleep disorders (Hrubos-Strøm et al., 2011). Both actigraphy and polysomnography can also be used to detect sleep-related movement disorders, e.g., presence of restless legs syndrome, periodic limb movement disorder, or sleep-related bruxism (i.e., grinding or clenching the teeth during sleep) (Merlino & Gigli, 2012).

Sleep Problems Across the Lifespan

Taken together, the preceding overview of sleep disorder diagnoses and examples of assessment tools highlight that however necessary and ubiquitous sleep may be to human health and well-being, the process of getting a good night's sleep may be interrupted in various ways. It is well established that untreated insomnia is associated with increased risk of a wide range of negative outcomes, including adverse medical and mental health consequences (Benz, 2020; Sivertsen et al., 2012). To further illustrate the magnitude of these issue at population level, the following paragraphs will elaborate on the prevalence of sleep problems across age groups, risk factors for developing sleep problems, comorbidities, and the persistence of sleep problems.

Prevalence Across Age Groups. In childhood, longitudinal data on self- and parent-reported problems (n = 832) indicate that difficulties with falling asleep affected 30% to 40% of children (ages 9 to 11 years) (Fricke-Oerkermann et al., 2007). Similarly, a US-based study showed that 30% to 40% of children and adolescents had problems with adequate sleep at least once a week (Singh & Kenney, 2013), whereas a study of self-reported sleep problems in Chinese adolescents (ages 12 to 18 years; n = 1365) found that ~17% reported insomnia symptoms (Liu et al., 2000).

A study on the prevalence of sleep problems in college students (ages 18 to 29 years; n = 7626) showed that ~27% experienced poor sleep quality and that ~36% slept less than 7 hours per night (Becker et al., 2018). A meta-analysis on the prevalence of sleep problems in medical students (n = 18,619) indicated that 55% of the students reported poor sleep quality and that 31% regularly experienced excessive daytime sleepiness (Jahrami et al., 2020). Based on data from a national survey in Norway (n = 50,054), the overall prevalence of a delayed sleep–wake phase disorder for young adults in higher education (ages 20 to 29 years) was 3.3%, with a significantly higher prevalence in males than females (4.7% vs. 2.7%) (Sivertsen, Harvey, Gradisar, et al., 2021).

In the adult population, a study of subjective sleep quality and self-reported sleep problems measured in a representative sample of Japanese adults (ages 20 to >80 years; n = 1871) found that the overall prevalence rates of sleep problems were between ~25% and ~30% (Doi et al., 2001). An epidemiological overview of sleep disorders in the general population found that 1–2 in 5 adults were dissatisfied with their lack of sleep (i.e., the sleep quantity) and that 1–3 in 10 reported insomnia symptoms with difficulty initiating and/or maintaining sleep (Ohayon, 2011).

For older adults, sleep problems are common. A cross-sectional study on sleep problems in the elderly (age > 60 years; n = 1402) found that 70% met at least one criteria for sleep problems, with interrupted sleep being the most common sleep complaint (Lindstrom et al., 2012). However, another study, using more stringent criteria, found that the prevalence of insomnia symptoms among older adults (age > 45 years; n = 72,262) in India was ~13% (Pengpid & Peltzer, 2021), which is comparable to the insomnia prevalence in the general population independent of age. A US-based study of 2800 adults (age > 53 years) found that the prevalence of insomnia was between 10% (three insomnia traits) and 26% (one insomnia trait) (Schubert et al., 2002).

Risk Factors. A risk factor is something that increases the chance of developing, e.g., a sleep disorder or another health condition in the future. For example, a longitudinal study on sleep problems and depressive symptoms in toddlers (age 1.5 years) and children (age 8 years; n = 35,075) demonstrated that there is a bidirectional association between sleep and internalizing/depressive symptoms from toddlerhood to middle childhood, meaning that short sleep duration (≤10 hours) and frequent nightly awakenings (≥3) in toddlerhood is a predictor of the development of depressive symptoms in middle childhood and, conversely, that internalizing problems in toddlerhood is a predictor of subsequent onset of short sleep duration (Sivertsen, Harvey, Reichborn-Kjennerud, et al., 2021). In middle childhood, the least-favorable social environments were associated with an increase in serious sleep problems compared with the most-favorable (10% vs. 16%) (Singh & Kenney, 2013). For adolescents, poor physical health and life stress experienced during the past 12 months are associated with an increased risk of insomnia (Liu et al., 2000). For adults, a study on insomnia as a risk factor for the development of medical health conditions in the working population (n = 24,715) concluded that insomnia is predictive of the cumulative incidence of several medical (e.g., fibromyalgia, whiplash, osteoporosis, headache, asthma, and

myocardial infarction) and mental health conditions (e.g., depression and anxiety) (Sivertsen et al., 2014). Being female and older age are risk factors associated with insomnia (Morin, Bélanger, et al., 2009), and a substantial number of women experience sleep difficulties in the approach to menopause and beyond, with 26% experiencing severe symptoms that impact daytime functioning, qualifying them for a diagnosis of insomnia (Baker et al., 2018). Lastly, a meta-analysis of sleep disturbances following traumatic brain injuries in adults (n = 1706) demonstrated that 1 in 2 suffered from some form of sleep disturbance after a traumatic brain injury (e.g., snoring, poor sleep maintenance, or reduced sleep efficiency) and that almost 1 in 3 was diagnosed with a sleep disorder (e.g., insomnia, hypersomnia, or sleep apnea) (Mathias & Alvaro, 2012).

In modern societies, another risk factor for poor sleep is that humans are frequently exposed to light from artificial light sources during the dark period (evenings and nights) of the day. While there are clear advantages of having access to artificial lighting, e.g., to aid vision and enhance performance and alertness at night (Badia et al., 1991; Souman et al., 2018), it is also well documented that exposure to artificial lighting may compromise the timing of sleep and wakefulness in humans, possibly compromising the quality of sleep and contributing to health problems (Vogel et al., 2012). For example, a study on the effects of exposure to normal indoor lighting (<200 lux) compared with dim light (<3 lux) 8 hours before bedtime on healthy volunteers (ages 18 to 30 years, n = 116) demonstrated that normal indoor lighting exerts a profound suppressive effect on melatonin, indicating that regular exposure to indoor lighting might have a negative impact on sleep (Gooley et al., 2011). Similarly, a study on the effects of reading an electronic book using a light-emitting device compared with reading a printed book on healthy volunteers (n = 12) showed that use of an electronic book was associated with a longer time taken to fall asleep, increased melatonin suppression, and reduced next-morning alertness (Chang et al., 2015). Worldwide, light pollution from

artificial light sources (e.g., street lamps) has a range of negative effects on both human health and natural ecosystems (Davies & Smyth, 2018; Falchi et al., 2019).

Taken together, there is evidence to support the impact of habitual exposure to artificial lighting during evenings and nights on the timing and rhythmicity of sleep. Although most individuals are able to get a good night's sleep and to function during the day despite the use of indoor lighting and electronic devices, a minority of the population develops severe issues related to the timing of sleep and wakefulness (e.g., a delayed sleep–wake phase disorder). A possible explanation for this is that some individuals display greater sensitivity to evening light exposure than others (Phillips et al., 2019; Watson et al., 2018). Data from a national survey in Norway (n = 50,054) on young adults (ages 20 to 29 years) showed that those with delayed sleep–wake phase disorder reported more sleep problems on weekdays as well as higher levels of somatic complaints and overall health problems than those without the disorder (Sivertsen, Harvey, Gradisar, et al., 2021).

That exposure to artificial light has negative effects on sleep and health are also of importance to shift workers, who regularly need to be awake and active during the dark period of the day. Working shifts or non-traditional hours is particularly common in the healthcare sector, where 24-hour services are required. Such work schedules are associated with an increased risk of, e.g., insomnia or shift work disorder (Åkerstedt et al., 2002; Pallesen et al., 2021; Vedaa et al., 2017) as well as a wide range of adverse health effects (Bonzini et al., 2006; Costa et al., 2010; Gan et al., 2015; Haines III et al., 2008; Knutsson & Bøggild, 2010; Li et al., 2019; Manouchehri et al., 2021; Morikawa et al., 2005; Nurminen, 1998; Pan et al., 2011; Stocker et al., 2014; Sun et al., 2021; Torquati et al., 2018, 2019; Vogel et al., 2012; Wang et al., 2015). A national survey of sleep problems in the US working population (n = 6338) showed that compared with all workers, night shift workers tend to more frequently report short sleep

durations (38% vs. 62%), poor sleep quality (19% vs. 31%), impairment in activities of daily living (25% vs. 36%), and insomnia symptoms (9% vs. 19%) (Yong et al., 2017).

Comorbidity. While risk factors precede the emergence of an issue, comorbidity refers to the simultaneous presence of two or more diagnoses. There is evidence of a reciprocal relationship between, e.g., insomnia and depression/anxiety (Sánchez-Ortuño & Edinger, 2012). Specifically, having two or more comorbid conditions may worsen symptoms as the conditions may aggravate each other, for example, as a result of daytime symptoms interfering with sleep, and sleep disturbances, in turn, may contribute to symptoms the next day (Jansson-Fröjmark & Lindblom, 2008; Sivertsen et al., 2012). A study of sleep problem prevalence and mental health correlates in college students (ages 18 to 29 years; n = 7626) found that symptoms of anxiety, but not depression, were associated with more sleep disturbances and sleep medication use, whereas symptoms of depression, but not anxiety, were uniquely associated with impaired daytime functioning (Becker et al., 2018). Overall, sleep disturbances or sleep disorders often co-occur in individuals with mental health conditions (affective disorders, anxiety disorders, substance use disorders, psychosis, attention deficit/hyperactivity disorders, etc.), and among those with sleep complaints compared to those without any, more individuals meet the criteria for a mental health diagnosis (~40% vs. ~15%) (Abad & Guilleminault, 2005).

A wide range of medical conditions also co-occur with sleep problems. For example, a meta-analysis (n = 591,945) demonstrated that there is a cross-sectional and prospective association between poor sleep and physical impairment (odds ratio 1.26 and 1.40, respectively) (Amiri & Behnezhad, 2021). Data from a national US-based survey (age > 20 years; n = 9848) demonstrated that individuals with diabetes were more likely to report multiple problems with sleep (e.g., inadequate sleep, excessive sleepiness, and sleep apnea) than those without (mean

3.1 sleep complaints vs. 2.5 sleep complaints, respectively) (Plantinga et al., 2012). In a sample of adults with attention-deficit/hyperactivity disorder (n = 252), nearly 1 in 2 reported symptoms consistent with an insomnia disorder diagnosis, and the presence of other medical or mental health comorbidities (e.g., mood disorders, anxiety, and substance use disorder) was associated with an increased risk of having insomnia in addition (Fadeuilhe et al., 2021). Similar trends have been observed for individuals with intellectual disabilities (van de Wouw et al., 2012), autism (Richdale, 1999; Richdale & Schreck, 2009), multiple sclerosis (Bamer et al., 2008), and in patients with active COVID-19 (Jahrami et al., 2021).

Persistence of Sleep Problems. Available data indicate that for more than half of children (ages 9–11 years), sleep problems last for more than one year (Fricke-Oerkermann et al., 2007). A study linking insomnia symptoms from adolescence (ages 16–18 years) to young adulthood (ages 22–25 years; n = 1257) demonstrated that 50% of those with insomnia symptoms in adolescence still reported insomnia symptoms 6 years later (Hysing et al., 2020). Additionally, the overall prevalence of insomnia increased from adolescence to young adulthood (Hysing et al., 2020). Similarly, a population-based longitudinal study on the persistence of insomnia in adults (n = 388) showed that almost 50% of the participants reported experiencing insomnia for the duration of the 3-year study period, and factors associated with chronicity were more severe insomnia symptoms, sex (female), and older age (Morin, Bélanger, et al., 2009). A longitudinal population-based study (ages 19–80 years; n = 24,175) found that 1 in 5 reported having insomnia for the duration of the 11-year study period (Sivertsen et al., 2012).

Daytime Consequences of Poor Sleep

The high prevalence rates of sleep problems across the lifespan, as well as the impact of risk factors, comorbidity, and the persistent nature of sleep problems, clearly support that insufficient sleep is a pervasive and prominent problem in our modern 24-hour society as well as a public health epidemic that is often unrecognized and associated with rather high economic costs (Chattu et al., 2018). Further, untreated sleep problems are associated with work-related impairment, particularly increased rates of presenteeism (Bolge et al., 2009; Johns, 2009), short- and long-term absenteeism from work (Caverley et al., 2007; Reynolds et al., 2017), and permanent work disability (Jansson et al., 2013; Léger & Bayon, 2010; Sivertsen et al., 2006, 2009) as well as daytime impairment outside of work and reduced quality of life (Ishak et al., 2012; Kyle et al., 2010). Focusing particularly on the daytime consequences of poor sleep, the following sections will elaborate on daytime impairment, work-related outcomes, and societal costs, beginning with some examples of how these outcomes can be measured.

To assess general daytime functioning and the impact of sleep problems, several questionnaires have been developed and validated. For example, the Work Productivity and Activity Impairment Questionnaire (WPAI) is 6-item instrument developed to quantitatively assess impairment at work and in activities outside of work (Reilly et al., 1993). Specifically, the reported data are used to derive information on presenteeism (defined as productivity loss while at work), absenteeism (missing scheduled work time), total work impairment (an aggregated score weighting the impact of presenteeism and absenteeism), and activity impairment (impairment in activities outside of work). The WPAI has good psychometric properties and has been more frequently used than any other metric of productivity across various occupations and disease areas (Bolge et al., 2009). Examples of similar work- and

performance-related instruments are the World Health Organization Health and Work Performance Questionnaire (Kessler, Barber, et al., 2003), the Lam Employment Absence and Productivity Scale (Lam et al., 2009), and the Work Limitations Questionnaire (Lerner et al., 2001).

Outside of work, other important areas of daytime functioning are, e.g., quality of life (i.e., an individual's perception of their current position in life with reference to their goals, expectations, standards, and concerns (WHO, 1995)), stress, and cognitive performance. Quality of life can be assessed with, e.g., the Medical Outcomes Study 36-Item (or 12-Item) Short Form Survey Instrument (Kosinski et al., 2007). The instrument is a multipurpose, generic health-related quality of life questionnaire with a physical and a mental component. To assess global stress (which might also be relevant for performance at work), the 10-item Perceived Stress Scale – designed to assess the extent to which individuals find their lives to be unpredictable – could be used (Cohen et al., 1983), whereas the Cognitive Failures Questionnaire, designed to measure the frequency of lapses in perception, memory, and action, could provide data on cognitive performance (Broadbent et al., 1982). Additionally, the inclusion of objective data on short- and long-term absenteeism, disability benefits, healthcare resource use, and medical and/or mental health diagnoses could be directly acquired (with individual permission) from employer records or from national registries on healthcare use and social benefits.

We now turn to impairment in daily activities, which is often caused by, e.g., fatigue or excessive daytime sleepiness that leads to less energy to, e.g., participate in family activities, maintain social relationships, or complete household tasks (Morin & Espie, 2004). Data from national health and wellness surveys (n = 137,000) revealed that patients with insomnia (either treated or untreated) report significantly worse health-related quality of life, greater

total impairment at work (measured with WPAI), and increased use of healthcare appointments compared with individuals without insomnia (DiBonaventura et al., 2015). Similarly, a review of the effects of insomnia on quality of life found that insomnia negatively affects individuals' quality of life and that increased severity of symptoms is associated with decreased quality of life, whereas treatment of insomnia symptoms had a positive effect on quality of life, including for individuals with comorbid mental health conditions (e.g., depression or anxiety) or comorbid medical conditions (Ishak et al., 2012).

Presenteeism affects a large number of individuals with untreated insomnia while at work, accounting for 20% to 40% of lost productivity for individuals recruited to insomnia randomized controlled trials (RCTs) (Espie et al., 2018, 2019; Kalmbach et al., 2019). A study on the effects of one of the most common symptoms of insomnia, nightly awakenings, on health status (measured with the SF-12), work and activity impairment (measured with WPAI), and costs (age 18+ years; n = 60,783) found that individuals with frequent nightly awakenings reported poorer medical and mental health status than those without insomnia (DiBonaventura et al., 2014). Further, poor sleep quality was found to be associated with higher presenteeism, activity impairment, and total work impairment, and the associated costs were estimated to amount to ~20% of the annual employee income (DiBonaventura et al., 2014). Similarly, a study on the association between insomnia and work-related outcomes (n = 19,711) found that individuals with insomnia, compared to those without, reported increased rates of presenteeism (29.2% vs. 7.6%) and absenteeism (10.7% vs. 1.77%) (Bolge et al., 2009). A study on the effects of health status on presenteeism and absenteeism (n = 884) found that poor self-reported health (from very poor to very good) was associated with a 20% reduction in both productivity while at work and number of hours worked (Böckerman & Laukkanen, 2010). Kessler and colleagues (2011) estimated the lost work performance specifically associated with untreated insomnia to be 2.3 weeks (11.3 days) per year per

individual and that complete eradication of insomnia would lead to proportional reductions of between 5.4% and 7.8% in all population-level lost work performance due to presenteeism.

For absenteeism, a prospective study of objectively assessed long-term sickness absenteeism (>3 weeks) during 1-year follow-up in a representative Danish population (n = 6538) found a cumulative incidence of absenteeism of 5.6% and that sleep disturbances at baseline are predictive of risk of absenteeism before the results were adjusted for depressive symptoms (Bultmann et al., 2013). Similarly, data from the Helsinki Health Study (n = 6535) and data on employees of the City of Helsinki (n = 6845) show that symptoms of insomnia were associated with objectively measured (by use of registry data) short-term (1-3 days), intermediate (4-14 days), and long-term (>15 days) absenteeism (Lallukka et al., 2013; Rahkonen et al., 2012). Data from a study on insomnia and days-out-of-role (i.e., being totally unable to work or carry out normal activities because of physical or mental health; n = 6791) found that insomnia was associated with more than 1 in 10 of all days-out-of-role (Hajak et al., 2011). Further, a cohort study (n = 3760) examining whether various sleep measures determined absenteeism found that having frequent insomnia symptoms was associated with an approximate doubling in absence due to sickness per year compared with not having insomnia symptoms (~5 days vs. ~10 days) (Lallukka et al., 2014), which is similar to other estimates (Léger, 2006).

Although several studies tend to distinguish between impairment at work and outside of work, the distinction between work and not work and how to define terms of daytime impairment across different areas of functioning are not clear cut. For example, the term ‘working individuals’ most often refers to individuals who are in paid employment. However, there is an increasing trend in social psychiatry/psychology to consider the concept of ‘home makers’ as ‘workers’ (even if they adopt this role when less able to undertake fulltime employment).

In this view, individuals who are not in paid employment but organize the home, undertake daily living tasks, and occupy care roles for children and parents, etc., are viewed as comparable to those working outside the home. As such, an important question arises: How should daytime impairment be measured in large populations? This pertains, e.g., to whether investigations on presenteeism only should include data from individuals who report being in paid employment or whether the impact of presenteeism on individuals who are productive but not in employment should also be included. Considering the societal importance of unpaid but productive activities, there is reason to argue that investigations on daytime impairment are relevant across traditional distinctions between work and not work.

Societal Costs. Economic costs associated with sleep problems can be divided into direct costs (e.g., increased use of healthcare services, medications, and hospitalization) and indirect costs (e.g., presenteeism, short- and long-term absenteeism, and disability benefits). In general, studies on the effects of treatment on sleep problems or secondary outcomes (e.g., work- and activity-related impairment, medical and mental health, etc.) does not provide any insights into the health economic aspects of digital cognitive behavioral therapy for insomnia (dCBT-I) because they only include outcomes from the patient perspective (Wickwire, 2019). Further, estimating the precise monetary costs of sleep problems is difficult due to the lack of hard epidemiological data (Léger & Bayon, 2010). However, available data indicate that the costs are substantial (Léger & Bayon, 2010), for example, equivalent to 0.95% of gross domestic product in the US in 2016 (Reynolds et al., 2017).

Focusing on the costs of presenteeism and absenteeism, there are different recommendations for calculating monetary costs. For example, Bolge and colleagues (2009) argued that indirect costs can be estimated by applying the percentage of presenteeism or absenteeism to various salary points (i.e., multiplying the percentage of productivity loss or absenteeism with the

yearly wage). Strömberg and colleagues (2017) recommend the use of wage multipliers (1.97 for absenteeism and between 1.54 to 1.70 for presenteeism), which reflect that the costs of absenteeism and presenteeism exceed the workers' wages. Independent of how the societal costs of sleep problems are calculated, data from several studies suggest that providing treatment for sleep problems to working individuals who need it is cost-effective (Darden et al., 2020; Thiart et al., 2016).

Treatment Interventions to Improve Sleep

As established in the preceding sections, sleep problems are associated with a range of negative outcomes both at the individual and the societal level and having a sleep problem is often a predictor of future health problems (sometimes years later). Experiencing short periods of poor sleep is considered normal, but if the problem becomes chronic (lasting for 3 months or longer), it can have detrimental effects on an individual's health and well-being, and it is recommended to seek professional help. From a public health perspective, correctly diagnosing and treating sleep disorders is of great importance even though it is estimated that this only occurs for as few as 1 in 5–10 affected individuals (Ohayon, 2011). To provide the best care, sleep problems are diagnosed based on stringent criteria and different treatments are provided based on the patient's symptoms (American Psychiatric Association, 2013; WHO, 2019). The following paragraphs will discuss pharmacological and non-pharmacological interventions aimed at improving sleep.

Pharmacological Treatments. Sleep medications (hypnotics) have a well-documented short-term effect and can be useful for treating acute insomnia, but it is important to keep in mind that none have been demonstrated to solve the underlying cause of a sleep problem. There is substantial evidence that the use of benzodiazepines to promote sleep (e.g., Imovane or Stilnoct) are effective in the short term (e.g., for sleep problems with a duration of

1–4 weeks) but only limited evidence that they retain their efficacy during long-term treatment (for sleep problems with a duration of <6 months) (Riemann & Perlis, 2009). Additionally, residual effects (i.e., hangover effects) of sleep medications are associated with impairment, e.g., at work (including presenteeism and absenteeism), in home management, and in social relationships (Fitzgerald & Vietri, 2015).

In Norway, sleep problems are recognized by primary care physicians, but drug therapies are still more widely prescribed in the long-term management of insomnia despite evidence that non-pharmacological treatment is superior (Sivertsen et al., 2010). Further, many individuals with sleep problems are unaware of the available treatment options and many use alcohol, alternative therapies, or undocumented health food products to improve their sleep (Morin, 2006). There has been a recent increase in the use of melatonin in Norway, likely because a prescription is no longer required for its purchase. A review on the efficacy of melatonin in treating insomnia concludes that melatonin promotes sleep initiation and increases sleep length, although the improvements might not be clinically meaningful (Low et al., 2020).

Shift workers regularly use pharmacological products to ameliorate the adverse effects of shift work, and data from a review of the effectiveness of such use indicate that caffeine and naps may reduce sleepiness during shifts and that melatonin is associated with increased sleep length after a shift (Liira et al., 2015). The use of wakefulness-promoting drugs (e.g., modafinil), on the other hand, causes side effects such as headaches and nausea as well as an increase in alertness and reduced sleepiness (Liira et al., 2015).

Non-Pharmacological Treatments. Independently of why an individual develops a sleep problem, it is important that suitable treatments are made available. A stepped-care approach has been suggested to solve the problem of treatment accessibility for insomnia (Rybarczyk & Mack, 2011), meaning that the most effective yet least resource-intensive

treatment is delivered first. Only those patients that do not substantially benefit from the first intervention are 'stepped up' to more intensive and specialized services. Self-help interventions (e.g., pamphlets, informational websites, or books) have been developed to provide information about good sleeping habits as well as tools to change problematic sleep-related habits (Bjorvatn, 2007; Hagatun et al., 2019; Ritterband et al., 2017). Telemedicine refers to the use of technology by medical professionals to diagnose and treat patients in a remote location, yielding similar improvements in sleep and daytime outcomes as traditional face-to-face therapy (Arnedt et al., 2020). Sleep restriction therapy works to decrease the variability in the timing of sleep while increasing its depth (Riemann et al., 2017; Spielman et al., 1987), which is shown to mediate improvements related to insomnia symptoms (Vestergaard et al., 2021).

Cognitive Behavioral Therapy for Insomnia. A recommended therapy for insomnia is cognitive behavioral therapy (CBT-I) (Qaseem et al., 2016; Riemann et al., 2017; Wilson et al., 2010, 2019). Traditionally, the treatment is provided face-to-face by trained professionals, either one-on-one or in groups, with components such as psychoeducation about sleep and sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relapse prevention (Morin, 1993; Morin & Espie, 2004).

Digital CBT-I. There is a gap between the availability of and demand for CBT-I due to a lack of professionally trained therapists (Morin, 2015). To overcome barriers regarding access to face-to-face therapy, CBT-I has been adapted for digital delivery via, e.g., websites or apps. The digital adaptations of CBT-I (dCBT-I) differ in the amount of support that is offered from clinicians, ranging from only the provision of information materials through therapist-guided programs and to fully automated adaptations of face-to-face CBT-I (Luik et al., 2017). Both face-to-face and digital adaptations of CBT-I have been shown to be effective

in reducing insomnia severity (Morin et al., 2006; Riemann et al., 2017; van Straten et al., 2018; Wilson et al., 2019; Zachariae et al., 2016). Both CBT-I and dCBT-I are also shown to be effective in alleviating insomnia symptoms for individuals with comorbid conditions (Wu et al., 2015), though less is known about the mechanisms by which CBT-I alleviates sleep problems and whether it has additional benefits beyond improved sleep.

Light and Dark Therapies. Therapeutic use of light and darkness, by manipulating exposure, aims to influence the timing of the sleep–wake cycle and improve sleep and may also alleviate the symptoms of some mental health conditions (Faulkner et al., 2020; van Maanen et al., 2016). The use of light therapy (i.e., exposure to bright light in the morning) for treating depression is associated with a reduction in the severity of symptoms (Golden et al., 2005), and a meta-analysis on the effects of light therapy on sleep problems showed that it can also yield a positive effect on symptom severity for individuals with insomnia or circadian rhythm disorders (van Maanen et al., 2016).

Dark therapy is roughly the converse of light therapy (Phelps, 2008). To treat bipolar disorder, for example, complete darkness has been applied for extended periods of time (e.g., from 18:00 to 08:00) to stabilize a patient's mood and help them recover faster than they would have without the treatment intervention (Barbini et al., 2005). Although effective, therapy intervention is highly impractical to administer and not accepted by patients (Phelps, 2008). As an alternative, the creation of 'virtual darkness' through the use of glasses blocking the light of blue wavelengths was found to benefit patient recovery by producing the same effects on the circadian system as complete darkness (Henriksen et al., 2016; Kimberly & James R., 2009; Phelps, 2008; Sasseville et al., 2006; van der Lely et al., 2015).

Although the use of blue-blocking glasses appears to have higher acceptance than the use of complete darkness, treatment adherence can prove too challenging for some patient

groups (e.g., psychiatric patients with severe symptoms). As such, the development of blue-depleted light environments in hospitals, through the installation of light technology to block blue-light frequencies and create a 'virtual darkness' environment during evenings and nights, might be more readily accepted and could prove beneficial in terms of the sleep and recovery of hospital inpatients (J. Scott et al., 2019). A clear advantage with the installment of blue-depleted light technology is that the building itself becomes a therapeutic non-intrusive intervention that does not require that the patients adhere to specific light and/or darkness exposure schedules nor wear any gadgets (such as blue-blocking glasses). While exposed to such environments, the human eye can see its surroundings, but the circadian physiological responses are equivalent to a situation of darkness (Sasseville et al., 2006; van der Lely et al., 2015).

Theoretical Models

Focusing on sleep disorders and their characteristics and available treatment options, theoretical frameworks can be used to organize case histories of symptoms and identify key symptoms of a disorder. In research and clinical practice, detailed case histories are important for comparisons of symptoms and treatment outcomes across individuals and populations. Additionally, keeping track of symptoms and outcomes may facilitate modifications of existing treatments to improve outcomes or the development of new treatments.

Spielman's '3P' Model of Insomnia. A classic model aiming to describe conceptual and practical aspects of the assessment of insomnia was proposed by Spielman (1986). He focused on the need for accurate diagnostic determination prior to treatment, and his '3P' model of insomnia has greatly influenced how insomnia disorder is understood and the development of treatments. Spielman proposed to categorize the clinical features of insomnia into 3 categories: predisposing conditions, precipitating circumstances, and perpetuating

factors (Spielman, 1986). Predisposing conditions are not, by themselves, sufficient to produce insomnia but refer to the factors that contribute to the development of insomnia. Precipitating circumstances take place at the same time as insomnia manifests. Perpetuating factors (i.e., thoughts and behaviors that contribute to the maintenance of insomnia symptoms) include too much time spent in bed, irregular bedtimes and rise times, napping during the day, the use of, e.g., sedative–hypnotics or alcohol, and conditioning (i.e., learned thoughts or behaviors). The '3P' model of insomnia is used to categorize clinical features of the insomnia as transient and situational or persistent. Further, it is important that the clinician has information about clinical features, such as any comorbid medical or mental health conditions, problematic alcohol or substance use, or other sleep disorders, as the symptoms of other disorders might also need to be addressed to facilitate improvement in insomnia symptoms (Spielman, 1986; Spielman et al., 1987).

Models of Sleep and Alertness Regulation. The mechanisms of both cognitive/behavioral and light/darkness therapies on sleep can be understood in terms of models of sleep and alertness regulation. The two-process model of sleep regulation provides a conceptual framework to understand the alternation between sleep and wakefulness, which includes interplay between a sleep–wake-dependent homeostatic process (S) and a circadian process (C) that, together, generate the timing of sleep and waking (Borbély, 1982). Process S describes how the need for sleep increases during wakefulness and decreases during sleep, while process C describes the daily cycles of physiological processes (e.g., variations in core body temperature and melatonin rhythms) that determine patterns of sleep and wakefulness (Borbély, 1982).

The element of sleep restriction in CBT-I aims to increase the homeostatic drive to sleep (process S) and thus facilitate the consolidation of sleep and increase sleep quality.

Light/darkness therapies (including blue-depleted light environments) aim to influence the circadian system (process C) by regulating the amount of light an individual is exposed to at different time points during the 24-hour day. Generally, increased exposure to bright light in the morning – but not earlier than the midpoint of an individual's sleep period – and reduced exposure to light during evenings and nights will phase advance the timing of the sleep period (Stothard et al., 2017; Wright et al., 2013). Conversely, exposure to artificial lighting during evenings and nights (e.g., by use of electronic screens or regular indoor lighting) will delay the timing of the sleep period (Chang et al., 2015; Cho et al., 2015; Stothard et al., 2017). To some extent, CBT-I also influences process C, e.g., through implementation of strict bedtimes and rise times, which often causes the individual to consistently get up earlier in the morning and thus be exposed to more daylight in the morning.

The phase-shifting effect of light is stronger when exposure occurs close to the approximate midpoint of an individual's sleep period (Minors et al., 1991). This is of particular importance to shift workers, who are regularly exposed to light during the dark period of the day and need to be alert and perform at times when they would normally sleep. To account for the impact of shift workers' sleep on alertness, the time course of waking up properly (or sleep inertia; process W) was added to the two-process model of sleep regulation to create the three-process model of alertness regulation (Åkerstedt & Folkard, 1997). This model can be used to predict alertness based on time spent awake (process S) and the circadian timing of sleep (process C). For example, during a night shift, the combined effect of a long time spent awake and circadian downswing (i.e., being awake when one would normally sleep) will yield a fall in alertness as the night progresses, with a slight increase in alertness toward the morning (i.e., when the body would normally start to wake up).

There is some evidence that dark therapy interventions might benefit the alertness of shift workers. By selectively filtering the blue short wavelengths of light (450–480 nm), a study on the effects of shift work on the sleep (measured with polysomnography) and performance (measured with a vigilance test) of nurses (n = 9) demonstrated that the altered light condition resulted in improved sleep and performance (Rahman et al., 2013). Similarly, to counteract the effects of shift work on alertness, an at least partial circadian adaptation to shift work (facilitated by artificial lighting) might be desirable and could potentially increase performance at work and reduce the risk of accidents as well as improve daytime sleep (Åkerstedt et al., 2001; Boudreau et al., 2013; Dinges, 1995; Santhi et al., 2008). A circadian adaptation to shift work is not always desirable, however, as it will compromise sleep and activity during days off work, when workers often wish to re-adapt to a daytime schedule. Further, it is important to keep in mind that long-time exposure to artificial light during evenings and nights can compromise the rhythmicity and timing of individual sleep and wakefulness patterns and contribute to the development of sleep problems (e.g., shift work disorder), medical conditions, or mental health conditions (Vogel et al., 2012).

The Overall Aim of the Thesis

The introduction illustrates the complex nature and high prevalence of sleep problems across the lifespan, likely impacting on the quality of life of individuals and their capacity to participate in work and other activities. There exist several different interventions that are efficacious for insomnia and other sleep disorders, such as face-to-face or digital CBT-I and light and dark therapies (where light exposure is manipulated). However, there is a gap in our understanding of whether these different treatment strategies also improve daytime functioning. As such, the main aim of the thesis was to investigate the effect of different interventions on both sleep and daytime functioning.

Aims of the Papers

Paper 1. The aims of paper 1 were to (i) test if individuals with insomnia disorder who received CBT-I demonstrated any improvements in levels of work productivity or daytime activity following therapy and (ii) examine if potential improvements in work-related outcomes differ according to observed changes in insomnia severity. The hypotheses were that levels of self-reported absenteeism, presenteeism, total work impairment, and activity 6 months post-CBT-I would be significantly lower than baseline levels and that individuals with an insomnia disorder who met recognized criteria for response or remission at follow-up would show significantly greater improvements across all work- and activity-related outcomes than those who did not meet these criteria.

Paper 2. The aims of paper 2 were to (i) examine any treatment-related between-group differences in improvements in work- and activity-related impairment at 6-month follow-up and (ii) test whether any changes in work- and activity-related impairment between baseline and 6-month follow-up were mediated by pre-to-post intervention changes in insomnia symptom severity (i.e., from baseline to 9-week follow-up).

Paper 3. The main aim of paper 3 was to test whether residing in an evening blue-depleted light environment, compared with exposure to a standard hospital lighting, influences the timing of dim light melatonin onset, melatonin suppression, and polysomnographic sleep variables in healthy controls. Secondary aims were to investigate if there were differences in neurocognitive functioning and subjective levels of sleepiness between light conditions and whether there are any side effects associated with residing in the blue-depleted light environment.

Paper 4. The main aim of paper 4 was to use subjective (work and sleep diaries) and objective (actigraphy) recordings to investigate nurses' sleep patterns, work functioning, levels of stress, and mood state over a 2-week period during which they either undertook shifts in a blue-depleted light environment or in a standard hospital light environment. Additionally, the nurses' self-reported physical and mental health when working in each light condition was explored.

Methods

Study Designs and Participants

Paper 1. Study 1 represents secondary analyses on a subset of a sample recruited to an RCT conducted at an outpatient public sleep clinic at St. Olavs Hospital (Østmarka) in Trondheim, Norway, between October 2014 and January 2016 in which the effectiveness of digital versus face-to-face CBT-I is examined (Kallestad et al., 2021). The key eligibility criterion for this study was that the individual reported being in paid employment at the time of entry into the RCT (n = 77). Data were extracted on sample characteristics and on work productivity and activity impairment at baseline and 6-month follow-up.

Paper 2. Study 2 used data from a large-scale RCT (n = 1721) that examined the effects of dCBT-I compared with a control condition (online patient sleep education (PE)) on self-reported insomnia symptoms, sleep–wake patterns, use of sleep medication, and other key markers of health and well-being in the general population (Vedaa et al., 2020). Data were extracted on demographic and clinical measures at baseline, insomnia severity at baseline and at 9-week follow-up, and work productivity and activity impairment at baseline and at 6-month follow-up.

Paper 3. Study 3 was a proof-of-concept study conducted in a newly built acute psychiatric hospital unit at St. Olavs Hospital (Østmarka) in Trondheim, Norway, in September 2017 (prior to opening the unit for patient admissions) to evaluate the effects of a blue-depleted light environment on healthy controls. The unit consisted of two separate wards, and new light technology installed during construction allowed for the introduction of a blue-depleted light environment during evenings and nights in one ward, whereas the other ward had standard hospital lighting. The study was designed as a randomized cross-over trial,

and the participants (n = 12) resided for alternating periods of 5 consecutive days in each ward. See Figure 1 in paper 1 for an overview of the study design.

Paper 4. Study 4 was originally designed as a non-randomized 12-week cross-over trial to investigate and compare the effects of an evening-and-night, blue-depleted light environment with those of a standard hospital light environment on nurses' sleep and work functioning in a naturalistic setting. Nurses working at least 50% of fulltime equivalent at the acute psychiatric hospital unit at St. Olavs Hospital (Østmarka) in Trondheim, Norway, when the study started in November 2018 (n = 86) were invited to participate, and 25 (29.1%) chose to do so for the first 6 weeks of data collection and 10 (11.7%) provided data after the cross-over (week 6 to 12 of the study). However, the comparatively small sample size limited the types of analyses that were considered feasible (e.g., analyses could not be carried out based on a cross-over design).

Assessments

Papers 1 and 2. Data were extracted on insomnia severity and work productivity and activity impairment.

Insomnia symptom severity was measured according to the Insomnia Severity Index (ISI). The ISI is a validated 7-item, self-report questionnaire that assesses the nature, severity, and impact of insomnia symptoms over the past two weeks, and it is recommended for use in insomnia research (Bastien, 2001; Buysse et al., 2006; Morin, Belleville, et al., 2011). Total scores range from 0 to 28, with higher scores indicating greater severity of insomnia symptoms.

The general health version of the Work Productivity and Activity Impairment Questionnaire (WPAI) (Reilly et al., 1993) was used to assess levels of absenteeism, presenteeism, total

work impairment, and activity impairment in activities outside of work, expressed as percentages. In study 2, absenteeism was instead measured as hours absent from work, and employment status (binary categorical measure) was included in the analyses. Total work impairment was not calculated in study 2.

In study 1, the Insomnia Interview Schedule, a semi-structured diagnostic interview, was administered at baseline to collect demographic and clinical information (Morin, 1993). In study 2, this same information was self-reported by participants prior to participation.

Paper 3. Data were collected on the participants' circadian rhythms, sleep, neurocognitive functioning, light exposure, and the acceptability of the indoor lighting and the ward itself.

Circadian rhythm was measured by analyzing melatonin concentrations in saliva samples hourly from 19:00 to 23:00 on 5 separate evenings while residing in either the blue-depleted light environment or in the standard hospital light environment. Saliva samples were collected in accordance with the protocol for the Dim Light Melatonin Onset test (Carlson & Chiu, 2008) in the evening before and after the participants entered or left each light environment.

Sleep was measured by use of an actiwatch (Actiwatch Spectrum, Philips Respironics Inc., Murrysville, PA) the last week before participants moved into the acute psychiatric unit and while they resided in the wards. While participants resided in the wards, sleep was also measured using novel radar technology based on changes in movement and respiration patterns (Xethru) (Pallesen et al., 2018) and by use of sleep diaries (Carney et al., 2012). Additionally, sleep was measured by use of polysomnography (PSG) for the 2 last nights spent in each condition.

Activity was assessed during evenings by use of data from the actiwatches worn by the participants. The Karolinska Sleepiness Scale (Åkerstedt & Gillberg, 1990) was used to estimate subjective sleepiness hourly during evenings between 19:00 and 23:00 and once each morning. Conners Continuous Performance Test version 3 (Homack & Riccio, 2006) was used to assess psychomotor vigilance and neurocognitive functioning between 21:00 and 22:00 on day 3 in each condition. The Karolinska Drowsiness Test (Putilov & Donskaya, 2013) with electroencephalography (EEG) was used to assess objective sleepiness between 21:00 and 22:00 on days 4 and 5 in each condition.

Light exposure was measured using a red–green–blue sensor (i.e., a small device measuring the amount of light it is exposed to) on one wrist throughout the study period and by placement of a red–green–blue sensor on their forehead during some evenings while residing in the acute psychiatric hospital unit.

Acceptability of the indoor lighting and the wards was assessed using the Committee of Clinical Investigations side effects rating scale (Lingjærde et al., 1987), the Farnsworth–Munsell 100-hue test (measuring the ability to discriminate colors in the different light conditions) (Rigby et al., 1991), and an open-ended interview.

Paper 4. Data were collected by use of work and sleep diaries, actigraphy, and validated scales and questionnaires.

A work diary was used for 14 consecutive days to gather information about worked shifts, number of cups of caffeinated beverages consumed, levels of sleepiness, and mood (i.e., positive and negative feelings) during each shift. The consensus sleep diary (Carney et al., 2012) was used in parallel with the work diary to provide subjective, daily estimates of sleep. An overview of the items from the work and sleep diaries are included in Table 3.

Table 3. An overview of items from the work and sleep diaries.

	Work diary		**Sleep diary**
1	What time did you start working?	1	What time did you get into bed?
2	What time did you finish working?	2	What time did you try to go to sleep?
3	How stressful was the shift?	3	How long did it take you to fall asleep?
	(from 'very calm' to 'very stressful')	4	How many times did you wake up, not
4	How sleepy were you during the shift?		counting your final awakening?
	(from 'not at all sleepy' to 'very sleepy')	5	In total, how long did these awakenings last?
5	How many caffeinated beverages did you	6	What time was your final awakening?
	consume during the shift?	7	What time did you get out of bed for the day?
6	How positive did you feel during the shift?	8	How would you rate the quality of your sleep?
	(from 'not at all positive' to 'very positive')		(very poor/poor/fair/good/very good)
7	How negative did you feel during the shift?		
	(from 'not at all negative' to 'very negative')		

Based on the information from the sleep diaries, the following measures were derived: Time in Bed (TIB), Sleep Onset Latency (SOL), number of nightly awakenings, Wake After Sleep Onset (WASO), Early Morning Awakening (EMA), Total Sleep Time (TST), Sleep Efficiency (SE), and Sleep Period Time (SPT), as well as an overall rating of the sleep quality (question 8 in the sleep diary). Actigraphy data (i.e., motor activity) was assessed in parallel with the diaries by use of actiwatches (GENEActive®) to derive estimates of WASO, TST, SPT, and number of sleep periods. Definitions of the measures derived from the sleep diaries and the actigraphy data are included in Table 4.

To assess symptoms of medical conditions, mental health conditions, and side effects associated with the light conditions, participants were asked to complete several validated scales and questionnaires: the Kessler Psychological Distress Scale (Kessler, Barker, et al., 2003), a short version of the Psychological Health Questionnaire (Schat et al., 2005), the Headache and Eyestrain Scale (Viola et al., 2008), an evaluation of beliefs about the lighting

Table 4. An overview and sleep measures derived from the sleep diaries and the actigraphy data.

Measure		Definition
Time in Bed	(TIB)	Time spent in bed between getting into bed at night and getting out of bed for the day in the morning
Sleep Onset Latency	(SOL)	How long did it take you to fall asleep?
Number of Nightly Awakenings		How many times did you wake up, not counting you final awakening?
Wake After Sleep Onset	(WASO)	In total, how long did the awakenings last?
Early Morning Awakening	(EMA)	How long before the intended awakening did you wake up?
Total Sleep Time	(TST)	Time spent asleep (i.e., SOL, WASO, and EMA subtracted from TIB)
Sleep Efficiency	(SE)	The ratio of TST to TIB expressed in percentages (i.e., TST divided by TIB)
Sleep Period Time	(SPT)	Time between falling asleep and the final awakening
Number of Sleep Periods		How many times an individual woke up and fell asleep again during the night

conditions (Smolders & de Kort, 2014), one item assessing work strain and three items assessing performance and effort from the Psychological Variables Questionnaire (Pilcher & Walters, 1997), 12 items assessing the negative side effects of the light conditions (Kallestad et al., 2018), and the Brief Horne–Östberg Morningness–Eveningness Questionnaire (Adan & Almirall, 1991).

Interventions

Cognitive Behavioral Therapy for Insomnia (CBT-I). CBT-I is a multicomponent treatment that consists of one or more behavioral and cognitive techniques (e.g., sleep restriction, stimulus control, and restructuring of unrealistic expectations and beliefs about sleep) traditionally provided in a face-to-face setting (Morin et al., 2006). In study 1, half of the participants received face-to-face CBT-I. Digital adaptations of CBT-I have been

developed (Espie et al., 2012; Ritterband et al., 2009). In studies 1 and 2, a Norwegian translation of a dCBT-I intervention (Sleep Healthy Using the Internet; SHUTi) was used. The SHUTi program consists of 6 cores and is a fully automated adaptation of traditional face-to-face CBT-I with components such as sleep restriction, stimulus control, cognitive restructuring, sleep hygiene, and relapse prevention (Hagatun et al., 2019; Ritterband et al., 2009, 2017). CBT-I is recommended as a first-line treatment of insomnia, and both face-to-face and digital adaptations of this treatment are shown to be effective in reducing insomnia severity (Morin et al., 2006; Riemann et al., 2017; Wilson et al., 2019, Zacharie et al., 2016, van Straten et al., 2018). For further details on the content of the dCBT-I and CBT-I provided in studies 1 and 2, see Table 5.

Patient Education about Sleep. Digital patient education about sleep is provided via a fixed website and is widely used as a control intervention in RCTs of insomnia treatments (Hagatun et al., 2019; Ritterband et al., 2017). The patient education website describes the prevalence, causes, and impact of insomnia, gives advice about when to seek help from a healthcare professional, and includes information about basic lifestyle, environmental, and behavioral strategies that may improve sleep–wake patterns (Ritterband et al., 2017).

A Blue-Depleted Light Environment. A blue-depleted light environment was created in one of two newly built wards in the acute psychiatric unit at St. Olavs Hospital by use of an LED lighting system that emits both colored and white light. The light system in one ward was programmed to remove all short-frequency blue light (<530 nm) from 18:30 to 07:00. Blue-blocking window filters were deployed during evenings and nights, and all screens in the ward have permanent blue-blocking filters. The main purpose of a blue-depleted light environment is to counteract the negative effects of artificial light exposure at night and help

Table 5. An overview of the content of each core of dCBT-I (studies 1 and 2) and the content of sessions in the face-to-face CBT-I (study 1). Adapted from (Kallestad et al., 2021).

Core/ session	**dCBT-I**	**Face-to-face CBT-I**
1	Overview: Review the nature of insomnia and how the program works; participants identify their sleep problems and set up personal treatment goals.	Focus on motivation and personal treatment goals. Psychoeducation about sleep and sleep hygiene (e.g., lifestyle and environmental factors that might interfere with sleep). Setting up sleep restriction (lower limit of 5 hours) and a plan for tapering of sleep medication (if relevant/wanted).
2	Behavior and sleep: Focus on how behavioral changes can improve sleep, with special emphasis on sleep restriction (lower limit of 5 hours).	Review of adherence to sleep restriction. Focus on beliefs and behaviors about sleep and specific changes that occurred due to sleep restriction. Motivational work to ensure patient adherence to sleep restriction.
3	Behavior and sleep 2: Focus on behavioral changes that can improve sleep, with special emphasis on stimulus control.	As session 2 plus adding stimulus control if necessary.
4	Sleep and thoughts: Focus on addressing and changing beliefs and thoughts that might impair sleep.	As sessions 2 and 3.
5	Sleep hygiene: Education on lifestyle and environmental factors that might interfere with sleep (e.g., caffeine and nicotine intake, use of electronic devices in bed).	As sessions 2 and 3.
6	Relapse prevention: Focus on integrating the behavioral, educational, and cognitive components from the previous cores to develop strategies to prevent future episodes of poor sleep from developing into full-blown chronic insomnia.	Final session: Evaluation of progress relative to treatment goals. Focus on relapse prevention: Check that the patient has understood the rationale behind sleep restriction and can implement use of sleep diaries and sleep restriction should sleep problems occur later.

stabilize the sleep–wake patterns of hospital inpatients (J. Scott et al., 2019), with positive effects being reported following similar interventions (Henriksen et al., 2016; Sasseville et al., 2006; van der Lely et al., 2015).

Statistical Analyses

Paper 1. SPSS version 25 was used for all analyses. Paired samples t-tests were conducted to test whether self-reported levels of absenteeism, presenteeism, total work impairment, and activity impairment 6 months post-CBT-I were significantly lower compared with baseline levels. Independent samples t-test were conducted to test whether individuals who met the criteria for response or remission 6 months post-CBT-I would report lower levels of impairment compared with non-responders or non-remitters, respectively. The data were checked for skewness in kurtosis, and values were deemed acceptable. Missing data were replaced by mean group values, an imputation method which is shown to work well in datasets with low levels of missing data (Cheema, 2014).

Paper 2. Mediation analyses were undertaken by an independent researcher using Mplus version 8.2 (Muthén & Muthén, 1998–2010). Direct and indirect effects of treatment on each of the outcome variables (presenteeism, activity impairment, absenteeism, and employment status) were estimated for the mediator (insomnia symptom severity) while adjusting for potential confounders (sex, age, educational attainment, relationship status, and comorbidities).

Sensitivity analyses were carried out to examine whether significant (in)direct effect estimates were robust to violations of no unmeasured mediator–outcome confounding (Muthén, 2011) and missing data assumptions (Enders, 2010). The effects of missing data were investigated

by regression of missing data on the outcome variables to mimic a missing-not-at-random scenario.

Paper 3. All statistical analyses were performed using R statistical package (version 3.5.2., R Core Team, Vienna, Austria, https://www.R-project.org/) by a statistician who was blinded to participant allocation. A within-subject approach was used in the main analyses to estimate the effects of blue-depleted compared with standard hospital lighting on melatonin phase shifts, melatonin suppression, sleep, and subjective sleepiness, neurocognitive functioning, and side effects. Post hoc analyses by condition order were performed on melatonin, polysomnography data, and sleep times across the study period.

Paper 4. STATA version 17 was used in all analyses of diary and actigraphy data. Fixed-effects regression models were fitted to capture the within-subjects effects using methods of maximum likelihood estimation. Results on comparisons between effects of the blue-depleted light environment compared with standard hospital lighting are shown for evening shifts and night shifts, both separately and combined.

IBM SPSS Statistics version 25 was used in exploratory analyses of questionnaire data (i.e., outcomes without multiple comparisons). One-way between-group ANOVAs were performed to examine differences in medical and mental health for participants working in blue-depleted compared with standard hospital lighting during the first round of data collection.

Ethics

Paper 1. The study protocol was approved by the Regional Ethical Committee of Southeast Norway (2013/1836). All participants provided written informed consent.

Paper 2. The study protocol was approved by the Regional Committee for Medical and Health Research Ethics in Southeast Norway (2015/134) and registered on the

ClinicalTrials.gov website (NCT02558647). The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Paper 3. The study protocol was approved by the Regional Ethical Committee of Central Norway (2017/916) and is registered on the ISRCTN website (ISRCTN12419665). Written informed consent was obtained from all participants, and the study was undertaken in accordance with the Revised Declaration of Geneva. The Patient User Group at the Division of Mental Health at St. Olavs Hospital were involved with the development of the new acute psychiatric unit at Østmarka and are involved in all research projects conducted in the unit. Specifically, the Patient User Group has helped develop tools to evaluate the subjective experience of residing in the unit and will contribute to the dissemination of findings to patients, hospital management, and policy makers.

Paper 4. The study protocol was approved by the Regional Ethical Committee of Central Norway (2018/1516), and the study was retrospectively registered on the ISRCTN website (ISRCTN21603406). Written informed consent was obtained from all participants, and they could withdraw at any time without providing a reason. The study was designed and implemented by external researchers in response to concerns raised by nurses and safety representatives about the possible negative side effects of working in a blue-depleted light environment. Both nurses and safety representatives were closely involved with the design and planning of the study. Participants were guaranteed anonymity and that collected data could not be traced back to individual participants.

Results

Paper 1: The Effect of Reducing Insomnia Severity on Work- and Activity-Related Impairment

The purpose of study 1 was to investigate whether CBT-I would impact on employee's levels of daytime functioning at 6-month follow-up, and whether any improvements in daytime functioning would coincide with reduced insomnia severity in a sample recruited from an outpatient sleep clinic.

Analyses of the data showed that participants reported lower levels of presenteeism ($p = .001$; Cohen's $d = 0.46$), total work impairment ($p < .001$; Cohen's $d = 0.48$), and activity impairment ($p < .001$; Cohen's $d = 0.66$) due to health problems at 6-month follow-up compared with baseline. There were no significant differences on absenteeism at 6-month follow-up compared with baseline. Response and remission analyses showed that both responders and remitters reported lower levels of total work impairment ($p = .017/< .001$; Cohen's $d = 0.61 / 0.88$) and activity impairment ($p = .023/.006$; Cohen's $d = 0.56/0.69$) compared with non-responders and non-remitters, respectively, and that remitters reported lower levels of presenteeism ($p = .002$; Cohen's $d = 0.45$) at 6-month follow-up compared with non-remitters. There were no effects of responder/remitter status on absenteeism.

Paper 2: The effects of digital CBT-I on work productivity and activity levels and the mediational role of insomnia symptoms: Data from a randomized controlled trial with 6-month follow-up

The purpose of study 2 was two-fold. First, whether dCBT-I was associated with better work- and activity-related outcomes at 6-month follow-up compared with a control condition (patient education about sleep) in the general population reporting insomnia symptoms was

investigated. Second, whether changes in work- and activity-related outcomes were mediated by change in insomnia symptoms between baseline and 9-week follow-up was explored.

Descriptive statistics of ISI scores at baseline and 9-week follow-up and work and activity-related outcomes (presenteeism, activity impairment, absenteeism, and employment status) at baseline and 6-month follow-up for the sample overall, and for either dCBT-I or patient education, showed that participants randomized to dCBT-I experienced a mean reduction in ISI score from 19.2 (SD = 3.9) to 10.4 (SD = 6.2) and participants in the control condition experienced a mean reduction from 19.6 (SD = 4.0) to 15.2 (SD = 5.3). For the whole sample, levels of presenteeism and activity impairment were reduced by 9.4% and 12.4%, respectively. Absenteeism in the study sample was reduced by 4.0 hours, and employment status for the sample overall remained virtually unchanged (69.2% vs. 70.6%).

The mediational analysis demonstrates a significant total effect of dCBT-I compared with psychoeducation on activity impairment outside of work (estimated effect −5.6%). There were no significant total effects on presenteeism, absenteeism, or employment status. Further, there were significant indirect effects of the mediator on presenteeism (estimated effect −5.4%) and activity impairment (estimated effect −5.5%) at 6-month follow-up but no significant indirect effects on absenteeism or employment status.

Sensitivity analyses of unmeasured confounders by use of correlated residual plots on presenteeism and activity impairment suggested that a residual correlation of at least 0.15 between the mediator and the outcome variable would be needed to reduce the indirect effects to zero. Although this can be considered a rather strict requirement, indirect effects should be interpreted with some caution. Sensitivity analyses assuming data missing-not-at-random were carried out and show the same results as the main analyses, in addition to an indirect

effect on absenteeism (1.8-hour increase) and a total effect of the mediator on presenteeism (estimated effect −4.3%).

Paper 3: The evening light environment in hospitals can be designed to produce less disruptive effects on the circadian system and improve sleep

The main aim of study 3 was to investigate the effects of a blue-depleted light environment (BDLE) compared with a standard hospital light environment (STLE) on biological markers of sleep in healthy controls. Secondary aims were to investigate effects of the blue-depleted light environment on neurocognitive functioning, subjective sleepiness, and side effects.

The most important findings in this study were the effects on circadian rhythms and sleep. First, after residing for 5 consecutive days in an BDLE, participants exhibited substantially reduced suppression of melatonin (18% in BDLE vs. 45% in STLE; $p < .001$) and a phase advancement of the circadian rhythm (as measured with the protocol for dim light melatonin onset) compared with baseline (1:20 hours in BDLE vs. 0:46 hours in STLE; $p < .001$). Additionally, melatonin levels in the BDLE did not differ from those in dim light (<3 lux), suggesting that the removal of all short-frequency, blue light (<530 nm) in a BDLE creates a 'virtual darkness' for the circadian system (Gottlieb et al., 2019). Second, residing in the BDLE increased total sleep time (by 8.1 min; $p = .032$) and time in rapid eye movement sleep (by 13.9 min; $p < .001$).

There were some indications of differences in neurocognitive functioning between conditions with higher variability in response times throughout the Conners Continuous Performance Test 3 (73.0 ms in BDLE vs. 65.3 ms in STLE; $p = .042$), but no differences were found on mean reaction time (356.7 ms in BDLE vs. 369.9 ms in STLE; $p = .85$) or number of omissions (0.3% in BDLE vs. 0.3% in STLE; $p = .93$) or commission errors (32.4% in BDLE

vs. 27.3% in STLE; p = .032). There were no significant differences on levels of evening subjective sleepiness (p = .16) or side effects (p = .091) between conditions, although tiredness/fatigue was more frequently reported in the BDLE (by 7 participants) than in the STLE (2 participants). There was a significant difference in the participants' ability to sort color hues between conditions (192 ± 33.4 error in BDLE vs. 39.3 ± 23.1 error in STLE; p < .001), reflecting low and average ability, respectively.

Paper 4: Sleep and Work Functioning in Nurses Undertaking Inpatient Shifts in a Blue-Depleted Light Environment

The main aim of study 4 was to investigate the effects of a blue-depleted light environment (BDLE) compared with a standard hospital light environment (STLE) on shift working nurses' sleep, mood, levels of stress, and caffeine use. Secondary aims were to investigate the effects of the blue-depleted light environment on medical conditions, mental health conditions, and side effects.

Results from the fixed-effects linear models comparing the blue-depleted light environment with standard hospital lighting showed within-subject differences of increased sleepiness (by 17%) during evening shifts in the BDLE compared with the STLE (p = .034; Cohen's *d* = 0.49) and a 0.2 increase in number of cups of caffeinated beverages consumed during night shifts in the STLE compared with the BDLE (p = .027; Cohen's *d* = 0.37). There were no significant differences between conditions on any other outcome variables from the diary or actigraphy data.

The exploratory one-way between-group ANOVAs on the questionnaire data revealed no significant differences between the groups except that nurses working in the BDLE reported

that they perceived the lighting as warmer ($p = .009$) and more relaxing ($p = .023$) than nurses in the STLE.

Discussion

The studies included in this thesis demonstrate that interventions to improve sleep also have some positive effects on daytime functioning at work and in activities outside of work and that it is possible to create a blue-depleted light environment that positively impacts on sleep in healthy volunteers without having a negative impact on the sleep and functioning of nurses undertaking shift work.

The main contributions of the presented studies are that they focus on knowledge gaps in the literature on sleep problems, sleep interventions, and their impact on daytime functioning. There is, for example, robust evidence that that CBT-I reduces the severity of insomnia symptoms (Arnedt et al., 2020; Barnes et al., 2017; Bostock et al., 2016; Espie et al., 2012, 2016, 2019; Hagatun et al., 2019; Kallestad et al., 2021; Ritterband et al., 2009, 2017; Vedaa et al., 2020; Zachariae et al., 2016), but there is limited research on its impact on different elements of daytime impairment, such as work productivity and general daily activities (outside of work). Further, there is evidence that use of blue-blocking glasses (Gottlieb et al., 2019) to create a 'virtual darkness' reduces the severity of, e.g., manic symptoms (Henriksen et al., 2016), but it remains to be investigated whether meaningful physiological effects could be achieved in healthy controls by creating blue-depleted light environments in naturalistic settings. Further, if blue-depleted light environments are shown to benefit inpatients' sleep and recovery time and are to be implemented as standard solutions in healthcare institutions, it is also highly warranted that it first be investigated whether they posit any benefit or harm to the nurses engaged in shift work under such conditions.

The Effects of Insomnia Treatment on Daytime Functioning

Presenteeism and Activity Impairment. Considering that untreated insomnia is associated with a wide range of negative outcomes including adverse health consequences (Sivertsen et al., 2012), increased rates of presenteeism (Bolge et al., 2009; Johns, 2009), short- and long-term absenteeism (Caverley et al., 2007; Reynolds et al., 2017), and permanent work disability (Jansson et al., 2013; Léger & Bayon, 2010; Sivertsen et al., 2006, 2009), it is of importance to investigate whether alleviation of insomnia symptoms after treatment also reverses the negative daytime effects associated with insomnia. In studies 1 and 2, the results demonstrated that CBT-I, in addition to its effect on insomnia symptom severity, has small to moderate positive effects on daytime functioning at work and in activities outside of work. Specifically, responder/remitter analyses of data from a subsample of adult patients recruited from an outpatient public sleep clinic (study 1) indicated that improvements in insomnia symptoms were associated with increased work productivity (i.e., reduced levels of presenteeism) and improvement in daytime activities outside of work at 6-month follow-up. Similarly, the mediation analysis on data from self-referred adults from the public with insomnia (study 2) demonstrated that it was specifically the improvement in insomnia symptoms from baseline to 9-week follow-up that led to improvements in work productivity and daytime activities outside of work.

The results on presenteeism and activity impairment from studies 1 and 2 are in line with previous research and add incremental evidence to support the results from similar studies on the effect of insomnia treatment on daytime outcomes (Espie et al., 2019; Kalmbach et al., 2019; Luik et al., 2020). Additionally, the mediation analysis highlights the mechanism that improvement of insomnia symptoms from baseline to 9-week follow-up led to improvement in these work- and activity-related outcomes at a later point in time (6-month follow-up),

showing that treatment of insomnia and reduction of insomnia symptom severity, to some degree, reverse daytime impairment.

Absenteeism and Employment Status. CBT-I did not have any effects on absenteeism nor result in changes in insomnia severity (studies 1 and 2) or employment status (study 2). A possible explanation for the lack of findings could be that insomnia is more closely related to presenteeism than to absenteeism or employment status (Caverley et al., 2007; Kessler et al., 2011) and that these outcomes may be influenced of many factors other than sleep. For example, national policies on absence from work, employment practices within companies, and "return to work" schedules (e.g., gradual return without monitoring presenteeism) will impact whether an individual decides to take a leave of absence or attend work.

Further, gaining employment after unemployment (or becoming unemployed and receiving social benefits) is usually a process that takes time, and 6 months might not be sufficient to capture the subtle effects of dCBT-I or a reduction in insomnia symptom severity on an individual's employment status. It may also be difficult to differentiate the effects of poor sleep by itself from those of, e.g., chronic diseases or work conditions that may simultaneously have an impact on sleep (Johns, 2009; Leger, 2014). As such, absenteeism might set a very high threshold for testing the direct or indirect impact of any therapy on work and social functioning (Johns, 2009), and employment status as a binary measure might not be sensitive to subtle changes in an individual's affiliation to working life.

It is also important to note that the data on absenteeism (studies 1 and 2) were extracted from RCTs not primarily designed to investigate the effects of CBT-I on work or other daytime outcomes. In study 1 (but not in study 2) absenteeism was calculated based on a validated scale (the general health version of the Work Productivity and Activity Impairment

Questionnaire (WPAI)) (Reilly et al., 1993). In study 2, a proxy measure of absenteeism (hours absent from work) was included instead of absenteeism as a percentage of work time missed (as in study 1) because information on regular working hours was not available. However, study 2 was estimated to have statistical power (80%) to detect significant differences ($p < 0.05$) in rates of absenteeism (Kallestad et al., 2018). To better capture absenteeism in future studies, collecting objective individual-level data on outcomes such as hours worked and hours absent over a defined period is recommended. Further, as employment status as a binary measure is not sensitive to subtle changes in an individual's affiliation to working life, future research should consider more sensitive measures of affiliation with working life (e.g., number of job adverts read, applications sent, or interviews attended).

Treatment Response and Remission Rates. Although CBT-I is demonstrated to be effective in terms of alleviating the severity of insomnia symptoms and some aspects of daytime functioning, the treatment does not work equally well for everyone. The effects of treatment on insomnia symptom severity itself can be discussed in terms of symptom reduction or in terms of clinical criteria for treatment response (i.e., marked clinical improvement defined as a reduction of at least 8 points on the ISI) (Morin, Belleville, et al., 2011) and remission (i.e., an ISI score of 7 or less) (American Psychiatric Association, 2013). In the subsample of working participants recruited from a public outpatient sleep clinic (study 1), the analyses showed that ~60% met the criteria for response and that ~50% of participants met criteria for remission at 6-month follow-up. In the sample recruited from the general public (study 2), available data show that ~60% of participants who received dCBT-I were in remission at 9-week follow-up (Vedaa et al., 2020). Similarly, a study on postmenopausal women found a remission rate of ~65% at 6-month follow-up after treatment with CBT-I (Drake et al., 2019). A study on the effects of telemedicine compared with face-to-face CBT-I

on diagnosed insomnia found a response rate of ~60% and a remission rate of ~45% (with minimal differences between treatment groups) at 3-month follow-up (Arnedt et al., 2020).

These response/remission rates reflect that insomnia research using RCT designs (as in study 2) can provide needed insight into the effectiveness and mechanisms of CBT-I on a group level. However, it is important to keep in mind that less is known about which individual patients are likely to benefit (or not) from, e.g., digital or telemedicine adaptations of CBT-I. Elevated dropout rates are evident in digital CBT-I trials (Wickwire, 2019), and it is important to further investigate barriers to completion (e.g., time demands or lack of individualization) and facilitators of engagement (e.g., individual support or convenience of use) (Hermes et al., 2019).

One possible explanation of why some individuals do not respond to treatment could be that treatment adherence proves overly demanding, e.g., because patients receiving CBT-I, either face-to-face or delivered online, are required to keep sleep diaries, adhere to strict bedtimes and rise times, and avoid napping during the day (Morin, 1993; Morin & Espie, 2004). Another possible explanation for the lack of response to treatment could be that some individuals are objectively short sleepers. There is evidence indicating that individuals with objective short sleep duration (i.e., sleep duration less than 5 hours as measured using polysomnography) have the most biologically severe phenotype of the disorder that is associated with an unremitting course (in contrast to insomnia with objective normal sleep duration), and patients with the biologically severe phenotype might respond better to biological treatments than CBT-I (Vgontzas et al., 2013). However, the usefulness of objective sleep length has been challenged by data indicating that only ~50% of short sleepers are consistent short sleepers (Galbiati et al., 2021). Further, objective short sleep duration

must not be confused with self-reported short sleep duration, as about 50% of individuals with insomnia underestimate how much they sleep (Vgontzas et al., 2013).

Comorbid Insomnia. A meta-analysis of 37 RCT studies on the efficacy of CBT-I with comorbid medical or mental health conditions shows that CBT-I is effective in alleviating insomnia symptoms for individuals with comorbid conditions (Wu et al., 2015), though attrition in online treatment of chronic insomnia could still be predicted based on symptom severity and comorbid mental health conditions (Hebert et al., 2010). In study 1, available data show that ~55% of patients recruited to the original RCT report at least one medical comorbidity and ~80% reported at least one comorbid mental health condition (Kallestad et al., 2021). However, this was based on self-reported symptoms and not a clinical evaluation of current presentation, patient history, or accompanying functional impairment, which introduces some uncertainty about the true comorbidity status of this sample. In study 2, ~50% of participants recruited from the general population reported having at least one medical comorbidity and ~55% reported at least one comorbid mental health condition.

Considering, for example, the high rates of medical comorbidities, there is a need for treatment options that could potentially help those who do not benefit substantially from CBT-I (e.g., do not respond to treatment nor achieve remission). An epidemiological overview of sleep disorders illustrated that diseases other than insomnia disorder can lead to an insomnia complaint (e.g., breathing-related sleep disorders, restless legs, poor sleep hygiene or environmental factors, or substance use) and can account for approximately 40% of the insomnia complaints (Ohayon, 2011). If many individuals experience comorbid insomnia because of another underlying and unidentified disorder (particularly comorbid medical conditions), it might be reasonable to investigate whether an individual who does not

respond to, e.g., CBT-I would benefit from receiving another treatment intervention targeting the other disorder, either alone or in parallel with CBT-I.

Focusing on mental health comorbidities, a review on the efficacy of cognitive and behavior therapies for insomnia on daytime symptoms has highlighted the need to better understand how psychological and physiological mechanisms are shared between disorders, pointing out that comorbidity may result in a vicious cycle whereby daytime symptoms of a mental health condition might interfere with sleep, and sleep disturbances, in turn, contribute to symptoms during the next day (Benz, 2020). This is further supported by a meta-analysis of RCTs showing that improved sleep had a positive effect on overall mental health, and that greater improvements in sleep quality led to greater improvements in mental health, suggesting that sleep is causally related to the experience of mental health difficulties (A. J. Scott et al., 2021).

Creating a Sleep-Friendly Environment

Although there is an important difference between diagnosed sleep disorders, such as insomnia, and intermittent poor sleep, most people tend to 'have a bad night' or sleep poorly every now and then and find that modern life might get in the way of sleep. Exposure to light and darkness over the course of a day is a major cue for entrainment of sleep and wakefulness in humans, but in modern societies, humans are frequently exposed to artificial light sources during the dark period (evenings and nights) of the day (Wirz-Justice, 2007). This likely has widespread and ongoing implications for health and sleep at the societal level (Münch et al., 2020). As such, there has been an increased focus on, e.g., reducing the use of electronics before bed time (Chang et al., 2015) and light pollution in large cities (Falchi et al., 2019). Further, the creation of blue-depleted light environments in, e.g., hospitals (J. Scott et al., 2019) or the use of blue-depleted light sources in patient rooms (Albala et al., 2019) might

counteract the negative effects of artificial light exposure at night and help stabilize the sleep–wake patterns of hospital inpatients. Although the installation of blue-depleted light environments in hospitals (and possibly in other institutions) could readily be provided as a potential therapeutic intervention to large numbers of inpatients with little increase in demands on staff or patients, there was a need to first investigate whether it affects physiological markers of sleep in healthy volunteers or has an effect on sleep and work functioning in nurses working shifts, without negative side effects.

Circadian Effects of Blue-Depleted Lighting. In study 3, the analyses indicated that it is possible to create a blue-depleted light environment during evening and nights in a naturalistic setting that has beneficial effects on the circadian system and sleep for healthy participants, moreover without negative side effects. Specifically, the participants who resided in the blue-depleted environment substantially reduced their suppression of melatonin and experienced a phase advancement of the circadian rhythm. They also experienced a slight increase in total sleep time and time spent in rapid eye movement sleep. It is important to keep in mind that these individuals did not report having sleep problems (and that high variability in day-to-day sleep times was one of the exclusion criteria of the study) or any mental or medical conditions prior to entering the study, such that even small improvements in the sleep of these healthy volunteers are of interest. Additionally, the study was not conducted in a laboratory setting, and the specific light exposure each participant was subjected to in the wards or when they left the unit during the day (from 08:00 to 17:00) was not controlled. This is both a novelty and a strength of the study, as it highlights that even healthy participants can benefit from reducing their exposure to artificial white light during evenings and nights. Further, it also highlights that alteration of light sources to block blue frequencies during the dark period of the day is feasible.

Virtual Darkness. Interestingly, the study also showed that levels of melatonin measured in the blue-depleted environment did not differ from melatonin levels measured in dim light, suggesting that the removal of all short-frequency blue light creates a 'virtual darkness' for the circadian system (Gottlieb et al., 2019). It has previously been shown that removing artificial light at night and keeping study participants in darkness after sunset for three days will phase advance the timing of melatonin onset and the sleep period (Stothard et al., 2017). This is comparable to observations of the healthy volunteers who resided in the blue-depleted light environment, supporting that it primarily is the short-frequency blue light of artificial light sources that has an effect on the circadian system and that it is possible to create sleep-promoting lighting environments using new light technologies.

Subjective Sleepiness and Alertness. There were no differences in the levels of subjective sleepiness between light conditions but some indication of reduced neurocognitive functioning (i.e., alertness) in the blue-depleted light environment. This might be because artificial white light (as opposed to blue-depleted lighting) has a direct alerting effect (Souman et al., 2018), which may impact on daytime functioning. It might also reflect that the drive for alertness varies over across the 24-hour day and that the additional phase advancement of the circadian rhythm experienced by participants in the blue-depleted light environment might have resulted in a lower circadian drive for alertness earlier in the evening (i.e., when the Conners Continuous Performance Test was administered) (Vandewalle et al., 2007). As the participants in this study did not have any specific responsibilities or, e.g., work-related tasks to perform while residing in the acute psychiatric unit, the indications of reduced alertness was likely inconsequential to them. After the hospital opened for admissions, however, the same statement is not applicable to staff working and performing tasks during evenings and nights, as both reduced alertness and increased sleepiness may

compromise their performance and/or safety (Åkerstedt & Wright, 2009; Dinges, 1995; Kecklund & Axelsson, 2016).

Side Effects. Further, very low numbers of side effects were reported in both light conditions, and no overall differences were detected, suggesting that the blue-depleted light environment does not have an obvious adverse impact on exposed individuals. The overall absence of side effects is encouraging, as it indicates that residing in a blue-depleted light environment is acceptable, at least to healthy individuals. However, these findings need to be confirmed in future larger-scale studies to establish, with significant certainty, that a blue-depleted light environment is not harmful. This is important for several reasons. First, this study included only a small number of participants, and the comparisons between self-reported side effects based on only 5 consecutive days might not be sufficient to detect subtle yet important nuances between conditions that might appear with longer exposure. Second, some of the most widely used medications in psychiatric disorders, as well as some diagnoses (e.g., bipolar disorder, seasonal affective disorder, and circadian rhythm disorders), appear to increase the light sensitivity of the circadian system (Gottlieb et al., 2019; McGlashan et al., 2018; Nathan, 1999; Watson et al., 2018), likely resulting in differential effects of the light for particular patient groups. Third, the installation of blue-depleted lighting may also affect the sleep and functioning of staff working shifts, and as shift work itself is associated with a range of negative health consequences, it is also highly warranted to determine whether exposure to a blue-depleted light environment at work results in any benefits or harm to the nurses.

Blue-Depleted Lighting in the Workplace

The main aim of study 4 was to investigate the effects of blue-depleted compared with standard hospital lighting on nurses' sleep and work functioning. There were no significant

differences between light conditions on variables from the work and sleep diary or actigraphy data, with the exception of some indications of increased sleepiness during evening shifts in the blue-depleted light environment and a slight increase in the number of caffeinated beverages consumed during night shifts under standard hospital lighting.

A systematic review on studies of simulated shift work demonstrated that caffeine consumption might be effective in improving alertness in shift workers (Ker et al., 2010), and while the slight increase in caffeine use during night shifts in standard hospital lighting is interesting, the available data do not allow us to determine whether this is best explained by differences in energy levels or perceived alertness during night shifts in different light conditions or individual fluctuation in caffeine intake (related to spurious factors), etc.

The small increase in sleepiness associated with evening shifts in the blue-depleted light environment may compromise the nurses' safety, e.g., if they need to react instantly to adverse events at work or when they commute home after work (Åkerstedt & Wright, 2009). The differing levels of sleepiness between light conditions likely reflects that white light (as opposed to blue-depleted light) has a direct activating effect, e.g., by increasing alertness (Smolders & de Kort, 2014; Souman et al., 2018; Viola et al., 2008). As such, it is surprising that the same increase in sleepiness was not observed for night shifts undertaken in the blue-depleted light environment. Considering the three-process model of alertness regulation, which is used to predict alertness (process W) based on time spent awake (process S) and the circadian timing of sleep (process C) (Åkerstedt & Folkard, 1997), it would be expected that the blue-depleted light environment exerted stronger effects on subjective sleepiness during night shifts compared with evening shifts. When working nights, the nurses will likely have spent more time awake compared with nurses working evening shifts (unless the nurses napped prior to the shift), and the circadian drive to sleep will be stronger (unless the nurses

have shifted their circadian rhythms and are fully adapted to being active during the night and sleep during the day). It could be that the comparatively small sample size included in the study resulted in a lack of statistical power to detect the small effects of light conditions on sleepiness or that the included measure of sleepiness (a single item in the work diary assessing sleepiness from 'not at all sleepy' (1) to 'very sleepy' (5) after each shift) is not satisfactorily suited to distinguishing between the nuances in the levels of sleepiness during shifts.

To the best of our knowledge, this study was the first to investigate nurses' sleep and functioning while working in a blue-depleted compared with a standard hospital light environment. One other study has investigated the effect of overnight use of a blue-depleted light source (instead of overhead patient room lighting) on nurse (and patient) experience when providing overnight care tasks in patient rooms. In that study, 82% of the nurses reported that the blue-depleted light source provided adequate lighting and improved caregiver satisfaction (Albala et al., 2019). The studies are not directly comparable as the adequacy of lighting and caregiver satisfaction was not measured in study 4, but exploratory analyses of between-group differences on the questionnaire data in our study did not reveal any differences in experienced suitability of blue-depleted compared with standard hospital lighting in the workplace nor on other measures of side effects associated with the lighting. The only difference on the questionnaire data were that the blue-depleted lighting was perceived as warmer and more relaxing.

In summary, although the amount of available data on the effect of blue-depleted lighting on nurses' sleep, work function, and satisfaction with the work environment is scarce, there is reason to be optimistic that blue-depleted lighting in the workplace will be accepted by nurses. However, replication and confirmation of the findings from this study are

recommended before blue-depleted light environments can be implemented across healthcare institutions. With time, these findings may prove relevant across a variety of hospital units and might also possibly be extended to other settings where control over ambient and incident light may be feasible, such as trains, planes, and hotels.

Methodological Considerations and Limitations

A major challenge in research projects is the recruitment and retainment of participants, increasing uncertainty in the representativeness of samples. Methodological issues can also cause problems with the analysis of data and limit the conclusions that can be drawn. Specifically, issues associated with inclusion and exclusion criteria, low participation rates, attrition, durability of results, statistical power, and self-reported compared with objective data will be discussed in the following paragraphs.

Inclusion and Exclusion Criteria. A survey among self-reported insomnia patients investigating the inclusion and inclusion criteria of clinical trials for insomnia indicates that eligible participants might not be representative for the insomnia patient population as a whole as a result of applying too many or overly restrictive eligibility criteria (Huls et al., 2018).

In study 1, 77 (76.2%) of 101 randomized participants in the original RCT reported that they were in paid employment at baseline (and were therefore eligible for inclusion in the study). The flow diagram of the original RCT (Kallestad et al., 2021) shows that 288 individuals were assessed for eligibility, 265 (92.0%) completed the clinical evaluation, 98 (33.6%) were excluded because they did not meet the inclusion and exclusion criteria, and 66 (22.9%) were excluded because they declined to participate. Finally, 101 (35.0%) participants were randomized to receive either digital or face-to-face CBT-I. For study 2, available data show

that 5349 individuals were assessed for eligibility by use of online screening. Of those, 2131 (39.9%) discontinued the screening for unknown reasons, 1497 (28.0%) were excluded (e.g., due to reporting of excessive sleepiness, engagement in nighttime shift work, or only mild insomnia symptoms), and 1721 (32.2%) were randomized to receive either dCBT-I or psychoeducation (Vedaa et al., 2020).

Application of less stringent criteria for research participation in research trials could yield information on the effectiveness of insomnia treatment for the whole insomnia population. For example, some individuals with insomnia self-medicate with, e.g., alcohol to improve their sleep (Morin, 2006), and these individuals are excluded from insomnia trials due to substance use. On the other hand, fewer defined criteria would complicate the analysis of data and the interpretation of results, creating a need for future large-scale trials designed to untangle the effects of treatment from the effects of, e.g., other sleep disorders and comorbidities. Such studies would also be resource-demanding, as inclusion of patients with comorbid disorders that could possibly be associated with adverse effects when exposed to CBT-I would require close monitoring to determine how each individual responds to treatment.

Low Participation Rates. Recruitment and retainment of participants is not only a challenge in clinical insomnia trials. In study 4, 25 (23.6%) of 106 nurses were excluded from participation in the study because they worked less than 50% of fulltime equivalent or were on leave (e.g., maternity or sick leave). Of the 86 nurses who met the criteria for inclusion in the study, 25 (29.1%) agreed to participate and provided data for the first 6 weeks of data collection, whereas only 10 (11.7%) participants provided data for the last 6 weeks of data collection. This low participation rate introduces uncertainty about the representativeness of the sample, and although other single-site studies in small workplaces (less than ~100

employees) will also necessarily be bound by an upper limit of available participants, having high participation rates would ensure that any drawn conclusions will be representative of all employees.

Attrition. Attrition or withdrawal of eligible participants before, during, or after exposure to treatment presents a major threat to the internal and external validity of RCTs (Sidani et al., 2015), and the phenomenon of participants stopping usage and/or being lost to follow-up is one of the fundamental characteristics and methodological challenges in the evaluation of digital adaptations of healthcare in general (Eysenbach, 2005). Regarding intervention use (study 2), which is a form of attrition, slightly less than 50% of individuals allocated to dCBT-I completed all six core elements of the intervention (Vedaa et al., 2020). Although this is comparable to other large-scale CBT-I trials (Buysse et al., 2006; Freeman et al., 2017; Ritterband et al., 2017) and data showing that ~40% of patients with chronic conditions correctly collect and take their prescribed medication (Neiman et al., 2017), taking steps to increase adherence rates could improve outcomes. For example, attrition in online treatment of chronic insomnia has been predicted based on symptom severity and comorbid mental conditions (Hebert et al., 2010), but no such predictor variables were found in group CBT-I (Ong et al., 2008), possibly indicating that symptom severity might be related to a preference for person-to-person contact over computer-based formats. A study on attrition from computer-based CBT-I programs (n = 29) found that, e.g., staff support could facilitate engagement, and it is recommended that future studies include weekly follow-up phone contact for individuals who desire this (Hermes et al., 2019). Individual weekly follow-up would probably not be feasible in large-scale online trials, but there are some indications that allocation to a preferred treatment option (as opposed to randomization) yields a lower rate of attrition (Sidani et al., 2015).

Statistical Power. The comparatively small sample sizes in studies 1, 3, and 4 limited the types of analyses that were feasible to conduct. For example, a larger sample size and the use of multivariate analyses in study 1 could have allowed for the detection of small effects of CBT-I on the work-related outcomes and consideration of the effect of covariates or mediators of improvement. Additionally, studies 1 and 2 were not primarily designed to investigate the work-related impact of sleep. In study 2, this meant that the measure of absenteeism was a proxy measure, with participants only reporting the number of hours absent from work (instead of, e.g., percentage of work hours absent), complicating comparisons with other studies that include absenteeism. It is also important to note that in studies with high dropout rates (as in study 2), efficacy measures may underestimate the impact of an application on a population that continues to use it (Eysenbach, 2005). However, sensitivity analyses assuming data missing-not-at-random did not significantly alter the results even though the results of the mediation analyses should be interpreted with some caution as the possibility of the significant mediator–outcome having a confounding impact on the estimated indirect effects could not be excluded.

There were also uncertainties related to statistical power in studies 3 and 4, as only 12 and 25 participants were included, respectively, but the within-subject design applied in both studies is a strength as it eliminates intra-individual variations in sensitivity to light exposure (Phillips et al., 2019). In study 4, it was not feasible to carry out analyses based on the cross-over design or investigate the effects of confounding factors (e.g., if patients exposed to the blue-depleted light environment were calmer and, as such, influenced the nurses).

Measurements. With some exceptions (e.g., measures of melatonin and neurocognitive functioning in study 3 and the use of actigraphy data in studies 3 and 4), most of the data included in this thesis was self-reported by participants (e.g., insomnia symptoms

and daytime impairment in studies 1 and 2, sleep diary data in studies 1, 2, and 4, side effects in study 3 and 4, and symptoms of medical and mental health conditions in studies 1, 2, and 4). Although self-report questionnaires on symptoms and degree of impairment are vulnerable to biases such as social desirability or recall bias (Demetriou et al., 2015), the majority of the included variables were based on standardized and validated questionnaires, and many of the targeted outcomes (e.g., insomnia symptoms and side effects) are subjective by their very nature. Further, a clear advantage of questionnaires is that they are easy to use in research (and clinical practice) to gather information about topic of interest. However, considering that it is necessary to limit the number of questionnaires that study participants are asked to fill out, secondary analyses of data from large-scale trials often investigate outcomes based on limited available information (e.g., a single item assessing absenteeism as in study 2). A such, there is a need for future studies focusing primarily on sleep and daytime outcomes. In such studies, it would be useful to also include other measures relevant for performance at work, e.g., the 10-item Perceived Stress Scale (a global stress measure to assess the extent to which individuals find their lives to be unpredictable) (Cohen et al., 1983) or the Cognitive Failures Questionnaire (designed to measure the frequency of lapses in perception, memory, and action) (Broadbent et al., 1982). The total effect of sleep on daytime impairment could also be assessed using e.g., the Insomnia Daytime Symptoms and Impacts Questionnaire (a global measure of daytime functioning) (Hudgens et al., 2021) or the WHO Quality of Life Questionnaire (assessing health and well-being) (Kosinski et al., 2007).

In addition to self-reported outcomes, studies on the effects of poor sleep on daytime functioning could include neurocognitive tests (such as Conners Continuous Performance Test in study 3) of cognition and/or psychomotor activity (e.g., card sorting, digit symbol substitution, pegboard, or finger tapping) to objectively assess daytime impairment. Generally, sleep studies that include both objective and subjective daytime measures have

found an agreement between the two types of measures, although available data indicate that the most common finding is that neither subjective or objective measures indicate daytime impairment in cognition or psychomotor activity (Riedel & Lichstein, 2000). As such, the administration of neurocognitive tests would increase the need for resources to conduct a study, and whether such tests would yield useful information about daytime functioning would depend on the research question investigated.

Lastly, the inclusion of data from registries, as opposed to self-reporting, could be a source of objective, high-quality information on how different interventions affect the participants. Objective data are relevant to studies on the effects of both CBT-I and blue-depleted light environments and could provide information on, e.g., levels of short- and long-term absenteeism, disability benefits, healthcare resource use, and medical or mental health diagnoses. Data on these outcomes could be directly acquired (with individual permission) from employer records or from national registries on absenteeism/unemployment (although the latter is only feasible in countries with a system of developed and universally available healthcare and where tracking of individuals across health, social, and employment registries is permitted). Additionally, data from objective sources could also be used to estimate the direct and indirect societal costs of insomnia treatment and associated gains (Bolge et al., 2009; Darden et al., 2020; Kessler et al., 2011), which would be of great use to, e.g., employers or healthcare policy makers.

Future Directions

The recommended first-line treatment for insomnia is CBT-I (Qaseem et al., 2016; Riemann et al., 2017; Wilson et al., 2019), but few individuals with this diagnosis seek help from a medical professional (Morin, LeBlanc, et al., 2011; Ohayon, 2011). Future studies should investigate whether it is feasible for, e.g., primary care physicians to prescribe/provide access

to dCBT-I also to patients who report only minor problems with their sleep. Such studies might also provide needed insight into how the clinical utility of dCBT-I is perceived and how dCBT-I might be incorporated into real-world clinical practice (Wickwire, 2019). Even though individuals with minor sleep problems do not meet the formal criteria for an insomnia diagnosis, they might experience small benefits from an increased focus on their sleep (and having the tools to make behavioral changes) through access to an intervention, which might have a large impact on the societal level. The prevention paradox describes that a population-based health measure, such as easy access to a sleep intervention, may lead to large benefits to the community but, at the same time, have relatively small influence on the health of a single individual (Hunt & Emslie, 2001; Rose, 1985).

Further, considering that the reduction in insomnia symptoms appear to reverse some of the impairment in work and other activities but that, e.g., stringent inclusion and exclusion criteria are often applied in research, possibly indicating that insomnia trials might not be representative of the whole insomnia population, and another avenue for future studies would be to further investigate the effect of CBT-I on insomnia and daytime impairment in individuals with comorbid symptoms/conditions (e.g., alcohol or substance use, excessive levels of sleepiness, etc.). There is also a need to further investigate how the impact of sleep problems on daytime impairment should be measured in individuals who are productive but not in paid employment (e.g., ‘home makers’). These issues are not only of theoretical importance but also likely to impact how sleep problems are addressed in research and clinical practice. Another example is that the structure of working life itself has changed over the past few decades, and employees now tend to work more with their heads than their hands. As such, ensuring that employees are fit to perform mentally demanding tasks is of importance to the success of businesses, making the impact of poor sleep on daytime functioning far more critical than ever before. It would be in the interest of both employers

and employees to investigate how focusing on sleep in the workplace could benefit both productivity and well-being. For example, occupational health services could offer sleep interventions in a low-threshold setting, e.g., sleep hygiene education, introductions to sleep restriction therapy/CBT-I, or light and dark therapy in group format. Additionally, access to dCBT-I could be provided. If such projects were instigated, it would be important to investigate their efficacy, but it would also be interesting to determine whether simple measures (e.g., instructing workers to minimize sleep-time variability and expose themselves to daylight in the morning) could yield a positive effect.

The development of blue-depleted environments might benefit psychiatric inpatients who often experience disrupted sleep–wake cycles (Gazendam et al., 2013; J. Scott et al., 2019; Wulff et al., 2010). The installment of blue-depleted lighting (or use of blue blocking glasses) in healthcare institutions may benefit patients (without having detrimental effects on staff working under such conditions). The effect of blue-depleted lighting on inpatients' sleep and recovery time has been investigated at the acute psychiatric unit at St. Olavs Hospital (Østmarka) in Trondheim, Norway (J. Scott et al., 2019), but results from the trial await publication (as of April 2022). Recently, another project aiming to evaluate the effects of, e.g., blue-blocking glasses on patient delirium in an intensive care unit was proposed at the University of Texas (Montgomery, 2021), suggesting that there is an interest in the medical field to improve inpatient outcomes by implementing broad circadian interventions to improve sleep. Positive effects have been found following similar interventions (Henriksen et al., 2016; Sasseville et al., 2006; van der Lely et al., 2015), and if large-scale trials and projects are deemed feasible to implement (i.e., without large increase in demands on staff) and lead to positive outcomes for various patient groups, this line of research could influence, e.g., healthcare policy makers to provide non-pharmacological treatment options such a

implementing blue-depleted light environments as a standard solutions in healthcare institutions, possibly improving the quality of care.

Blue-depleted lighting in hospitals has potential benefits to patients and no clear negative impact on nurses undertaking shifts in such an environment, but there is a need to further investigate the effect of a blue-depleted work environment on shift workers. For example, it would be important to investigate whether a blue-depleted work environment in combination with other interventions (e.g., wearing of blue-blocking glasses when travelling home from work to avoid exposure to artificial light) can positively impact the sleep or functioning of shift working nurses. As such, there is a need for large-scale trials to examine the effects of a blue-depleted light environment on nurses' sleep and circadian rhythms and the acceptability of such lighting in the work environment. Large-scale trials would allow for multivariable analyses on the effects of a blue-depleted light environment or the effects of switching between light conditions. Additionally, as exposure to artificial lighting also has an impact on the general population, it would be of great interest to also investigate the feasibility and effect of installing blue-depleted lighting in, e.g., private homes or other settings where control over ambient and incident light may be feasible, such as trains, planes, and hotels. If such interventions were deemed feasible and effective, it could help mitigate some of the negative effects of light exposure on human health and well-being.

Clinical and Public Health Implications

There are some important clinical and public health implications of the thesis that should be considered. Independent of why some individuals experience compromised sleep, it is important that the issue is addressed in an adequate manner and evidence-based interventions be offered. Evidence-based practice refers to the integration of science and practice to enhance public health by applying empirically supported principles to assessment, therapy,

and interventions (American Psychological Association, 2006). Considering that the reduction in insomnia symptoms appears to reverse some of the associated daytime impairment and that scalability is a key benefit of dCBT-I (Wickwire, 2019), making the treatment readily available to the general population might improve health outcomes for individuals with insomnia and contribute to a reduction in societal costs (e.g., by lowering the need for healthcare services or reducing levels of presenteeism and absenteeism). Additionally, combining cognitive/behavioral and pharmacological treatment interventions when appropriate (e.g., for individuals with persistent sleep problems, comorbid conditions, or objectively measured short sleep duration) may prevent sleep problems from becoming chronic and exerting a negative impact on health and daytime functioning (Morin, 2015; Morin, Vallières, et al., 2009; Riemann & Perlis, 2009).

Exposure to artificial light (e.g., from indoor lighting or use of electronic devices) during evenings and nights impacts negatively on health and sleep (Chang et al., 2015; Davies & Smyth, 2018; Falchi et al., 2019; Gooley et al., 2011; Vogel et al., 2012). Additionally, some individuals display greater sensitivity to evening light exposure than others (Phillips et al., 2019; Watson et al., 2018), possibly contributing to issues with the timing of sleep and wakefulness. To counteract the effects of light exposure, blue-depleted light environments could be widely installed, e.g., when building or renovating private homes (independent of whether the residents have problems with insufficient sleep) to create sleep-friendly environments. If altered light environments were to be broadly applied in private spheres, this intervention might, over time, contribute to a slight increase in sleep quality or deter the development of sleep problems for numerous individuals.

Considering the prevention paradox, even minimally improved sleep could have a large impact on the overall quality of life and capacity to participate in work and other activities on

a societal level. A clear advantage with installing blue-depleted lighting is that the environment itself will have a therapeutic effect on exposed individuals, without clear side effects. However, it would also be important to reduce the impact of exposure to light from electronic devices. While it is not realistic to reduce screen time during evenings and nights on a population-wide level, blue-depleted filters could offer a solution. A blue-depleted filter is directly applied on the screen and, similarly to blue-depleted lighting, alters the quality of the emitted light. By increasing the availability of blue-depleted filters and communicating the beneficial effects to the community, the effects of evening and nighttime use of electronic devices may be counteracted. Alternatively, blue-depleted filters could be provided by primary care physicians as a low-effort stepped-care intervention, e.g., to patients who report trouble with falling asleep at night. If the intervention is not effective, they patient may 'step up' to receive a more comprehensive treatment (e.g., dCBT-I).

Conclusions

Sleep is essential for health and well-being, yet its nature and true purpose remain enigmatic. It has fascinated observers for thousands of years and will likely continue to do so in the foreseeable future. While insomnia and poor sleep affect many individuals, available interventions (e.g., CBT-I or use of blue-depleted lighting) may be beneficial. Taken together, the findings from this thesis show not only that CBT-I improves insomnia symptoms but that it is specifically the reduction in the severity of insomnia symptoms that leads to the positive effects on work and daily activities. However, few individuals with sleep problems are correctly diagnosed, and even fewer are provided with the optimal, guideline-recommended interventions. Scalability is a key benefit of digitally available treatments, such as dCBT-I, and improving access to such interventions might have large positive impacts on public health. Further, this thesis suggests that, compared with a standard lighting condition, a blue-

depleted light environment was associated with improved sleep in healthy volunteers and did not have any significant adverse effects on nurses' sleep or functioning when engaged in shift work. Exposure to artificial lighting during evenings and nights tends to impact negatively on sleep quality and the timing of sleep and wakefulness and, consequently, individual health outcomes. Given the potential benefits of blue-depleted light, it would be worthwhile raising public awareness of how a relatively simple change in their exposure to different lighting conditions might resolve or even prevent some of the most widely experienced sleep problems. It is acknowledged that the reported findings in this thesis should be supported by future larger-scale studies specifically designed to test the direct and indirect effects of sleep and altered light interventions on daytime functioning However, the findings from this sequence of studies point toward the positive impact of sleep interventions on work and other activities, and the absence of negative effects on those exposed to different lighting environments implicate that blue-depleted lighting is well tolerated in naturalistic settings.

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Papers 1-4

Paper 1

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The Effect of Reducing Insomnia Severity on Work- and Activity-Related Impairment

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ABSTRACT

Objective/background: The effectiveness of Cognitive Behavioral Therapy for Insomnia (CBT-I) for alleviating sleep problems is well established. However, few studies have explored its impact on work productivity and activity.

Participants: Seventy-seven currently employed adults with insomnia disorder (59 females) recruited to a randomized trial of digital versus face-to-face CBT-I.

Methods and Materials: The general health version of the Work Productivity and Activity Impairment questionnaire was used to measure absenteeism, presenteeism, total work impairment, and activity impairment. We assessed changes in work productivity and activity pre-to-post-therapy for the total sample and then for subgroups categorized according to response or remission of insomnia disorder (evaluated using the Insomnia Severity Index).

Results: Study participants showed significant improvements in presenteeism ($p = .001$; Cohen's $d = 0.46$), total work impairment ($p < .001$; $d = 0.48$), and activity ($p < .001$; $d = 0.66$), but not absenteeism ($p = .51$; $d = 0.084$) between baseline and follow-up assessment. Individuals meeting criteria for remission showed significantly greater improvement in presenteeism ($p = .002$), total work impairment ($p < .001$), and activity ($p = .006$), but not absenteeism ($p = .064$).

Conclusion: This study suggests that the benefits of CBT-I extend beyond improvement in sleep to encompass moderate-to-large improvements in work productivity and activity levels particularly for individuals who achieve remission from insomnia. Given the importance of these behaviors, there is a need for future large-scale randomized trials and cohort studies which should strive to include objective measurement of daytime activity and work performance more frequently.

Background

The predominant complaints of individuals with insomnia are difficulties initiating or maintaining sleep despite adequate opportunity, and significant distress or impairment in important areas of daytime functioning, such as work or daily activities outside of work (American Psychiatric Association, 2013). Insomnia affects 10%–15% of the population (Pallesen et al., 2001, 2014), and

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untreated insomnia is associated with reduced quality of life (Kyle et al., 2010) and adverse health consequences (Sivertsen et al., 2012), as well as increased rates of short- and long-term absenteeism and permanent work disability (Overland et al., 2008; Sivertsen et al., 2006, 2009, 2012). Given that impaired daytime functioning is a diagnostic criterion for insomnia, it is important to establish if treatment of insomnia can also improve levels of functioning at work and activity outside of work.

Data from the 2005 US National Health and Wellness Survey (n = 41,184) found that individuals with insomnia symptoms experienced significant work productivity loss with 11% missing their scheduled work time (absenteeism), 29% demonstrating productivity loss while at work due to health problems (presenteeism), and 24% showing overall work impairment (work productivity loss) (Bolge et al., 2009). Compared with the non-insomnia group – when adjusting for demographics and comorbidities – this amounts to a 6% excess of absenteeism, 13% of presenteeism, and a 10% increase in overall work impairment. This equates to five full working weeks per annum per individual with insomnia when compared with the non-insomnia group, corresponding to a cost of 10% of the individual's salary. The insomnia group also experienced significantly greater impairment in daily activities, reporting, on average, 48% impairment in activity outside of work, which is more than three times higher than that reported by the non-insomnia group (Bolge et al., 2009). A similar study found that employees with sleep problems were twice as likely to self-report absenteeism of 7 or more days (Hui & Grandner, 2015). Further, a study on the work-related correlates of insomnia of 369 matched pairs of individuals diagnosed with the insomnia disorder (matched with individuals without any sleep difficulties, i.e., "good sleepers"), the authors found a two-fold increase in objectively assessed absenteeism for the individuals with insomnia. Also, individuals with insomnia had lower self-reported efficiency at work, poorer job satisfaction, and lower self-esteem at work compared with the "good sleepers" (Léger, 2006).

Cognitive Behavior Therapy for Insomnia (CBT-I) is the recommended first-line treatment for insomnia (Morin et al., 2006; Riemann et al., 2017; Wilson et al., 2019), which is associated with demonstrable improvements in daytime symptoms such as fatigue, mood, and mental functioning (Batterham et al., 2017; Sandlund et al., 2018). However, less is known about the potential effects of CBT-I on other life domains, such as work, or activity outside of work. It has been shown that individuals who receive CBT-I report increased job satisfaction (Barnes et al., 2017). In a randomized controlled trial (RCT) of postmenopausal women diagnosed with insomnia, CBT-I and sleep restriction therapy had a positive effect on work productivity and activity impairment, whereas sleep hygiene had no significant effect (Kalmbach et al., 2019).

A RCT in a UK community sample comparing digital CBT-I and sleep hygiene education showed that CBT-I was associated with reduced presenteeism (i.e., less impairment in productivity whilst at work), but not reduced absenteeism, and the investigators did not report on the effects on activity impairment outside of work (Espie et al., 2019). Similarly, in an American study of office-based employees with self-identified sleep problems, individuals treated with CBT-I reported lower levels of presenteeism, but not reduced levels of absenteeism, compared with wait-list controls (Bostock et al., 2016).

In summary, there is substantial evidence that work productivity and activity impairment are adversely affected by insomnia, but the evidence regarding potential beneficial effects of CBT-I on work-related outcomes remains limited. Therefore, it is important to test if the successful treatment of insomnia with CBT-I is associated with improved work-related functioning and activities outside of work.

Aims and hypotheses

This study focuses on a subsample of employed adults who recently participated in a RCT that compared two modalities of CBT-I (face-to-face or digital). The aims of the current study are (1) to test if individuals with insomnia disorder who receive CBT-I demonstrate any improvements in levels of work productivity or day-time activity following therapy, and (2) to examine if potential

improvements in work-related outcomes differ according to the observed change in insomnia severity. We hypothesize that:

(1) Levels of self-reported absenteeism, presenteeism, total work impairment, and activity 6 months post-CBT-I will be significantly lower than baseline levels;
(2) Individuals with an insomnia disorder who meet recognized criteria for response or remission at follow-up will show significantly greater improvements across all work- and activity-related outcomes than those who do not meet these criteria.

Methods and materials

Study design

The current study represents secondary analyses of data on a subset of a sample recruited to a recent RCT of digital versus face-to-face CBT-I (Kallestad et al., submitted). This study is registered on ClinicalTrials.gov (NCT02044263) and details of the protocol are available on that open access site.

Ethics

The study protocol was approved by the Regional Ethical Committee of South-East Norway (REK reference number: 2013/1836).

Study sample

The sample was recruited from the outpatient public sleep clinic at St. Olavs University Hospital, Department of Psychiatry, Trondheim, Norway, between October 2014 and January 2016. The 101 trial participants were randomized to digital (N = 49) or face-to-face CBT-I (N = 52) provided they met the following inclusion criteria: (1) age ≥ 18 years old; (2) met the DSM-5 diagnostic criteria for insomnia (American Psychiatric Association, 2013); and (3) willing and able to give written informed consent. The exclusion criteria were (1) evidence of circadian rhythm disorder; (2) evidence of an organic sleep disorder or sleep apnea; (3) working night shifts and being unable to discontinue this work pattern during the trial; (4) previous exposure to CBT-I; (5) a current alcohol and/or substance misuse problem; (6) medical conditions where CBT-I is deemed inappropriate; (7) insufficient fluency in Norwegian; and/or (8) insufficient computer skills. The key eligibility criterion for the current study was that the individual reported being in paid employment at the time of entry into the RCT.

2.4 Therapy Intervention. In CBT-I, both cognitive and behavioral techniques are used to target and alleviate insomnia symptoms (Morin & Espie, 2004). Face-to-face CBT-I was delivered by trained practitioners whilst digital CBT-I was made available via a fully automated web-based program called Sleep Healthy Using the Internet (SHUTi) (Ritterband et al., 2009). Full details of the interventions are described elsewhere (Vedaa et al., 2020).

Measures

The insomnia interview schedule (IIS)

The IIS is a semi-structured diagnostic interview used to collect information on demographic variables (age, sex, relationship status, educational attainment, and employment status), duration of insomnia, comorbid mental disorder(s), physical disorder(s), and current use of sleep medications (Morin, 1993). The IIS was only administered at baseline.

Insomnia severity index (ISI)

The ISI was administered at baseline and at 6-month follow-up. The ISI is a validated seven-item, self-report questionnaire that is recommended for use in insomnia research (Bastien, 2001; Buysse et al., 2006; Morin et al., 2011). The scale assesses the nature, severity, and impact of insomnia symptoms over the past two weeks. A 5-point Likert scale from 0 (no problem) to 4 (very severe problem) was used to rate each item, yielding a total score ranging from 0 to 28. Two markers of clinically meaningful improvement were calculated: (1) patients with response to treatment (responders) and (2) patients who are in remission from insomnia (remitters). Responders had marked clinical improvement, defined as a reduction in ISI score of at least 8 points from baseline to 6-month follow-up (Morin et al., 2011), whereas remitters were defined by an ISI score of seven or less at 6-month follow-up (American Psychiatric Association, 2013).

The work productivity and activity impairment questionnaire: general health (WPAI)

The general health version of the WPAI is a 6-item instrument developed as a quantitative assessment of work and activity impairment (Reilly et al., 1993). The WPAI was administered at baseline and at 6-month follow-up. The WPAI has good psychometric properties and has been more frequently used than any other metric of productivity across various occupations and disease areas (Bolge et al., 2009). Participants are asked about hours of missed work due to health problems (Q2) and hours actually worked (Q4). Participants are also asked to report hours of missed work due to other reasons (Q3). This helps participants appropriately categorize their work hours. The degree to which health problems affected productivity while working (Q5) and the ability to do regular daily activities outside of work (Q6) was recorded on a scale from 1 to 10, with a higher score indicating higher impairment. The reported data were used to calculate the following scores (expressed in percentages): (1) absenteeism (missed work time due to health problems); (2) presenteeism (productivity loss while at work due to health problems); (3) total work impairment (WI; an aggregated score weighting absenteeism and presenteeism); and (4) activity impairment (AI; impairment in daily activities outside of work due to health problems) (Reilly et al., 1993).

Statistical analysis

As the purpose of the current study was to explore the association between change in insomnia and change in work productivity and day-time activity, data from all individuals were combined into a single group (irrespective of prior random allocation).

SPSS version 25 were used for all analyses with $p < .05$ (2-tailed tests) regarded as indicative of statistical significance. Paired sample t-tests were conducted to test our hypothesis that levels of self-reported absenteeism, presenteeism, total work impairment, and level of activity 6 months post-CBT-I would be significantly lower compared with baseline levels. Independent sample t-tests were conducted to test the hypothesis that at 6-month follow-up, individuals with baseline insomnia disorder who then met criteria for insomnia response or remission would report lower work impairment scores compared with non-responders and non-remitters, respectively. Supplemental independent t-tests were conducted to test differences in WPAI variables between participants who received CBT-I either face-to-face or digitally. Considering that baseline severity is expected to be associated with treatment outcome (Nunes et al., 2011), we chose not to include clinical variables as covariates. The impact of age and sex as covariates were analyzed, and their inclusion did not alter any of the results (analyses available from the authors upon request).

The data were checked for skewness in kurtosis, and values were acceptable (1.0–1.4) for presenteeism, overall work impairment and activity impairment, although the value for absenteeism (2.3) reflects that a large proportion of respondents report zero absenteeism. Cohen's *d* was calculated as the difference in mean scores divided by the pooled standard deviation and interpreted as small (<0.4), moderate (0.5–0.7) and large (≥0.8) effect sizes (Cohen, 1988). Missing data were replaced by mean group values. This method was chosen due to low levels of missing data. Simulated data from research

investigating the impact of different imputation methods show that mean imputation work well as long as the percentage of missing data is low (Cheema, 2014). Additionally, there were no differences between participants who did and did not provide data at 6-month follow-up regarding age, gender, level of absenteeism or severity of sleep difficulties at baseline. At study entry, data were complete except for 1 (1.2%) participant who did not provide data on absenteeism. At 6-month follow-up, 16 (20.7%) participants did not provide data on absenteeism and 9 (11.6%) participants did not provide data on presenteeism and activity impairment. The rate of missing data on absenteeism is at the upper limit of the recommended cutoff rate for using mean substitution. However, both the mean value and the median value of reported absenteeism is zero, and therefore other methods of imputation would not significantly deviate from the values imputed by use of mean substitution.

Results

Sample characteristics

Of the 101 randomized participants (76 females; 75.2%), 77 (59 females; 76.6%) reported that they were in paid employment at baseline (and were therefore eligible for this study). Table 1 describes the key demographic and clinical characteristics of the study sample overall and for participants who received face-to-face and digital CBT-I, respectively.

Follow-up data were available on 68 of the 77 (88.0%) study participants. In a preliminary comparison of patients randomized to receive either digital CBT-I or face-to-face CBT-I, there were no differences in absenteeism, presenteeism, total work impairment, or activity impairment at 6-month follow-up. See Table 1S in the supplementary materials.

Work and activity outcomes at 6 months

As shown in Table 2, participants at 6-month follow-up reported lower mean scores of presenteeism, WI, and AI, but not absenteeism compared with baseline mean levels. There were no significant differences in mean number of hours worked at baseline (M = 101.6, SD = 49.1) and at 6-month follow-up (M = 99.5.1, SD = 57.7; t(76) = 3.1; p = .76), or mean hours of absenteeism due to health problems at baseline (M = 18.3, SD = 34.8) and at 6-month follow-up (M = 11.3, SD = 29.0; t (76) = 1.5; p = .13).

Table 1. Demographic and clinical information of the study sample.

	All (n = 77)	Face-to-face CBT-I(n = 39)	Digital CBT-I (n = 38)
Age, years (SD)	42.4 (10.5)	42.8 (11.6)	41.8 (9.3)
Sex, n (%)			
Female	59 (76.6)	30 (76.9)	29 (76.3)
Male	18 (23.4)	9 (23.1)	9 (23.7)
Relationship status, n (%)			
Married or cohabitant	51 (66.3)	26 (66.6)	25 (65.8)
Divorced, separated or never married	26 (33.7)	13 (33.3)	13 (34.2)
Education attainment, n (%)			
Less than high school	2 (2.6)	2 (5.1)	0
Completed high school	18 (23.4)	10 (25.6)	8 (21.0)
College or bachelor's degree	42 (54.6)	20 (51.3)	22 (57.9)
Higher degree	15 (19.5)	7 (18.0)	8 (21.1)
Employment status, n (%)			
Full-time	47 (61.0)	24 (61.5)	23 (60.5)
Part-time	19 (24.7)	10 (25.6)	9 (23.7)
Duration of insomnia, years (SD)	12.4 (12.2)	12.6 (12.7)	12.3 (11.9)
Current use of sleep medication (yes), n (%)	50 (64.9)	27 (69.2)	23 (62.2)
At least one comorbid disorder (yes), n (%)	42 (66.2)	23 (59.0)	19 (50.0)
ISI score at baseline, mean (SD)	18.6 (3.9)	18.0 (3.8)	19.1 (4.1)

Table 2. Changes in mean levels of work and activity impairment[a] from baseline to 6 months post-CBT-I in a sample of working participants diagnosed with insomnia.

	Baseline	6-month follow-up	Paired sample t-test		
	Mean (SD)	Mean (SD)	Difference (95% CI)	Cohen's *d*	p-value
Absenteeism[1], %	14.9 (27.0)	12.6 (27.7)	−2.3 (−9.2 to 4.6)	0.084	0.51
Presenteeism[2], %	36.0 (29.6)	22.4 (29.5)	−13.6 (−21.5 to −5.8)	0.46	0.001
Total work impairment[3], %	42.8 (31.0)	27.3 (33.0)	−15.5 (−23.9 to −7.1)	0.48	<0.001
Activity impairment[4], %	46.8 (29.4)	27.2 (30.0)	−19.5 (−26.6 to −12.5)	0.66	<0.001

[a]From the "Work Productivity and Activity Impairment Questionnaire: General Health (WPAI). [1] Absence from work due to health problems; [2] Average reduced productivity while working; [3] Reduced total work impairment; [4] Average reduced productivity in daily activities outside of work.

Table 3. Differences in work and activity impairment scores[a] between responders and non-responders, and remitters and non-remitters at 6 months post-CBT-I in a sample of working participants diagnosed with insomnia.

	Responders (n = 37)	Non-responders (n = 31)	Independent samples t-test		
	Mean (SD)	Mean (SD)	Difference (95% CI)	Cohen´s *d*	p-value
Absenteeism[1], %	6.8 (20.6)	20.1 (36.4)	13.5 (−0.6 to27.5)	0.45	0.074
Presenteeism[2], %	15.9 (28.2)	30.0 (33.7)	14.1 (−0.9 to 29.0)	0.45	0.066
Total work impairment[3], %	17.5 (29.0)	38.2 (38.7)	20.8 (3.9 to 37.7)	0.61	0.017
Activity impairment[4], %	19.2 (27.8)	36.8 (34.4)	17.6 (2.5 to 32.6)	0.56	0.023
	Remitters (n = 30)	Non-remitters (n = 38)	Independent samples t-test		
	Mean (SD)	Mean (SD)	Difference (95% CI)	Cohen´s *d*	p-value
Absenteeism[1], %	5.9 (19.2)	18.5 (34.8)	12.5 (−0.8 to 25.8)	0.45	0.064
Presenteeism[2], %	10.0 (22.7)	32.1 (34.0)	22.1 (8.3 to 35.9)	0.76	0.002
Total work impairment[3], %	11.3 (24.5)	39.2 (37.4)	27.9 (12.8 to 43.0)	0.88	<0.001
Activity impairment[4], %	15.7 (25.8)	36.3 (33.7)	20.6 (6.2 to 35.0)	0.69	0.006

[a]From the Work Productivity and Activity Impairment Questionnaire: General Health (WPAI). [1] Absence from work due to health problems; [2] Average reduced productivity while working; [3] Reduced total work impairment; [4] Average reduced productivity in daily activities outside of work.

Work and activity outcomes in groups defined by response or remission at 6 months

Data were unavailable for the follow-up ISI rating on nine participants (12%), so they were excluded from the response/remission analyses.

At 6-month follow-up, 37 participants (48.1%) met the response criteria, whereas 31 (40.3%) did not. However, if outcome used the more stringent remission criteria, it was found that 30 participants (39.0%) were in remission, whereas 38 (49.4%) were not.

Responders reported lower levels of WI and AI, but there were no significant differences in absenteeism and presenteeism. Participants who were in remission from insomnia reported significantly lower mean levels in presenteeism, WI, and AI, but not in absenteeism compared with participants who were not in remission at follow-up (see Table 3 for details). There were no significant differences in mean hours worked for responders (M = 112.0, SD = 58.3) compared with non-responders (M = 84.6, SD = 62.6, difference of −27.3, 95% CI −56.7 to 2.0, p = .067) or hours of absenteeism for responders (M = 7.7, SD = 25.1) compared with non-responders (M = 15.6, SD = 26.7, difference of 7.9, 95% CI −22.9 to 7.1, p = .30). There were no differences in mean hours worked for patients who were in remission from insomnia (M = 107.4, SD = 55.8) compared with patients who were not in remission (M = 93.3, SD = 65.6, difference −14.5, 95% CI −44.0 to 15.8, p = .35) or in hours of absenteeism for remitters (M = 7.4, SD = 24.1) compared with non-remitters (M = 14.4, SD = 35.5, difference 7.3, 95% CI −8.1 to 22.1, p = .36).

Discussion

The purpose of this study was to investigate whether CBT-I would impact on employees' levels of daytime functioning at 6-month follow-up, and whether any improvements in daytime functioning

would coincide with reduced insomnia severity. In line with our first hypothesis, we found moderate improvement in the levels of presenteeism, work impairment, and activity impairment outside of work from baseline to 6-month follow-up. In line with our second hypothesis, patients who achieved remission or response status after the treatment period reported lower levels of work impairment and activity impairment compared with those who did not achieve remission or responder status. Patients who were in remission after the treatment period also demonstrated improvements with regards to levels of presenteeism. There were no significant changes in the levels of absenteeism in any of the analyses. Overall, we found partial support for our hypotheses, and our findings indicate that patients with insomnia disorder who receive CBT-I appear to also experience moderate-to-large effect size improvements in work functioning and activity impairment, but not in levels of self-reported absenteeism. Further, our results allow us to speculate on whether clinically meaningful improvements in insomnia severity catalyzes the improvements observed in work- and activity-related domains.

Our findings are in line with several previous studies on the effects of treatment of insomnia symptoms on improved daytime functioning at work and outside of work (Bostock et al., 2016; Espie et al., 2019; Kalmbach et al., 2019) which show that CBT-I is associated with moderate-to-large effect size improvements on work- and activity-related outcomes. This study adds incremental evidence to previous studies demonstrating the effects of CBT-I on daytime functioning at work and extends this body of research by demonstrating additional effects of CBT-I on out-of-work activity levels. Participants in the current study had slightly higher levels of impairment pre-intervention compared with those in previous studies; which for example, included more selected samples such as employees recruited within a single company (Bostock et al., 2016) and menopausal women in a primary care setting recruited by community advertisement in another study (Drake et al., 2019; Kalmbach et al., 2019). In the latter study, the baseline rate of absenteeism was 10-times lower than reported here (1.4% vs. 14.9%). This could reflect actual differences in impairment between the samples prior to the intervention. Alternatively, it could be attributed to our use of the general health version of the WPAI, which captures the impact of general health problems on work and other activities and not only the portion attributed by the participant to a specific condition or illness (e.g., poor sleep or insomnia).

Absenteeism

Considering the reciprocal relationship between insomnia and other mental and somatic conditions and illnesses (Sánchez-Ortuño & Edinger, 2012), it is reasonable to argue that while treating the insomnia itself might be beneficial, it would not always be sufficient to reverse all the negative effects associated with insomnia. In our study, we only found a tendency toward an effect of change in insomnia severity on absenteeism. This could be because insomnia is much more strongly related to presenteeism than absenteeism (Kessler et al., 2011) or that absenteeism sets a very high threshold for testing the impact of any therapy due to the complexity of the relationship between health and work. An individual's needs may vary depending on their actual work role, personal economic drivers, and e.g., the presence or nature of comorbid health problems, and all of these factors can affect absenteeism (and presenteeism) in different ways (Johns, 2009). Further, national policies on absence from work, employment practices within companies and "return to work" schedules (e.g., gradual return without monitoring presenteeism) will impact an individual's decision to go absent or attend work. Statistical modeling can account for some of these confounders, and even multivariate analyses will allow future consideration of other covariates that may explain the associations between change in insomnia severity and absenteeism. This is important because even small effects could have a large societal impact given the direct and indirect costs of absenteeism (Léger & Bayon, 2010; Strömberg et al., 2017). However, the current study was exploratory and the RCT was not powered to detect modest changes in absenteeism. To better capture absenteeism in future studies, we recommend collecting objective data on an individual level such as hours worked and hours absent over a defined period of time. These data could be acquired (with individual permission) directly from employer records or

from national registries on absenteeism (although the latter is only feasible in countries with a system of developed and universally available health care and where tracking of individuals across health, social, and employment registries is permitted).

Presenteeism

Presenteeism is associated with sleep problems, productivity loss and most often discussed in terms of impairment in daytime functioning (Johns, 2009). Sleep problems are highly prevalent and, therefore, even a minor reduction in presenteeism and associated costs would be valuable. Overall, our sample reported a productivity gain of 13.5% after treatment with CBT-I. This equates to 5 more hours of effective work time during a 37.5-h working week. Assuming a work year of 48 weeks, we can extrapolate that exposure to CBT-I may be associated with a productivity gain equivalent to 6.4 weeks per year per individual compared with untreated insomnia. The reduction in indirect costs can be estimated by applying the 13.5% work productivity gain to various salary points (Bolge et al., 2009). However, when looking specifically at remitters and responders, we only found a significant improvement in presenteeism in individuals who achieved remission compared with individuals who did not, and there was no significant improvement for responders compared with non-responders. This might be due to residual insomnia symptoms experienced by responders that interfere with performance at work, possibly implying that some of the daytime impairment associated with insomnia will remain until the problem is completely reversed. Thus, there might be a need for new treatment options for individuals not achieving remission with CBT-I. Still, it is reasonable to argue that "good presenteeism" (i.e., substituting absenteeism with presenteeism while experiencing minor discomfort), and the productivity gain of presenteeism relative to absenteeism, may be beneficial to both the employer and the employee compared with absenteeism and zero work productivity (Johns, 2009). The individual might experience less social isolation, which may benefit their mental health and can help prevent long periods of absenteeism and permanent work disability.

Activity impairment

We also found that alleviating insomnia symptoms is associated with improvement in activities outside of work. There may be several reasons why patients who received treatment with CBT-I report less activity impairment at 6-month follow-up. First, improved sleep could lead to restored daytime energy, which in turn may lead the individuals to pursue more leisure activities. This could be associated with an increase in the quality of life for these individuals (Espie et al., 2019) as well as improved social functioning. Second, an integral part of CBT-I is in sleep restriction and stabilizing of the circadian rhythm, in particular, the rise time. Sleep restriction causes the individuals to have more time out of bed, which leads to more time to pursue daily activities. Thus, treatment of insomnia symptoms can improve daytime impairment, which may also lessen the burden on the individual, family, and friends, as well as lessening the burden on society (Kessler et al., 2011; Strömberg et al., 2017; Thiart et al., 2016; Zhang et al., 2017).

Limitations

There are some important limitations of the current study. First, by including only working participants, our analysis and findings are limited to a subsample of the original RCT and inclusion of insomnia patients who are unemployed prior to treatment is necessary to examine whether treatment of insomnia may help people regain employment. Second, we did not include a control group and, therefore, cannot ascertain whether the observed changes in work-related impairment are attributable to the insomnia treatment. Third, the sample size of the current trial limited the type of analyses we were able to conduct (i.e., the sample size was insufficient for reliable and for meaningful covariate analysis). A larger sample and the use of multivariate analyses could have allowed for the detection of

small effects, and it is needed to test whether the effects of CBT-I on work impairment are mediated through other demographic and clinical variables (e.g., comorbidity, pain, or fatigue). Further, lack of consideration of covariates means we can only speculate on the effects of these factors on the reported outcomes of the insomnia treatment. Fourth, the data on absenteeism was slightly skewed. However, two-tailed t-tests with equal sample sizes are robust with respect to departures from normality (Posten, 1978). They are robust to false positives (type II errors) and produce appropriate significance levels even in the presence of small samples (≤50) with decidedly non-normal datasets in which as many as 50% of the subjects attained scores of zero (Lumley et al., 2002), and we therefore chose to use parametric statistics. Fifth, self-report questionnaires on symptoms and degree of impairment are vulnerable to biases such as social desirability or recall bias (Demetriou et al., 2015), and we have not obtained objective data on sleep or work-related impairment.

Conclusion

In conclusion, the effects of CBT-I in terms of leading to reduced symptoms of insomnia is well known. However, the findings from this exploratory study suggest that the benefits of reducing insomnia might result in improvements in work productivity and day-time activity, particularly for participants who achieve remission from insomnia. It is important that future RCTs and cohort studies focus on the daytime impairment associated with insomnia and investigates the impact of therapies such as CBT-I on functional outcomes that are important for the individual as well as society in general. Preferably, such studies should recruit larger samples, apply more sophisticated statistical approaches such as mediational analysis, and collect objective as well as subjective or observer data on work performance and activities to ensure a complete picture is obtained of any important associations or inter-relationships between disturbed sleep, interventions, and functional domains.

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Disclosure statement

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Paper 2

The effects of digital CBT-I on work productivity and activity levels and the mediational role of insomnia symptoms: Data from a randomized controlled trial with 6-month follow-up

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Declarations of interest: none

Abstract

Study Objectives: Cognitive behavioral therapy for insomnia (CBT-I) is a well-established treatment for insomnia, but few studies have explored its impact on work and activity impairment. ***Methods:*** Data stem from 1721 participants enrolled in a randomized controlled trial comparing the efficacy of digital CBT-I compared with Patient Education. Baseline and 6-month follow-up assessments included self-reported ratings of presenteeism and general impairment (Work Productivity and Activity Impairment Questionnaire), and absenteeism (hours of missed work) and employment status. Insomnia was measured using the Insomnia Severity Index (ISI). Mediation analyses were conducted for each outcome with ISI scores at baseline and 9-week follow-up as the mediator. The analyses were adjusted for potential confounders (e.g., sex, age, comorbidities). ***Results:*** dCBT-I was found to be associated with reduced activity impairment compared with PE (by 5.6%) but not presenteeism, absenteeism, or changes in employment status. Mediation analysis showed that changes in insomnia severity largely mediated improvements in presenteeism (by 5.4%) and activity impairment (by 5.5%). There were no significant mediational effects on absenteeism or employment status. ***Conclusions:*** This study shows that dCBT-I is not only effective in improving insomnia. but also demonstrates positive effects on work and daily activities in general, supporting the need for increased access to dCBT-I.

Keywords: Insomnia, Cognitive Behavior Therapy, Mediation, Work, Activities of daily living

Introduction

Insomnia has an estimated prevalence of 10-15% (Pallesen et al., 2001, 2014), and is characterized by difficulties with initiating or maintaining sleep, with associated daytime impairment (American Psychiatric Association, 2013). The disorder is associated with adverse health consequences (Sivertsen et al., 2012), reduced quality of life (Kyle et al., 2010) and may lead to reduced workplace productivity (presenteeism), short- and long-term absenteeism (missing scheduled work time), and permanent work disability (Léger & Bayon, 2010; Overland et al., 2008; Sivertsen et al., 2006, 2009, 2012).

The recommended first-line treatment for insomnia is Cognitive Behavioral Therapy for Insomnia (CBT-I) and both face-to-face and digital adaptations of CBT-I (dCBT-I) are shown to be effective in reducing insomnia severity (Morin et al., 2006; Riemann et al., 2017; van Straten et al., 2018; Wilson et al., 2019; Zachariae et al., 2016). In a recent publication using the same dataset as the current study, Vedaa et al. (2020) found a between-group Cohen's *d* effect size of 1.21 on the Insomnia Severity Index (ISI) when comparing dCBT-I with Patient Education about sleep. Furthermore, a systematic review of 86 studies (n = 15578) found that CBT-I has a small-to-moderate effect on daytime functioning and that positive effects on nighttime symptoms are associated with improvement in daytime symptoms (Benz, 2020). However, it is not known if a reduction in insomnia severity mediates any improvement in functioning at work or in activities outside of work, as only a few studies have looked at the effects of CBT-I on work specific variables. For example, a randomized controlled trial (RCT) in a UK community sample showed that, unlike sleep hygiene education, dCBT-I is associated with reduced presenteeism (i.e., less impairment in productivity whilst at work) but not absenteeism (Espie et al., 2019). Interestingly, secondary analysis of the baseline (n = 906) and 48-week post-randomization data (n = 365) in the CBT-I group found reduced levels of presenteeism and absenteeism (Luik et al., 2020). However,

these findings should be treated with caution given the high attrition within the CBT-I group and absence of any follow-up data on the control group. Finally, our research group recently reported findings from a small-scale study on work- and activity-related impairment of employed adults (n = 77) with insomnia disorder who received either face-to-face or digital CBT-I (Kjørstad et al., 2021). Using the Work Productivity and Activity Impairment Questionnaire (WPAI; Reilly et al., 1993), we demonstrated that post-intervention remission is associated with improvements in presenteeism and in activities outside of work (irrespective of modality of CBT-I) (Kjørstad et al., 2021).

Taken together, although there is robust evidence that dCBT-I significantly reduces insomnia, there is limited research on its impact on different elements of daytime impairment, such as work productivity or general daily activities (outside of work). Further, the existing studies are small scale and/or hampered by sample attrition. As such, there is a need for more research in this field.

Aims

This study uses data from a large-scale community-based RCT comparing the efficacy of dCBT-I with Patient Education about sleep in self-referred adults with insomnia and aims to (1) examine any between-group differences in improvements in work- and activity-related impairment and (2) test whether change in work- and activity related impairment between baseline and 6-month follow-up is mediated by pre-to-post-intervention changes in the severity of insomnia symptoms (i.e., baseline to 9-week follow-up).

Methods and Materials

De-identified data were obtained on the 1721 participants in our recent RCT comparing the efficacy of a fully automated, self-guided dCBT-I with a control condition for the treatment of

insomnia (Vedaa et al., 2020). The trial received ethical approval from the Regional Committees for Medical and Health Research Ethics in Southeast Norway (2015/134) and is registered on the ClinicalTrials.gov website (NCT02558647). Full details of the protocol are available elsewhere (https://ntnuopen.ntnu.no/ntnu-xmlui/handle/11250/2611758) (Kallestad et al., 2018). A flow diagram of the study is shown in the supplementary materials (Supplementary Figure A1). Below, we summarize key information about the RCT and then detail the measures and analyses employed in this study.

Participants and eligibility

Between February 2016 and July 2018, 5349 individuals commenced the screening process for the RCT. Forty percent of these individuals (n = 2132) discontinued the screening process and a further 28% (n = 1479) declined to participate or were ineligible. The eligibility criteria were as follows: (1) age ≥ 18 years, (2) scored ≥12 on the Insomnia Severity Index (ISI) (Morin et al., 2011), which is the most sensitive score indicator of insomnia disorder in Norway (Filosa et al., 2020), and (3) willing to sign an online consent form. Individuals were excluded if they met one or more of the following criteria: (1) score >10 on the Epworth Sleepiness Scale (ESS) or reported regular snoring, breathing difficulties and difficulties staying awake during the day, which is indicative of an organic sleep disorder (e.g. sleep apnea or hypersomnia), (2) self-reported a medical condition for which self-guided dCBT-I may be contra-indicated (i.e., epilepsy, bipolar disorder, schizophrenia or psychotic disorders, and recent cardiac surgery), and/or (3) were currently engaged in night shift work and unable to discontinue this work pattern during the trial.

Interventions

Digital Cognitive Behavioral Therapy for Insomnia (dCBT-I). A Norwegian translation of Sleep Healthy Using the Internet (SHUTi) was used. The SHUTi-program is a fully automated adaptation of traditional face-to-face CBT-I with components such as sleep restriction, stimulus control, cognitive restructuring, sleep hygiene, and relapse prevention (Hagatun et al., 2019; Ritterband et al., 2009, 2017).

Patient Education about sleep. Digital PE is provided via a fixed website and is widely used as a control intervention in RCTs of insomnia treatments (Hagatun et al., 2019; Ritterband et al., 2017). The PE site describes the prevalence, causes, and impact of insomnia, giving advice about when to seek input from a health care professional and includes information about basic lifestyle, environmental, and behavioral strategies that may improve sleep-wake patterns (Ritterband et al., 2017).

Assessments

For this study, we extracted data on the following-

Demographic and clinical measures. Participants self-reported demographics and information about any ongoing medical (e.g., cardiac, endocrine, renal, respiratory, skin, joint, and other problems) or mental health (e.g., anxiety, depression, post-traumatic stress disorder (PTSD), alcohol and/or substance use disorder (SUD), eating disorders, attention deficit hyperactivity disorder (ADHD), psychosis, and personality disorders) conditions were noted. The information about the presence or absence of comorbidities was categorized as no comorbidity, medical comorbidity, psychiatric comorbidity, or both.

Insomnia Severity Index (ISI). The ISI was administered at baseline and at 9-week follow-up. The ISI is a validated 7-item, self-report questionnaire that assesses the nature, severity, and impact of insomnia symptoms over the past two weeks and is recommended for

use in insomnia research (Bastien, 2001; Buysse et al., 2006; Morin et al., 2011). The total score ranges from 0 to 28, with a higher score indicating greater severity of insomnia symptoms.

Work Productivity and Activity Impairment. Data on the work- and activity-related outcomes due to health problems were collected at baseline and 6-month follow-up. Presenteeism (productivity loss while at work due to health problems) and activity impairment (impairment in daily activities outside of work due to health problems) were assessed using single items from the general health version of the Work Productivity and Activity Impairment Questionnaire (WPAI; Reilly et al., 1993). The WPAI items were scored on a scale from 1 to 10, with a higher score indicating higher impairment. The reported data on presenteeism and activity impairment were then transformed to express levels of impairment in scale percentages. The WPAI has good psychometric properties and has been more frequently used than any other metric of productivity across various occupations and disease areas (Bolge et al., 2009). Two additional items were used to measure absenteeism (hours absent from work) and employment status (binary categorical measure).

Statistical analysis

Mediation analyses were undertaken by an independent researcher using Mplus version 8.2 (Muthén & Muthén, 1998-2010). For each outcome, we estimated the direct and indirect effects of the exposure (treatment) on the outcome variable for the mediator (ISI) while adjusting for potential confounders (sex, age, educational attainment, relationship status, and comorbidities). Continuous baseline covariates were grand mean centered. As recommended, we included the exposure-mediator interaction in the model (VanderWeele, 2015). Sensitivity analyses were carried out to examine whether significant (in)direct effect estimates were robust to violations of no unmeasured mediator-outcome confounding (Muthén, 2011) and

missing data assumptions (Enders, 2010). The former (no unmeasured mediator-outcome confounding) was tested by developing correlated residual plots in which the size of the residual correlation between outcome and mediator was plotted against the size of the (in)direct effect. For the latter (missing data assumptions), selection models were estimated in which binary missing data indicators were regressed on the dependent variables in the model to mimic a missing-not-at-random scenario. As noted, 9-week ISI scores were available for 1118 (64.9%) of the sample. Data on presenteeism, activity impairment, absenteeism, and employment status were available for 707 (41.1%), 765 (44.5%), 689 (40.0%), and 839 (48.8%) participants, respectively.

All mediators and outcomes were treated as continuous variables, except for employment status. A Bayesian estimator with 95% credibility interval (CI) was used for all models. For employment status, the Bayesian estimator used the probit link function. The Bayesian estimator uses all available data and is valid under the assumption of data missing-at-random (MAR), similar to maximum likelihood estimation.

All indirect/direct effects were derived using the potential outcomes and counterfactual framework. As such, we distinguish between the direct effect (more precisely the pure natural direct effect (PNDE)), the indirect effect (more precisely the total natural indirect effect (TNIE)), and the total effect. Formally, the direct effect represents the effect that would have been realized if the exposure was administered while keeping the mediator at the level it would have taken in the absence of the exposure. In other words, it reflects differences in the outcome measures at 6-month follow-up depending on treatment allocation at baseline controlled for age, sex, education attainment, relationship status, and comorbidities as well as baseline levels of each outcome variable and the baseline level of the mediator (ISI score). The indirect effect represents the difference between the mean in the treatment group with the mediator varying as it would have under the treatment condition and the mean in the

treatment group with the mediator varying as it would have under the control condition (i.e., the counterfactual). In other words, the indirect effect represents the effects on the outcome measures related to the changes in the mediator (insomnia symptom severity) from baseline to 9-week follow-up. The total effect is the sum of the direct and the indirect effect. If there are significant total effects, but no direct effects, the total effect will be driven by the indirect effect and vice versa. The analysis model is illustrated by the directed acyclic graph (DAG) in Figure 1. An example of Mplus input commands is shown in the supplementary material (Appendix A).

[Figure 1 about here.]

Results

Descriptive statistics

Table 1 describes key demographic and clinical characteristics of the RCT participants included in this study. The sample had a mean age of 44.4 years (SD = 13.9 years), was predominantly female (73.3%), mostly married or cohabitating (63.3%), and college educated or higher (73.8%). The mean duration of self-reported insomnia was 13.7 years (SD = 10.8 years), and more than half (58.1%) self-reported at least one comorbid disorder.

[Table 1 about here.]

Table 2 shows ISI scores at baseline and 9-week follow-up and work and activity-related outcomes (presenteeism, activity impairment, absenteeism, and employment status) at baseline and 6-month follow-up for the overall sample, and for dCBT-I and PE, respectively.

Participants randomized to dCBT-I experienced a mean reduction in ISI score from 19.2 (SD = 3.9) to 10.4 (SD = 6.2), and participants in the control condition experienced a mean reduction from 19.6 (SD = 4.0) to 15.2 (SD = 5.3). For the overall sample, levels of presenteeism and activity impairment were reduced by 9.4% and 12.4%, respectively. Absenteeism in the study sample was reduced by 4.0 hours and employment status for the overall sample remained virtually unchanged (69.2% vs 70.6%); see Table 2 for further details. Between-group Cohen's *d* effect sizes on the mediator and the work- and activity-related outcomes are reported in the supplementary material (Appendix A).

[Table 2 about here.]

Effect of dCBT-I on work-related outcomes and the mediational role of insomnia symptoms

Treatment effect. As shown in Table 3, the analysis demonstrated a significant total effect of dCBT-I compared with PE on activity impairment outside of work (estimated effect -5.6% in favor of dCBT-I). There were no significant total effects on presenteeism, absenteeism, or employment status.

Mediation effects. In the mediation analysis, we found a significant indirect effect of the mediator on presenteeism (estimated effect -5.4%) and activity impairment (estimated effect -5.5%) at 6-month follow-up. There were no significant indirect effects on absenteeism or employment status.

[Table 3 about here.]

Results from the sensitivity analyses of unmeasured confounders and the MNAR selection models can be found in the supplementary material (Appendix A).

Discussion

The purpose of the present study was two-fold. First, we investigated if dCBT-I was associated with better work and activity-related outcomes at 6-month follow-up compared with PE. We found that participants randomized to dCBT-I demonstrated significantly less activity impairment, but there were no statistically significant changes in presenteeism, absenteeism, or employment status depending on treatment allocation. Second, we explored whether changes in work- and activity-related outcomes were mediated by change in severity of insomnia symptoms between baseline and 9-week follow-up. This analysis showed that changes in presenteeism and activity impairment, but not absenteeism or employment status, were largely mediated by change in insomnia severity.

Baseline assessment demonstrated that some form of work or social impairment occurs in at least 40% of individuals recruited to an RCT of interventions for insomnia. This degree of impairment is similar to that of other studies. For example, an RCT about the effect of insomnia treatment (sleep restriction therapy or CBT-I) on daytime functioning and work performance in postmenopausal women reported similar levels of impairment in activities outside of work (~40% impairment) and at work (~30% productivity loss) prior to treatment (Kalmbach et al., 2019). Kalmbach and colleagues (2019) reported that trial participants reported moderate improvements in both activity impairment (~20% improvement; Cohen's d = .63) and presenteeism (~15% improvement; Cohen's d = 0.50) at 6-month follow-up. On average, our study sample reported 12.4% less impairment in daytime activities outside of work and a 9.4% productivity gain at work (i.e., reduced presenteeism attributed to health problems). The differences in the observed effects on activity impairment (~20% vs. 12.4%) and presenteeism (~15% vs. 9.4%) between these two studies might partly be explained by slight differences in how the outcomes were measured (impairment due to work-specific issues vs. impairment due to health problems).

Further, Kalmbach and colleagues did not control for the effects of covariates nor explore the mediational role of insomnia symptoms on daytime impairment. In our study, we found that the changes in both presenteeism and activities outside of work were largely mediated by change in insomnia symptom severity. As such, participants randomized to dCBT-I appear to experience 5.6% less activity impairment compared with participants in the control condition, not only as an effect of treatment allocation but likely also because participants randomized to dCBT-I showed more improvement in insomnia symptoms. Although this issue is under-explored, some support for this idea comes from an RCT that showed that change in insomnia symptom severity mediates a moderate reduction in presenteeism after approximately 2 months (8 weeks; Cohen's d = -0.41) and 6 months (24 weeks; Cohen's d = -0.42) (Espie et al., 2019).

The major difference between the two conditions is that the dCBT-I intervention presents information over a 6-week course and introduces the participants to a significantly larger volume of comprehensive therapeutic material, in addition to conducating a partially individually tailored follow-up of the participants. In particular, the tailoring of the sleep restriction regime and participant adherence to a strict rise time would allow participants more time to pursue daily activities by spending more time out of bed. It could also be that they feel less tired and have more energy to pursue daily activities (i.e., their productivity improves in parallel with reductions in a range of insomnia symptoms).

Overall, the participants in our study (independent of treatment allocation) reported a 9.4% productivity gain at work (i.e., reduced presenteeism attributed to health problems). Approximately half of the gain (5.4% divided by 9.4% = 57%) was mediated by lessening of insomnia symptoms. As there was no direct effect of treatment allocation on presenteeism (i.e., no total effect), the estimated, but nonsignificant, 4.0% difference between conditions in favor of dCBT-I (as shown in Table 3) is likely explained by the fact that participants who

received dCBT-I experienced more improvement in insomnia symptoms than participants in the control condition (i.e., the mediational effect).

Focusing on work functioning, the overall reduction in the levels of presenteeism in our sample (~10%) may sound modest but equates to approximately 4 more hours of effective work time during a 37.5 hour working week. Assuming a work year of 48 weeks, we can extrapolate that offering interventions for insomnia could lead to an overall productivity gain equivalent to 4.4 weeks per year per individual compared with not getting access to such an intervention (Bolge et al., 2009). However, the overall estimate of improvement in presenteeism is based on descriptive data, and it cannot be ascertained whether the observed ~10% improvement is attributable to the dCBT-I, improvements in insomnia symptoms, or other non-specific factors, but the mediation analyses demonstrate that approximately half of the 4.4 weeks of productivity gain (i.e., 57% or 2.5 weeks per year per individual) is directly attributable to the improvements regarding insomnia symptoms during treatment. Kessler and colleagues (2011) similarly estimated the lost work productivity associated specifically with insomnia to be 2.3 weeks (11.3 days) per year per individual (adjusted for age, sex, and education attainment) and that complete eradication of insomnia would lead to proportional reductions of between 5.4% and 7.8% of all population-level lost work performance due to presenteeism. Likewise, Darden and colleagues (2020), employing more conservative assumptions, estimated that untreated insomnia was associated with a productivity loss of 1.9 weeks per individual per year, and that insomnia was associated with 1 extra week of absence from work compared with individuals without insomnia (extrapolated by dividing estimates of annual costs by median hourly salary). Their estimates did not consider the effect of comorbidity, whereas our sample included insomnia alone (42%) or in combination with comorbid conditions (58%), which may partly explain the slightly higher estimate of presenteeism in our study. However, this should be considered a strength rather than a

weakness of our project, as insomnia in the community frequently co-occurs with physical and mental disorders.

Taken together, the findings on activity impairment and presenteeism support the established connection of insomnia with reduced work productivity and activity impairment, and they suggest that treatment of insomnia and reduction of insomnia symptoms, to some degree, reverse daytime impairment. Nonetheless, we need to consider why we find that insomnia symptoms only play a limited role in mediatingactivity impairment and presenteeism. As argued in the systematic review performed by Benz and colleagues (2020), we speculate that the findings reflect that while there are effects on daytime symptoms (such as reduced daytime sleepiness, stress, improved daytime and social functioning, etc.), they will predominantly be small to moderate compared to the far stronger effects on the core symptoms of insomnia unless therapeutic techniques that directly address daytime symptoms are added.

We found no effects of dCBT-I or changes in insomnia severity on absenteeism. Similarly, the RCT on postmenopausal women showed no effect on absenteeism 6 months after treatment (Kalmbach et al., 2019). In another recent study, we were also unable to demonstrate an effect of CBT-I (face-to-face or online) on absenteeism in patients referred to treatment with CBT-I at an outpatient public sleep clinic (Kjørstad et al., 2021). One possible explanation for this could be that insomnia is more closely related to presenteeism than absenteeism (Johns, 2009), and that absenteeism may be a reflection of many factors other than sleep. It may further be difficult to differentiate the effects of poor sleep by itself from those of e.g., chronic diseases or work conditions that may simultaneously have an impact on sleep (Leger, 2014). Therefore, we speculate that in considering absenteeism, a very high threshold is set for testing the direct or indirect impact of any therapy on work and social functioning (Johns, 2009). However, Espie and colleagues (2019) found a significant but

small effect in terms of reduced absenteeism attributed specifically to poor sleep after approximately 6 months (Cohen's $d = 0.013$) but not at earlier time-points (mid-treatment and post-treatment). This implies that reversal of absence from work caused by insomnia takes time to manifest, although we cannot ascertain whether the participants of their study had ineed increased work attendance, or, rather, had started attributing their absence to causes other than poor sleep.

Lastly, we found no effects of dCBT-I or changes in insomnia severity on employment status. Gaining employment after unemployment (or becoming unemployed and receive social benefits) is usually a process that takes time, and 6 months might not be sufficient to capture the subtle effects of dCBT-I or a reduction in insomnia symptom severity on an individual's employment status. Individual needs when applying for, changing, or quitting jobs may vary depending on profession (e.g., physically demanding work versus a desk job), personal economic drivers (e.g., national policies on social security), workload (e.g., the possibility of a gradual return to the work force), or e.g., the presence or nature of comorbid health problems. Thus, employment status assessed as a binary measure is not sensitive to subtle changes in an individual's affiliation with working life. Future research should consider more sensitive measures of affiliation with working life (e.g., number of job adverts read, applications sent, or interviews attended) and make use of employer and/or national registry data.

Strengths and limitations

There are some strengths of the present study. One strength was the RCT design with a sufficient sample size to detect small effects and to investigate whether the effects on work- and activity at 6 months are mediated by change in insomnia severity during the intervention.

This reduces the risk of false negatives (type I errors). Further, the statistical analyses were performed as recommended in the literature (VanderWeele, 2015).

The present work has some limitations that should be addressed. For instance, there is significant participant attrition at the 6-month follow-up (~60%). This is a major challenge in research involving repeated measures, and the observed effects may be explained by the differences between individuals who leave a study and those who do not (Nunan et al., 2018). To address this possibility, preventive steps were taken when designing the present study (e.g., recruitment of a sufficiently large sample and randomized allocation to either the intervention or the control condition) and sensitivity analyses of the data were performed to investigate whether there were systematic differences in symptom severity, age, sex, relationship status, educational attainment, or comorbidities prior to the intervention between those who completed the 6-month follow-up assessment and those who did not (see Supplementary Table A2). We did not find evidence that the attrition was associated with systematic differences in any of the abovementioned variables or that the attrition biased the results of the mediation analysis. However, results from the mediation analyses should be interpreted with caution, as sensitivity analyses indicated that the possibility for the impact of significant mediator-outcome confounding on the estimated indirect effects could not be excluded. Furthermore, the present study was a secondary analysis of data from an RCT, and its main aim was to investigate the effects of digital CBT-I on insomnia disorder symptom severity compared with a control condition (Patient Education). As such, some of the participants were unemployed at baseline. Further, the included measure of absenteeism in the present study is a proxy measure with participants only reporting the number of hours absent from work, and, therefore, we were unable to calculate, e.g., percentage of work hours absent. The RCT was, however, designed with a large enough sample size to have sufficient statistical power (80%) to also detect significant differences ($p<0.05$) in rates of sick leave

(Kallestad et al., 2018), so although the measure included here is not perfect, we are confident that any effects of insomnia severity on sick leave would have detected them with our proxy measure. Another limitation of this work is that we have not obtained objective data on sleep or daytime impairment. The usefulness of objective sleep data for insomnia is in itself questionable, as it does not predict the outcome of treatment with CBT-I (Galbiati et al., 2021), but the lack of objective data on absenteeism and employment status over longer time periods implies that our results regarding these outcomes should be interpreted with some caution. Finally, self-report questionnaires on symptoms and degree of impairment are vulnerable to biases (e.g., recall bias or social desirability as discussed above) (Demetriou et al., 2015). Therefore, another important consideration is that individuals interested in digital mental health interventions are likely older, females, separated/divorced, and highly educated compared to those who chose not to participate, for which the ease and convenience of use versus finding time to participate is a major barrier to their participation (Crisp & Griffiths, 2014). Thus, a possible self-selection bias in the sample might indicate that digital versions of mental health interventions, while being effective, might not be suitable for or preferred by all individuals who need treatment for a mental health condition such as insomnia. Therefore, future studies should investigate whether a brief version of dCBT-I, which requires a lower time commitment, could benefit individuals who are hesitant to participate due to busy schedules.

Conclusions

The results of this trial suggest that dCBT-I is not only effective in improving insomnia symptoms but also demonstrates positive effects on work and daily activities in general. In addition, improvements related to the severity of insomnia symptoms serve as a mediator of these benefits. These results demonstrate that interventions targeted at insomnia can have

positive benefits on the around-the-clock symptoms associated with this problem. Given that CBT-I is one of the most effective interventions available, this study offers evidence of potential clinical, social, and economic benefits that further support calls for increased access to this therapy. We acknowledge that these findings need confirmation and that future studies designed to specifically examine work and social impairment are also needed. These might include studies that explore whether face to face CBT-I demonstrates a bigger effect size for changes in work and social impairment than dCBT-I. This is relevant as access to face-to-face therapy is more restricted than access to digital therapies. Moreover, given that even subtle changes in an individual's work productivity can have personal and societal impacts, additional, more detailed health economic analyses are required that include examination of employer record data on work participation and function as well as objective data from national work and disability registries.

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Declaration of interest

The authors declare that they have no competing interests.

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Tables

Table 1. Demographic and clinical information of the study sample.

	Digital CBT-I (n. = 868)	Patient Education (n. = 853)	All (n. = 1721)
Age, mean (SD), years	44.2 (14.1)	44.7 (13.8)	44.4 (13.9)
Female, %	75.3	71.3	73.3
Relationship status, n (%)			
Married/cohabiting with partner	551 (63.5)	543 (63.6)	1094 (63.6)
Divorced, separated, or never married	316 (36.5)	310 (36.4)	626 (36.4)
Education attainment, n (%)			
High school or less	230 (26.5)	219 (25.7)	449 (26.1)
College or bachelor's degree	391 (45.1)	418 (48.9)	809 (47.0)
Higher degree	246 (28.4)	216 (25.3)	462 (26.8)
Insomnia duration, mean (SD), years	13.9 (10.8)	13.5 (10.9)	13.7 (10.8)
Comorbidity, n (%)			
No comorbidity	380 (43.9)	339 (39.8)	719 (41.9)
Medical comorbidity	102 (11.8)	109 (12.8)	211 (12.3)
Mental health comorbidity	303 (35.0)	286 (33.6)	589 (34.2)
Medical and mental health comorbidity	81 (9.4)	118 (13.8)	199 (11.6)

Table 2. Descriptive statistics of the mediator (ISI score) at baseline and 9-week follow-up, and the outcome variables at baseline and 6-month follow-up.

	n	dCBT-I	n	Patient Education	n	Total
ISI score, mean (SD)						
Baseline	868	19.2 (3.9)	853	19.6 (4.0)	1721	19.4 (3.9)
9-week follow-up	584	10.4 (6.2)	534	15.2 (5.3)	1118	12.7 (6.3)
Presenteeism[a1], % mean (SD)						
Baseline	785	28.1 (25.4)	773	30.5 (27.0)	1558	29.3 (26.2)
6-month follow-up	370	17.5 (24.0)	337	22.5 (25.1)	707	19.9 (26.6)
Activity impairment[a2], % mean (SD)						
Baseline	867	41.6 (29.6)	853	43.9 (28.8)	1720	42.7 (29.2)
6-month follow-up	400	27.9 (28.8)	365	33.0 (29.5)	765	30.3 (29.2)
Absenteeism, mean (SD), hours						
Baseline	805	10.5 (26.5)	792	10.3 (23.5)	1597	10.4 (25.1)
6-month follow-up	359	6.6 (19.8)	330	6.2 (17.0)	689	6.4 (18.5)
Employed, n (%)						
Baseline	867	590 (68.1)	853	601 (70.5)	1720	1191 (69.2)
6-month follow-up	433	296 (68.4)	406	296 (72.9)	839	592 (70.6)

[a]From the "Work Productivity and Activity Impairment Questionnaire: General Health (WPAI). [1]Average reduced productivity while working; [2] Average reduced productivity in daily activities outside of work.

Table 3. The direct effect, indirect effect, and total effect of treatment on the outcome variables at 6-month follow-up for the mediator (insomnia symptom severity; ISI) at 9-week follow-up. The analyses are adjusted for sex, age, educational level, relationship status, and comorbidities, as well as for the baseline value of the ISI and the outcome variable. 95% confidence intervals are shown in parentheses. The analyses assume a data missing-at-random scenario.

	Presenteeism, %	Activity impairment, %	Absenteeism, hours	Employment, probit link scale
ISI				
Direct effect	1.4	-0.2	2.18	-.021
	(-3.5 to 6.3)	(-5.4 to 5.3)	(-1.31 to 5.82)	(-.11 to .065)
Indirect effect	**-5.4***	**-5.5***	-.90	.008
	(-7.8 to -3.1)	**(-8.1 to -3.0)**	(-2.68 to .77)	(-.031 to .045)
Total effect	-4.0	**-5.6***	1.29	-.012
	(-8.1 to 0.1)	**(-9.9 to -1.0)**	-1.71 to 4.19)	(-.090 to .057)

****p<.05***

Figures

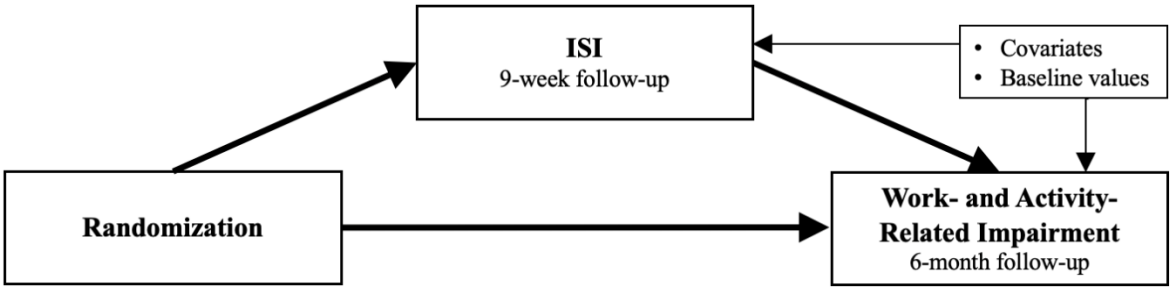

Figure 1: A directed acyclic graph showing the analysis model. In addition, an interaction between treatment and ISI 9-week post-randomization was included in the model.

Appendix A: Supplementary Materials

Title

The effects of digital CBT-I on work productivity and activity levels and the mediational role of insomnia symptoms: Data from a randomized controlled trial with 6-month follow-up

Authors

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Example of commands used in Mplus (MAR model)

```
DATA:

File is "Digital_CBT-I_mediation_on_work_and_activity_levels.dat";

VARIABLE:

names = id group age sex rstatus
preisi postisi
employed0 absenteeism0 presenteeism0 activity0
employed6 absenteeism6 presenteeism6 activity6
comorbidity education;
usevariables = activity6 postisi group activity0 preisi
age sex rstatus edu1 edu2 co1 co2 co3 int;

Missing is all(-99);
!Categorical=activity6;

Define:

edu1 = education == 1;
edu2 = education == 2;
co1 = comorbidity == 1;
co2 = comorbidity == 2;
co3 = comorbidity == 3;

int = group*postisi;

center age preisi (grandmean);

Analysis: estimator = bayes;
          biterations = (10000);
          processors = 2;
          mediator=observed;

Model:

activity6 ON group postisi activity0 preisi
age sex rstatus edu1 edu2 co1 co2 co3 int;

postisi ON group activity0 preisi
age sex rstatus edu1 edu2 co1 co2 co3;

Model indirect:

activity6 MOD postisi int group;

Output: tech1 standardized cinterval;

Plot: type=plot3 sensitivity;
```

Supplementary Results

Effect sizes (Cohen's d)

Based on the descriptive data reported in Table 2, between-group Cohen's *d* effect size was estimated as the difference in mean scores divided by the standard deviation (Carlson & Schmidt, 1999; Morris, 2008). Cohen's *d* was calculated for the mediator at baseline and 9-week follow-up and for each of the outcome variables at baseline and 6-month follow-up (except absenteeism which is a binary measure). As a benchmark for interpreting Cohen's *d*, 0.8 is regarded as large, 0.5 as moderate, and 0.2 as small (Cohen, 1988).

The estimated effect sizes for the mediator at baseline and 9-week follow-up when comparing dCBT-I with patient education were -0.1 and -0.8, respectively. At baseline, estimated effect sizes for presenteeism, activity impairment, and absenteeism were -0.09, -0.08, and 0.008, respectively. At 6-month follow-up, the estimated effect sizes for presenteeism, activity impairment, and absenteeism were -0.2, -0.2, and 0.002, respectively.

Sensitivity analyses

Information for the regression estimates of the outcome variables at 6-month follow-up on covariates included in the mediation analysis is included in Supplementary Table A1.

Unmeasured confounders. Correlated residual plots for the statistically significant indirect effects on presenteeism and activity impairment suggest that a residual correlation between the mediator and the outcome variable would need to be at least 0.15 to reduce the indirect effects to zero (see Supplementary Figure A2). Requiring the residual correlation to be lower than 0.15 can be considered a rather strict requirement. The results regarding the significant indirect effects should therefore be interpreted with caution.

MNAR selection models. Sensitivity analyses assuming data missing-not-at-random were carried out and show the same results in addition to an indirect effect on absenteeism

and a total effect of the mediator on presenteeism (see Supplementary Table A2 for additional details).

Supplementary Table A1. Regression estimates of outcome variables at 6-month follow-up on covariates included in the mediation analysis.
*One-tailed p-value <0.025. Values are estimates (95% CI).

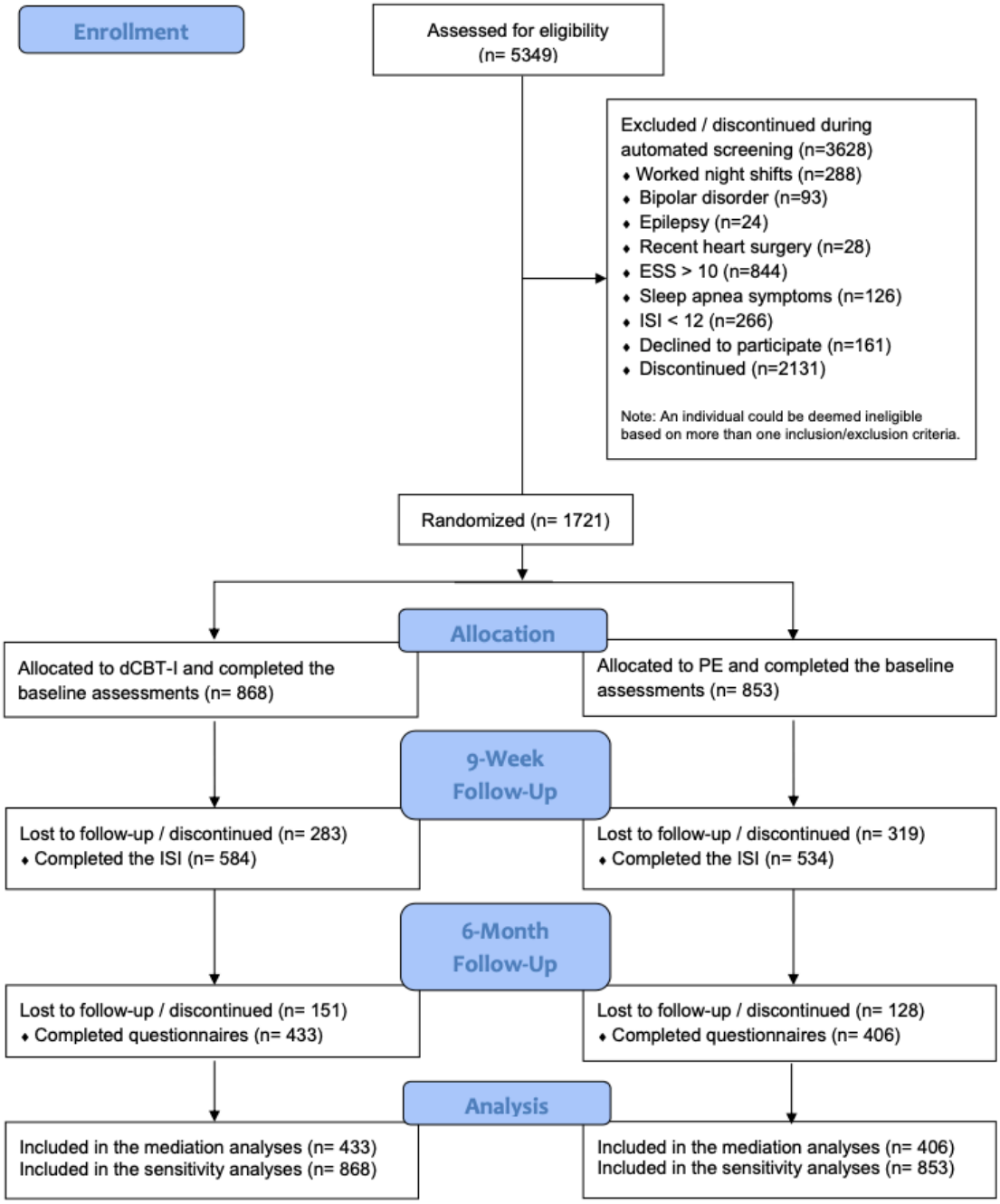
	Presenteeism		Activity impairment		Absenteeism		Employment status	
	MAR	MNAR	MAR	MNAR	MAR	MNAR	MAR	MNAR
dCBT-I	.061	-.13	-.44	-.53	.023	1.99	-.337	-.14
	(-.86 to 1.02)	(-1.075 to .81)	(-1.46 to .58)	(-1.56 to .54)	(-7.41 to 7.61)	(-5.14 to 9.00)	(-1.12 to .40)	(-.42 to .15)
ISI, 9-week	**.099***	**.11***	**.072***	**.086***	.043	-.23	-.025	-.018
follow-up	**(.045 to .15)**	**(.050 to .16)**	**(.009 to .13)**	**(.027 to .15)**	(-.38 to .49)	(-.64 to .17)	(-.067 to .018)	(-.043 to .006)
ISI, baseline	-.034	-.012	.007	.019	.14	-.33	-.037	**-.042***
	(-.087 to .018)	(-.066 to .042)	(-.051 to .065)	(-.040 to .078)	(-.28 to .55)	(-.71 to .050)	(-.075 to .001)	**(-.079 to -.007)**
Presenteeism,	**.34***	**.32***						
baseline	**(.26 to .41)**	**(.24 to .39)**						
Activity			**.39***	**.38***				
impairment,			**(.32 to .46)**	**(.31 to .45)**				
baseline								
Absenteeism,					**.096***	.050		
baseline					**(.033 to .16)**	(-.004 to .10)		
Employment,							**2.25***	**2.25***
baseline							**(1.97 to 2.55)**	**(1.99 to 2.52)**
Age	**-.017***	**-.019***	.001	-.001	-.098	-.088	**.020***	**-.015***
	(-.031 to -.003)	**(-.033 to -.005)**	(-.014 to .017)	(-.017 to .014)	(-.21 to .014)	(-.20 to .019)	**(-.030 to -.010)**	**(-.024 to -.005)**
Female sex	-.37	**-.50***	-.34	**-.44***	-2.014	-.13	.19	.16
	(-.76 to .012)	**(-.90 to -.10)**	(-.78 to .11)	**(-.89 to -.002)**	(-5.11 to 1.15)	(-3.28 to 2.94)	(-.14 to .50)	(-.11 to -.45)
Relationship	.12	.087	-.17	-.14	-.91	-.91	-.14	-.091
status	(-.26 to .51)	(-.30 to .47)	(-.60 to .24)	(-.56 to .28)	(-4.040 to 2.19)	(-3.83 to 2.053)	(-.42 to .18)	(-.38 to .17)
College or	-.13	-.056	.091	.093	-.31	-.63	.27	.23
bachelor's degree	(-.59 to .33)	(-.52 to .41)	(-.41 to .59)	(-.41 to .60)	(-4.02 to 3.56)	(-2.79 to 4.12)	(-.066 to .60)	(-.069 to .55)
Higher degree	-.27	-.25	-.26	-.30	-.67	1.82	**.52***	**.54***
	(-.77 to .23)	(-.76 to .26)	(-.82 to .29)	(-.86 to .25)	(-4.74 to 3.52)	(-2.029 to 5.66)	**(.13 to .92)**	**(.17 to .90)**
Medical	**.77***	**.91***	**1.42***	**1.39***	3.84	1.081	-.34	-.26
comorbidity	**(.052 to 1.48)**	**(.21 to 1.61)**	**(.70 to 2.13)**	**(.67 to 2.10)**	(-1.42 to 9.06)	(-3.66 to 5.72)	(-.80 to .12)	(-.67 to .16)
Mental health	-.032	-.074	.090	.092	-3.19	-2.19	-.047	.096
comorbidity	(-.45 to .39)	(-.51 to .35)	(-.39 to .55)	(-.39 to .56)	(-6.51 to .24)	(-5.44 to 1.07)	(-.38 to .28)	(-.22 to .41)
Medical and	.034	.094	-.36	.41	.49	-.85	-.092	-.051
mental health	(-.54 to .62)	(-.043 to .092)	(-.28 to .98)	(-.24 to 1.03)	(-4.16 to 5.28)	(-5.20 to 3.58)	(-.50 to .33)	(-.45 to .34)
comorbidity								

Supplementary Table A2. Sensitivity analyses assuming data missing-not-at-random for the direct effect, indirect effect, and total effect of treatment on the outcome variables at 6-month follow-up for the mediator (insomnia symptom severity; ISI) at 9-week follow-up. The analyses are adjusted for sex, age, educational level, relationship status, and comorbidities, as well as for the baseline value of the mediator (insomnia severity) and baseline level of each outcome variable. 95% confidence intervals are shown in parentheses.

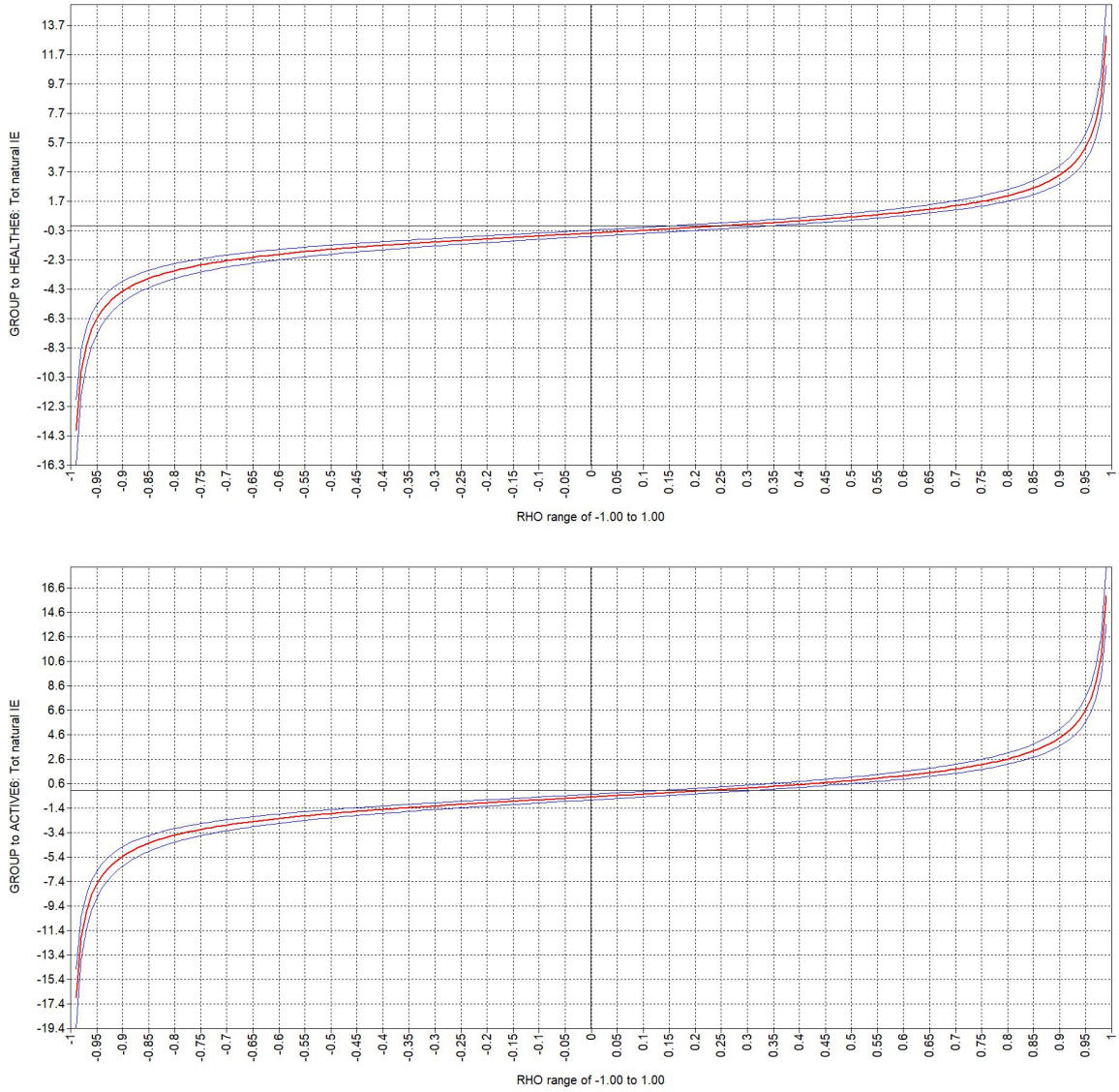
	Presenteeism, %	Activity impairment, %	Absenteeism, hours	Employment, probit link scale
ISI				
Direct effect	2.5	0.7	-.061	-.030†
	(-2.3 to 7.5)	(-4.6 to 6.0)	(-3.19 to 3.08)	(-.098 to .035)
Indirect effect	**-6.8***	**-6.8***	**1.80***	.019†
	(-9.4 to -4.4)	**(-9.6 to -4.3)**	**(.26 to 3.40)**	(-.008 to .046)
Total effect	**-4.3***	**-6.2***	1.75	-.011†
	(-8.4 to -0.1)	**(-10.6 to -1.7)**	(-.87 to 4.40)	(-.074 to .047)

**p<.05*

† Model with exposure-mediator interaction did not converge – reported results for the binary outcome are based on a selection model without the interaction.



Supplementary Figure A1. Flow diagram of the study: participant inclusion, timing of assessments, and completion rates.
dCBT-I = digital cognitive behavioral therapy for insomnia.



Supplementary Figure A2. Sensitivity plots of the indirect effect on presenteeism (top) and activity impairment outside of work (bottom) at 6-month follow-up suggesting that a residual correlation between the mediator (insomnia severity) and the outcome variable would need to be at least 0.15 to reduce the indirect effects to zero.

Paper 3

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Original Article

ORIGINAL ARTICLE

The evening light environment in hospitals can be designed to produce less disruptive effects on the circadian system and improve sleep

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Abstract

Study Objectives: Blue-depleted lighting reduces the disruptive effects of evening artificial light on the circadian system in laboratory experiments, but this has not yet been shown in naturalistic settings. The aim of the current study was to test the effects of residing in an evening blue-depleted light environment on melatonin levels, sleep, neurocognitive arousal, sleepiness, and potential side effects.

Methods: The study was undertaken in a new psychiatric hospital unit where dynamic light sources were installed. All light sources in all rooms were blue-depleted in one half of the unit between 06:30 pm and 07:00 am (melanopic lux range: 7–21, melanopic equivalent daylight illuminance [M-EDI] range: 6–19, photopic lux range: 55–124), whereas the other had standard lighting (melanopic lux range: 30–70, M-EDI range: 27–63, photopic lux range: 64–136), but was otherwise identical. A total of 12 healthy adults resided for 5 days in each light environment (LE) in a randomized cross-over trial.

Results: Melatonin levels were less suppressed in the blue-depleted LE (15%) compared with the normal LE (45%; $p = 0.011$). Dim light melatonin onset was phase-advanced more (1:20 h) after residing in the blue-depleted LE than after the normal LE (0:46 h; $p = 0.008$). Total sleep time was 8.1 min longer ($p = 0.032$), rapid eye movement sleep 13.9 min longer ($p < 0.001$), and neurocognitive arousal was lower ($p = 0.042$) in the blue-depleted LE. There were no significant differences in subjective sleepiness ($p = 0.16$) or side effects ($p = 0.09$).

Conclusions: It is possible to create an evening LE that has an impact on the circadian system and sleep without serious side effects. This demonstrates the feasibility and potential benefits of designing buildings or hospital units according to chronobiological principles and provide a basis for studies in both nonclinical and clinical populations.

Statement of Significance

Evening and night exposure to blue light exert particularly disruptive effects on the circadian system, but tunable LED-systems allow for blue-depleted evening lighting more adapted to human circadian biology. We demonstrate that when a blue-depleted light environment is integrated into a large-scale building complex, this has quantifiable effects on the circadian system and sleep. Our study was performed in a new acute psychiatric hospital unit where healthy participants resided for 5 days, a similar duration as patient admissions. This shows that it is possible to use the evening light environment to target circadian disruption and sleep in such a setting and it may have additional applications in a range of settings where control over incident and ambient light is feasible.

Key words: circadian rhythms; lighting; sleep; arousal; hospitals

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Introduction

Light is the most important time-giver for the human circadian system [1–3]. Throughout evolution, this system has continuously adapted to the signal created by the cyclic shifts in nature from daylight to nighttime darkness. The advent of electric lighting transformed visual perception in evening environments, increasing the number of hours available for both productivity and recreation. However, exposure to artificial light during normal dark periods exerts additional effects because of the nonvisual effects of light, such as delaying the circadian phase, suppressing melatonin production, delaying sleep onset, changing sleep architecture, and increasing alertness [4–6]. Furthermore, circadian disruption can have negative effects on both mental and somatic health and can contribute to depression, insomnia, metabolic abnormalities, obesity, immune impairment, poor cognitive performance, and a greater risk of cancer [7]. These substantial changes in timing, color, and intensity of evening light have occurred at a rapid pace with regard to the evolutionary perspective and likely have widespread and ongoing implications for health and sleep at a societal level [8]. In contrast, residing in natural darkness at night has been shown to phase-advance circadian rhythms and sleep timing [5, 9]. It remains unknown whether it is possible to create a scalable and usable indoor light environment (LE) that mitigates the negative effects of artificial evening light on circadian rhythms, sleep, and arousal.

The effects of light on the circadian system are primarily mediated by the intrinsically photosensitive retinal ganglion cells (ipRGCs) [10–12], which project to the circadian pacemaker in the suprachiasmatic nucleus of the hypothalamus. ipRGCs are primarily sensitive to short-wavelength, blue light (λ_{max} ~ 480 nm) [10], suggesting the potential to mitigate the negative effects of evening artificial light by modifying the spectral composition of the indoor LE [8]. It has previously been shown that selectively filtering out short-wavelength, blue light in the evening or night reduces melatonin suppression and alertness [13–18], indicative of impeded ipRGC signaling. However, these effects were established under laboratory conditions, whereas a naturalistic setting introduces large variability in irradiance and illuminance resulting from general movement, changes in direction of gaze, light emitting screens, and ambient light. Therefore, it remains to be determined whether meaningful physiological effects can be achieved when such lighting modifications are applied in general housing or institutional settings.

The application of evening blue-depleted lighting may extend to many situations where it is feasible to exert a high level of control over all light sources. It may, however, hold potential in hospitals in which sleep–wake disruptions are ubiquitous and light levels at times may exceed those in household settings. It is known that patients with critical illnesses often have disrupted circadian rhythms [19], a phenomenon that is associated with a subsequent increase in morbidity and mortality [20, 21]. Moreover, disrupted circadian rhythms and sleep–wake cycles are equally, if not more apparent, in severe mental disorders compared with physical illnesses [22], highlighting the need for non-pharmacological interventions that can be used to target sleep–wake disruption and arousal in clinical psychiatry. Notably, the application of extended darkness in the evening and night [23–25], or filtering out short-frequency, blue light using blue-blocking glasses [26] has been shown to reduce manic symptoms in patients acutely admitted with mania [27]. Given the potential benefits to this population, we decided to examine the potential application of an evening blue-depleted LE as implemented in a large-scale, multiroom complex such as a hospital by integrating such a lighting system in a new psychiatric unit.

The new hospital unit contains two wards that have identical, mirror-image layouts, and similar levels of photopic lux, albeit different light spectrum compositions in the evening: evening blue-depleted or standard hospital LE. Prior to opening of the unit for patient admissions, we undertook a proof-of-concept study to evaluate the effects of the evening blue-depleted LE on healthy subjects. In a randomized cross-over trial, healthy, young adult volunteers resided for alternating periods of 5 consecutive days in each ward. Our main aims were to test whether residing in the evening blue-depleted LE influenced the timing of dim light melatonin onset (DLMO), melatonin suppression, and polysomnographic sleep variables as compared with the effects of exposure to standard LE. Secondary aims were to determine whether differences in neurocognitive arousal and subjective levels of sleepiness could be identified and whether any side effects might be associated with residing in the blue-depleted LE.

Methods

Study design

Participants completed a comprehensive screening procedure, 7-day pre-randomization monitoring, and the 13-day study protocol. Prospective participants were eligible for inclusion in the research if their habitual sleep–wake patterns were within normal parameters (defined for the purposes of the study as weekday bedtime between 10:30 pm and 12:00 am and weekday rise time between 06:30 am and 08:00 am), with small intraindividual variations (<2 h) between weekdays and weekends and they tested negative for color blindness on the Ishihara plate test.

Exclusion criteria were evidence of any current medical or psychological conditions, current use of prescription medication(s), family history of severe mental illness, current sleep disorders, night shift work in the preceding 2 years, trans-meridian travel in the preceding 2 months exceeding one time-zone, and/or current use of nonprescription drugs or illicit substances (not including alcohol or nicotine).

During the 7-day pre-randomization monitoring, all participants were asked to maintain a fixed sleep–wake schedule (bedtime: 11:00 pm–12:00 am, rise time: 07:00 am–08:00 am) and wear an actiwatch. Participants were asked to refrain from the ingestion of alcohol and/or caffeine after 12:00 pm for the duration of the project.

A randomized cross-over design (see Figure 1 and Supplementary Figure S1) was chosen for this study as within-participant variation was expected to be lower for our main outcomes compared with between-participant variation, thus allowing for a smaller number of participants. Participants resided for a total of 10 days (2 conditions of 5 days each) in late September 2017 in a new 40-bedded acute psychiatric unit at St. Olavs Hospital in Trondheim, Norway. Individuals were randomized to first reside 5 days in one of two wards followed by an intermission day and then to reside the next

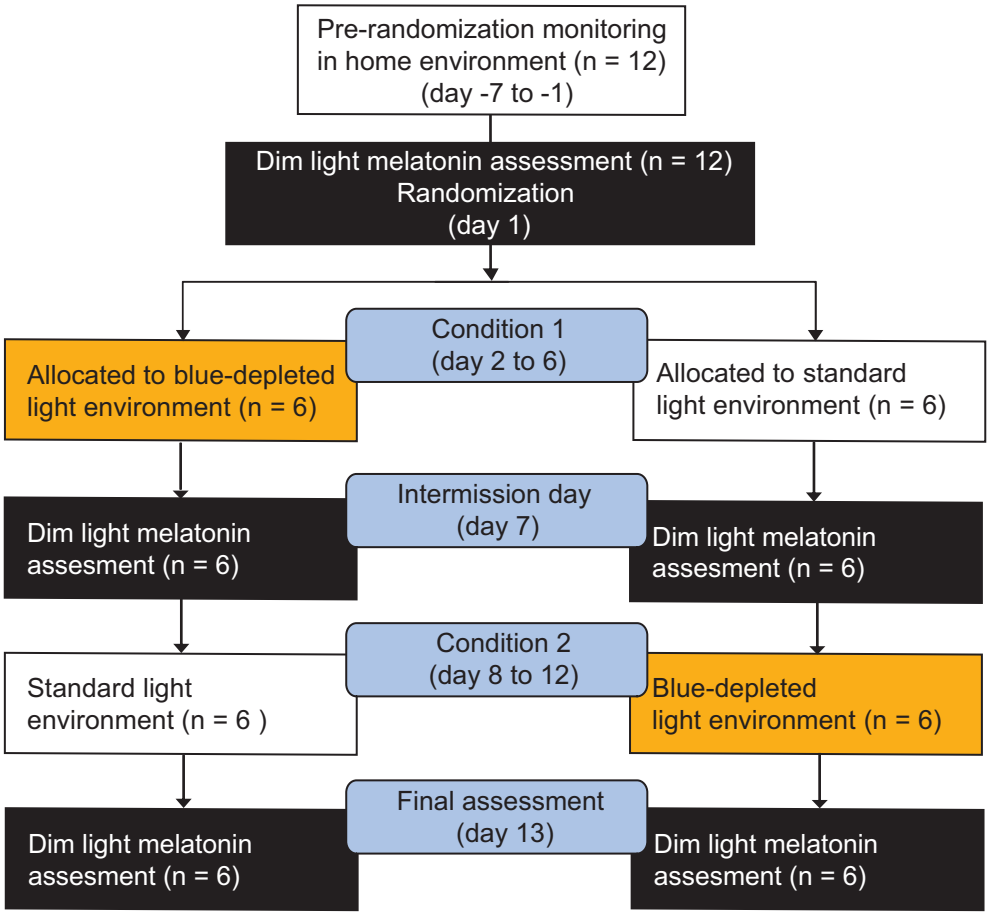

Figure 1. Overview of the study design. Flowchart of the randomized cross-over design describing the location of the participant at each key time point in the trial along with information regarding the nomenclature for the different phases in the study.

5 days in the other ward. The only difference between the two wards was the light spectrum to which residents were exposed during the evening and night (see Supplementary Figure S2 for an overview of the unit). One ward provided a blue-depleted LE in the bedrooms, bathrooms, hallways, and common areas from 06:30 pm until 06:50 am and standard hospital lighting throughout the day, whereas the other ward utilized standard LE at all times. In addition, participants in the blue-depleted LE were asked to use blue-blocking filters (lowbluelights.com) on their electronic media devices in the evenings. Each ward consisted of 20 bedrooms with common areas for socializing and dining.

Participants were given a timetable at the beginning of each 5-day condition that detailed the type and timing of assessments. Hospital staff members were present to maintain safety and assist in the day-to-day running of the wards (e.g. delivery of meals).

During residency at the hospital unit, all participants were awoken by 07:00 am and expected to leave the unit by 08:00 am and return by 05:00 pm. Between 05:00 pm and 06:00 pm, participants had dinner in a common dining room (with standard hospital lighting). At 06:00 pm, participants returned to the LE they were currently allocated to and were free to spend their time in their rooms or the common areas. Participants were requested to retire to their bedrooms for sleep by 11:00 pm and turned the lights off during the sleep opportunity.

Ethics

The protocol was approved by the Regional Ethical Committee in Trondheim (Central Norway; REK: 2017/916) and is registered on the ISRCTN website (Reference: 12419665). Written informed consent was obtained from all participants and the study was undertaken in accordance with the Revised Declaration of Geneva.

Overview of each hospital LE

The lighting fixtures and fittings in each ward were identical and included round downlights, recessed square lights, and built-in reading lights by the desk in the bedrooms (Glamox AS, Oslo, Norway).

Blue-depleted LE (experimental condition)

The blue-depleted LE was created using a LED lighting system that emits both colored and white light. The LED modules inside the light fittings contained a mix of red, green-white, and blue diodes that can be programmed individually to emit different light intensities at different times of the day. To create the evening blue-depleted LE, only the green-white and red diodes emitted light, whereas the blue diode was switched off. The green-white diode emitted a small amount of blue light as it is a blue-chip covered with yellow phosphorus. Blue-blocking

window filters were also deployed in the evening and all televisions had permanent blue-blocking filters (Supplementary Figure S3 shows an example of the bedrooms).

From 07:00 am to 06:00 pm, the light was comprised of standard hospital light (3,000 K). From 06:00 pm to 06:30 pm, there was a transition period from normal to blue-depleted lighting. All light sources were blue-depleted from 06:30 pm to 06:50 am. From 06:50 am to 07:00 am, the lighting underwent a further transition returning it to standard hospital lighting.

Normal LE (control condition)

In this ward, the light spectrum remained constant throughout the 24 h cycle (3,000 K).

Light measurements

Prior to commencing the trial, the light spectrum was assessed using a Mavospec Base light meter (Gossen Foto- Und Lichtmesstechnik GmbH, Nürnberg, Germany). The light measurements demonstrated that the LE in the two wards had similar levels of photopic lux but the levels of melanopic lux were lower in the blue-depleted LE than in the standard LE (see Table 1 for details) [28]. Light exposure will vary with the direction of gaze. However, for the purposes of this study, light measurements were performed horizontally at eye level at standardized locations and times in both units. These locations were patient rooms (1 m into the room, facing windows, standing, with measurement performed horizontally at eye level [160 cm]); bathrooms (standing in front of mirror, with measurement performed horizontally at eye level [160 cm]); common areas such as the TV room (seated in a sofa, facing TV-screen, with measurement performed horizontally at eye level [100 cm]); and hallway (standing beneath a hallway luminaire: the brightest lit area in the hallway).

Assessments

Melatonin

Saliva samples were collected hourly between 07:00 pm and 11:00 pm on study days 1, 6, 7, 12, and 13 using Salivette Cortisol Code blue (Sarstedt AG & Co, Nümbrecht, Germany). Immediately following sample collection, the samples were centrifuged at 2,200*g* for 10 min and frozen at –18°C overnight, before they were moved into storage at –80°C the following day. Samples were analyzed using enzyme-linked immunosorbent assay (Direct Saliva Melatonin, EK-DSM, Bühlmann, Schönenbuch, Switzerland).

Melatonin assessment in dim light Participants were exposed to dim light (<3 lux) from 06:00 pm until 11:00 pm on three separate occasions (days 1, 7, and 13). The clock time at which melatonin levels were >4 pg/mL was defined as the DLMO.

Melatonin assessment in blue-depleted and standard LE Evening melatonin concentrations were assessed on study days 6 and 12 (i.e. when participants had been exposed to the different LEs for 5 consecutive days).

Sleep

Participants underwent polysomnography (PSG) on study days 5, 6, 11, and 12. Electrodes were applied to the scalp according to the 20/20 system for electroencephalography recording (F3, F4, C3, C4, O1, O2); electrooculogram, submental electromyogram, electrocardiogram, peripheral pulse oximetry, and electrodes on the legs were also measured. The PSG data were collected using SOMNO HD (SOMNOmedicsGmbH, Randersacker, Germany). Signals were sampled at 256 or 128 Hz, low-pass filtered, and stored at 128 Hz. Evaluation of sleep stages (according to the American Academy of Sleep Medicine criteria version 2.4) [29] was undertaken by a clinical neurophysiologist with >10 years of experience with PSG who was blinded to key participant details (such as current LE or order of LE exposure). Time spent in each sleep stage, sleep onset latency, time awake after sleep onset, rapid eye movement (REM) sleep onset latency, and sleep efficiency (percentage of time in bed spent asleep) were estimated.

Subjective sleepiness

Participants rated their subjective sleepiness on the Karolinska Sleepiness Scale (KSS), a 9-point Likert scale (from 1 = "extremely

Table 1. Light measurements in the two LEs

Light measurements	Photopic	Cyanopic		Melanopic		Rhodopic		Chloropic		Erythropic		Irradiance (μW/cm²)	photon flux	Log photon flux	peak irradiance (nm)
	Lux	Lux	EDI	Lux	EDI	Lux	EDI	Lux	EDI	Lux	EDI				
Standard LE															
Patient room	93	34	34	49	44	58	52	78	75	92	94	28.3	8.28E+13	13.9	605
Patient bathroom	64	17	17	30	27	37	33	53	51	64	65	18.9	5.58E+13	13.8	610
Common area, TV room	86	30	30	46	41	54	48	72	69	86	87	26.5	7.75E+13	13.9	610
Common area, hallway	136	48	48	70	63	83	74	113	109	135	138	42.3	1.24E+14	14.1	610
Blue-depleted LE															
Patient room	87	1	1	16	15	24	21	52	47	97	97	28.3	8,66E+13	13,9	625
Patient bathroom	49	2	2	7	6	11	10	29	26	54	55	14.8	4.49E+13	13.7	620
Common area, TV room	55	0	1	9	8	14	12	32	28	61	61	17.5	5.35E+13	13.7	620
Common area, hallway	124	1	2	21	19	33	28	74	66	139	139	39.7	1.21E+14	14.1	620

Light measurements taken inside the hospital in both the blue-depleted and the standard LE. α-opic illuminance (lux) levels for each of the five photopigments are given in concordance with Lucas et al [28], whereas the α-opic equivalent daylight illuminance (EDI) are reported according to the CIE S026:2018 standard [71].

alert" to 9 = "extremely sleepy—fighting sleep"), at 06:00 pm, 08:00 pm, and 10:00 pm on each night spent in the unit, and again at 07:00 am, the following morning [30].

Neurocognitive arousal

As a neurocognitive measure of arousal, participants completed the Connors Continuous Performance Test-3 (C-CPT-3) [31] between 09:00 pm and 10:00 pm on study days 4 and 10. In brief, the C-CPT-3 is a computerized test in which the letters A–Z are presented consecutively on a monitor (physical blue-blocking filters were used in front of monitors in both LEs). The test consists of 360 trials and lasts for 14 min. The participants are asked to press a response button each time a letter (targets, 80% of trials) was presented but to withhold their response when the letter was X (nontargets, 20% of trials). The participants were asked to respond as quickly and accurately as possible. Outcomes are reported on four commonly derived measures of response speed, consistency throughout testing, and accuracy; that is, reaction time, standard deviation of the reaction times, omissions (failure to respond to targets), and commissions (response to nontargets) [32, 33].

Actigraphy

Participants wore an actiwatch on their nondominant wrist (Actiwatch Spectrum, Philips Respironics Inc., Murrysville, PA), for both the 7 days of pre-randomization monitoring and throughout the 13-day study period. Sleep–wake data (divided into 30-s epochs) were used to estimate the sleep regularity index (SRI). The SRI indicates the percentage of epochs in each 24-h in which sleep–wake states are similar to the corresponding epoch in the previous 24 h [34]. Rise times were generated automatically from actigraphy recordings using an actigraphy software program (Actiware version 5.70.1, Philips Respironics Inc., Murrysville, PA). For bedtimes, participants indicated time they went to bed using an event-marker press on the actiwatch. If this information was missing, we used the reported bedtime recorded in the sleep diary.

Side effects

Subjective side effects Participants completed the Committee of Clinical Investigations (UKU) side effect rating scale on days 7 and 13. Although generally used in the evaluation of new psychotropic drugs, this scale was selected for the present trial as it assesses potential side effects across several important domains (i.e. psychiatric, neurological, autonomic, and other) [35]. The scale has 40 core items in addition to some sex-specific ratings (3 for males and 5 for females). The total score ranges from 0 to 129 for men and 0 to 135 for women, with higher scores indicating the presence of more side effects. However, as increased sleepiness and longer/deeper sleep duration represent desired benefits rather than side effects of exposure to blue-depleted LE, these items were excluded from our analysis.

Color perception Ability to discriminate colors was assessed using the Farnsworth–Munsell 100 Hue Color Vision Test (FM-100) on two occasions (day 2 or 3 and day 8 or 9). The FM-100 measures the amount of errors an individual makes in a color-hue sorting task. Superior color discrimination ability is defined as an error score <20, average ability as a score of 20–100, and low ability by a score >100 [36].

Sample size

A previous study reported that 3 days in a natural light–dark environment (without artificial lighting at night) advanced melatonin onset by 1.4 h and 6 nights advanced DLMO by 2.6 h (without artificial lighting at night) [5]. Other studies had reported that blue-blocking glasses at night had the same effect as darkness on melatonin secretion [15, 37]. As such, we assumed a priori that melatonin onset could be advanced by approximately 1.5 h following 5-day exposure to a blue-depleted LE with an estimated standard deviation of 45 min (a *SD* similar to that reported for melatonin onset in healthy controls [38] and the above-mentioned studies [5, 15, 37]. We estimated that a sample size of eight individuals would give a 90% chance of detecting these differences with a significance level of 0.05 (two-sided testing). As dropouts from the cross-over design were difficult to predict reliably, we determined we should recruit 12 participants (to allow for 30% attrition).

Randomization

The random allocation sequence was generated by the Unit of Applied Clinical Research (Department of Medicine and Health Sciences, NTNU). The members of the research group could not influence the process in any way.

Statistics

All statistical analyses were performed using R statistical package (version 3.5.2., R Core Team, Vienna, Austria, https://www.R-project.org/) and all figures were generated using GraphPad Prism (version 8.1.2, GraphPad Software, San Diego, California, www.graphpad.com/). A statistical significance level of $p < 0.05$ was chosen for all analyses. A within-subject approach was used in the main analyses to estimate the effects between the two LEs. The analyses were performed by a statistician who was blinded to participant allocation.

Melatonin

The effect of LE on concentrations of salivary melatonin was assessed using a linear mixed model. The combination of study day (day of melatonin assessment), LE, and hour was taken as the fixed effect. The combination of participant ID number and LE were taken as random effects. The assumption of normality was met using a logarithmic scale for the outcome variable. This model estimates the concentrations of melatonin for each of the 5 h included in the melatonin assessments undertaken in the different LEs and dim light. This method implicitly accounts for missing values. The modeled values were in turn used to calculate melatonin suppression and DLMO phase-shifts. As the interaction between LE and study day was specified in the model, any differences in the effects of LE for the order of exposure to each LE could be estimated. Individual levels of melatonin suppression and phase-shifts were calculated from the observed melatonin concentration values.

Melatonin suppression Melatonin suppression is reported as a percentage, which represents the level of melatonin in the two different LEs relative to the level of melatonin the following night in dim light. It was calculated using the area under the

curve (AUC) from 07:00 pm to 11:00 pm on days 6 and 12 divided by the AUC from 07:00 pm to 11:00 pm on days 7 and 13.

Phase shift of DLMO Phase shift was taken as the difference between timing of DLMO after residing in an LE for 5 days (days 7 or 13) and timing of DLMO at baseline (day 1). Linear interpolation was utilized to find the timing of DLMO.

Sleep

Similar linear mixed models were specified to test overall differences in PSG variables between the LEs and by condition order, and to test differences in bedtime, rise time, and SRI between pre-randomization monitoring, condition 1, and condition 2.

Subjective sleepiness, arousal, and side effects

For mean subjective sleepiness (KSS) in the evening and morning, intraindividual differences were calculated and tested for significance using one-sample Student's *t*-tests. The same approach was used for the color perception test (FM-100). As some measures from the C-CPT-3 and scores on the UKU side effects rating scale were not normally distributed, we used a Wilcoxson signed-rank test to examine intraindividual differences between the two LEs for these outcomes.

Missing values were pairwise deleted in the calculation of individual mean scores for the UKU side effects scale and the KSS. One individual was missing all KSS-scores in the blue-depleted LE and was thus excluded from those analyses. There were no missing values on the C-CPT-3 or the FM-100.

Results

Subjects and study design

As shown in Figure 1, 12 healthy young adults (mean age ± *SD*: 23.0 ± 3.1 years, 7 women) completed the eligibility screening and pre-randomization monitoring and participated in the 13-day trial protocol. Complete data were obtained for the main outcome assessments of melatonin and PSG. Prior to undertaking the analyses, we checked data distributions, etc., for outliers. This resulted in the exclusion of one melatonin concentration value associated with one participant to avoid over-estimating the difference in melatonin suppression between conditions (at 11:00 pm when residing in the blue-depleted LE this participant had an extreme concentration of melatonin which was considered most likely to be a measurement error). All but one of the secondary outcome assessments had complete data (one individual did not complete the KSS evaluations).

Melatonin levels and DLMO phase shift

Melatonin suppression was significantly lower when participants resided in the blue-depleted compared with the standard LE (mean difference = 27%, 95% confidence interval (CI): 4% to 51%, $p = 0.020$). Melatonin suppression was 18% (95% CI: –3% to 34%, $p = 0.09$) in the blue-depleted LE and 45% (95% CI: 29% to 57%, $p < 0.001$) in the standard LE. From observed values, 10 out of 11 individuals with complete suppression data exhibited lower levels of melatonin suppression in the blue-depleted LE (see Supplementary Figure S4 for details). DLMO occurred 0:34 h (95% CI: 0:10 to 0:54 h) earlier following residence in the blue-depleted compared with the standard LE ($p = 0.008$). Compared with DLMO at baseline, DLMO was phase-advanced by 1:20 h (95% CI: 1:00 to 1:38 h, $p < 0.001$) following residence in the blue-depleted LE, and by 0:46 h (95% CI: 0:25 to 1:09 h, $p < 0.001$) after residing in the standard LE (Figure 2). From observed values, 11 of 12 individuals presented greater phase advancement of DLMO after residing in the blue-depleted LE (Supplementary Figure S5).

Changes in total sleep time and REM sleep

Total sleep time (TST) was 8.1 min longer in the blue-depleted compared with the standard LE ($p = 0.032$). Furthermore, participants exhibited 13.9 min more REM sleep when residing in the blue-depleted compared with the standard LE ($p < 0.001$). As shown in Table 2, no significant differences were observed between LEs with regard to the variables sleep onset latency, REM sleep onset latency, wake after sleep onset, sleep efficiency, or time in non-REM sleep stages 1–3.

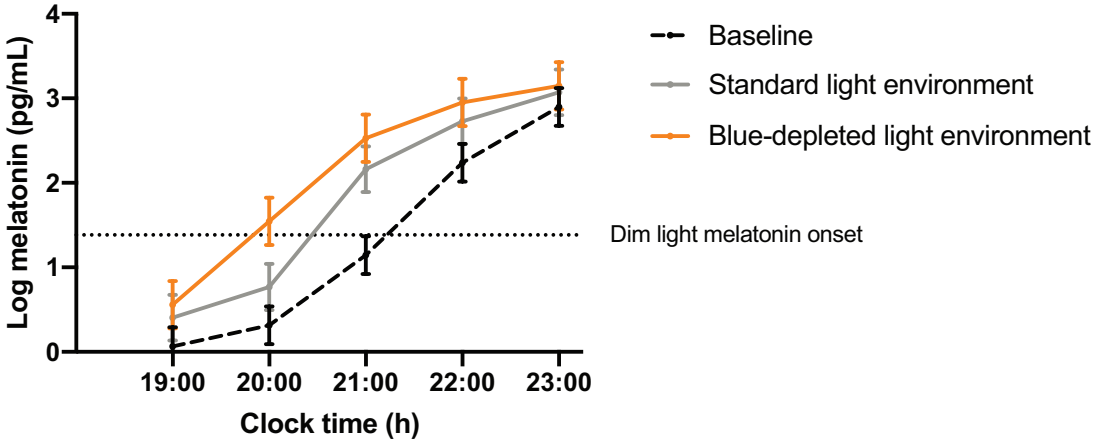

Figure 2. Melatonin concentration by hour and condition. Estimated mean dim light melatonin log concentrations hourly between 07:00 pm and 11:00 pm at baseline and after residing 5 nights in the blue-depleted and the standard LE. Error bars indicate the estimate ± standard error of the mean. The dotted line indicates the 4 pg/mL threshold for DLMO. Melatonin concentrations between 07:00 pm and 11:00 pm differed significantly when individuals resided in the blue-depleted LE compared with the standard LE.

Table 2. Sleep as measured by polysomnography

	Blue-depleted LE		Standard LE		Difference		
Sleep variables (min)	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	*P*
Total sleep time	440.2	432.6 to 447.8	432.1	424.5 to 439.7	8.1	0.7 to 15.5	0.03
Time in REM	89.7	80.8 to 98.6	75.8	66.9 to 84.7	13.9	6.0 to 21.7	0.001
Time in N1	30.8	26.6 to 35.1	33.5	29.3 to 37.8	–2.7	–7.9 to 2.4	0.30
Time in N2	225.6	213.7 to 237.6	224.8	212.8 to 236.7	0.9	–8.3 to 10.1	0.85
Time in N3	94.8	84.3 to 105.4	98.7	88.1 to 109.3	–3.9	–10.9 to 3.0	0.27
Sleep onset latency	10.3	7.6 to 12.9	11.9	9.3 to 14.6	–1.7	–5.1 to 1.7	0.34
REM onset latency	128.0	110.7 to 145.3	125.2	107.9 to 142.5	2.8	–21.0 to 26.6	0.82
Wake after sleep onset	23.0	16.8 to 29.3	22.6	16.3 to 28.8	0.5	–5.8 to 6.7	0.89
Sleep efficiency*	93.0	91.6 to 94.5	92.6	91.2 to 94.1	0.4	–1.0 to 1.8	0.59

Estimates of means in PSG-measured sleep-variables during the last 2 nights residing in the evening blue-depleted LE or the standard LE, and the estimated mean differences between LEs. Estimates, 95% confidence intervals and *p*-values were calculated from a mixed model with *n* = 12 participants. REM, rapid eye movement; N1, non-REM sleep stage 1; N2, non-REM sleep stage 2; N3, non-REM sleep stage 3.
*Sleep efficiency is given in percent.

Table 3. Neurocognitive test outcomes

	Blue-depleted LE		Standard LE		Estimated difference	
C-CPT3 test variables (ms)	Mean	*SD*	Mean	*SD*	*Z*	*P*
Hit reaction time	356.7	27.1	369.9	60.2	–0.18	0.85
Hit reaction time *SD*	73.0	13.0	65.3	16.2	–2.03	0.04
Commissions*	32.4	17.1	27.3	16.0	–0.98	0.32
Omissions*	0.3	0.3	0.3	0.5	–0.09	0.93

Mean scores with standard deviations (*SD*) on Connor's Continuous Performance Test-3 variables in both LEs and the estimated differences between the LEs (Wilcoxon signed-rank test with *n* = 12 participants).
*Commissions and omissions are reported in percent of targets.

Subjective levels of sleepiness and neurocognitive arousal

No significant difference (mean difference = 0.18, 95% CI: –0.09 to 0.47, $p = 0.16$) was detected between mean evening subjective sleepiness scores for the 11 individuals residing in the blue-depleted (4.98 ± 2.05) compared with the standard LE (4.79 ± 1.85). The mean morning subjective sleepiness also did not significantly differ (mean difference = 0.02, 95% CI: –0.82 to 0.86, $p = 0.96$) between the 11 individuals with complete data for subjective sleepiness residing in the evening blue-depleted versus standard LE (5.91 ± 2.24 vs. 6.04 ± 2.24, respectively). Supplementary Figure S6 details the mean subjective sleepiness scores as measured at different times of the day. Participants exhibited higher variability in their response times (standard deviations of hit reaction times) throughout the C-CPT-3 computerized response test in the blue-depleted compared with the standard LE ($p = 0.042$). No statistically significant differences were detected between the two lighting conditions in mean hit reaction time or number of omission or commission errors (see Table 3 for details).

Side effects and color perception

Participants reported very few side effects on the UKU rating scale in either the blue-depleted (0.17 ± 0.42) or standard LE (0.12 ± 0.39), with no significant difference between the LEs ($Z = –1.69$, $p = 0.091$). Tiredness/fatigue represented the side effect most frequently reported in the blue-depleted LE (7 reports compared with 2 in the standard LE). Participants made 152 more errors (95% CI: 128 to 177, $p < 0.001$) on the FM-100 color-hue sorting task when residing in the blue-depleted (192 ± 33.4) compared with the standard LE (39.3 ± 23.1). Mean number of errors in the blue-depleted and normal LE were categorized as evincing low and average ability, respectively.

Post hoc analyses of melatonin-data by condition order

For participants who first resided in the blue-depleted LE and then resided in the standard LE, melatonin suppression was respectively, 18% (95% CI: –16% to 41%, $p = 0.26$) in the first condition and 62% (95% CI: 47% to 73%, $p < 0.001$) in the second condition (mean difference: 44%, 95% CI: 16% to 79%, $p = 0.002$).

For participants who first resided in the standard LE and then resided in the blue-depleted LE, melatonin suppression was respectively 34% (95% CI: 8% to 53%, $p = 0.013$) in the first condition and 18% (95% CI: –10% to 39%, $p = 0.19$) in the second condition (mean difference: 16%, 95% CI: –17% to 50%, $p = 0.33$). There was no statistically significant effect of order on the difference between conditions (mean difference: 28%, 95% CI: –19 to 73, $p = 0.23$).

For participants who first resided in the blue-depleted LE, DLMO was phased advanced by 0:55 h (95% CI: 0:30 to 1:20, $p < 0.001$) compared with baseline. After residing in the standard LE as the second condition, there was no significant change in DLMO (mean difference: –0:19 h [delay], 95% CI: –0:49 to 0:14, $p = 0.19$) compared with DLMO after residing in the blue-depleted LE.

For participants who first resided in the standard LE, DLMO was phase advanced by 0:55 h am (95% CI 0:30 to 1:33, $p < 0.001$) compared with baseline. After residing in the blue-depleted LE as the second condition, DLMO was further phase advanced by another 0:50 h (95% CI: 0:11 to 1:15, $p = 0.01$) compared with DLMO after residing in the standard LE. There was an effect of order in that the effect of the blue-depleted LE was larger in condition 2 (mean difference: 1:10 h, 95% CI: 0:20 to 2:01, $p = 0.009$). Findings for melatonin concentrations by the condition are shown in Supplementary Figure S7, D and E.

Post hoc analyses of PSG by condition order

For participants first residing in the blue-depleted LE, there were no statistically significant differences between LE in PSG variables. For participants first residing in the standard LE, REM sleep was 19.6 min longer ($p < 0.001$) and TST was 11.9 min longer ($p = 0.02$) in the blue-depleted LE compared with in the standard LE. There was a significant order effect for one PSG variable in that the blue-depleted LE had a larger effect on reducing sleep onset latency in condition 1 (mean difference: 8.5 min, 95% CI: −16.7 to −0.2, $p = 0.04$).

Post hoc analyses of sleep times across study phases

These post hoc exploratory analyses are reported as they provide insights regarding potential effects on individuals of residing in a regularized environment (e.g. inpatient unit with fixed rise times, meal times, or bedtimes) during the two study conditions representing time spent in the unit compared with their usual living environment.

Participants went to bed 0:35 h (95% CI: 17 to 0:52, $p < 0.001$) earlier in condition 1 compared with the pre-randomization period (when the participants resided at home). There were no significant differences in bedtimes between condition 1 and condition 2 (mean difference: 0:10 h, 95% CI −0:09 to 0:30, $p = 0.31$). Furthermore, participants rose 1:26 h (95% CI: 1:09 to 1:44 h) earlier in condition 1 than in the pre-randomization period ($p < 0.001$); no significant differences in rise times were found between condition 1 and condition 2 ($p = 0.92$). There was statistically significant correlation between phase-shifts in bedtime and phase-shifts in DLMO for the pre-randomization period to condition 1 ($r = 0.66$, 95% CI: 0.13 to 0.89, $p = 0.02$), but no statistically significant correlation for condition 1 to condition 2 ($r = 0.26$, 95% CI: −0.36 to 0.73, $p = 0.40$). The SRI increased significantly from 85% (95% CI: 83% to 88%) in the pre-randomization period to 95% (95% CI: 93% to 98%) in study condition 1 ($p < 0.001$). However, there was no statistically significant difference in the SRI from condition 1 to condition 2 ($p = 0.14$). Details are provided in Supplementary Figure S7, A–C.

Discussion

In this study, we demonstrated that it is possible to create an evening LE in a large, multiroom complex such as a hospital that had a meaningful effect on objective measures of circadian rhythms, sleep, and arousal, albeit little or no influence on subjective assessments of sleepiness or side effects. Specifically, we found that when healthy adults reside for 5 consecutive days in an evening blue-depleted LE, they exhibit substantially reduced suppression of melatonin production and phase-advancement of endogenous circadian rhythms compared with when residing for a similar period in standard LE conditions. Moreover, melatonin levels in the blue-depleted LE did not differ from those in a dim LE (<3 lux), suggesting that it is possible to design a well-tolerated LE that is similar to near-darkness; that is, "virtual darkness" [27], with regard to its effect on melatonin production. Furthermore, residence in the blue-depleted LE also increased TST and time in REM sleep. We suggest that not only may these effects be relevant for general housing and the healthy population, but the potential therapeutic effect of these adaptations may be even more pronounced in hospital settings.

In particular, sleep disturbances are virtually ubiquitous in critically ill inpatients admitted to hospital units [39–42]. In inpatient psychiatry, sleep disturbances receive particular attention as they constitute trans-diagnostic symptoms of most major mental disorders [22, 43, 44]. These have primarily been treated with medication; however, although chronotherapeutic treatments of these symptoms have been tested [27], their use to date has been limited owing to low feasibility in the clinic as they require acutely ill individuals to adhere to strict treatment regimens. In addition, whereas several hospital units and nursing homes have been built with variations of circadian lighting [8], most have focused on altering indoor daylight properties rather than exerting rigorous control over evening ambient and electric light. To the best of our knowledge, this is the first demonstration that creating such an evening blue-depleted LE is possible in a multiroom complex and the first evaluation of the effects of residing in such an environment using a randomized cross-over trial including objective markers of circadian rhythms, sleep, and arousal. Furthermore, the minimal individual input required by participants together with the failure to detect serious side effects suggests that this design could be applicable in numerous inpatient settings, allowing for effective dissemination of a non-pharmacological intervention targeting circadian rhythms and sleep in hospitals, and in psychiatry in particular. Thus, these findings with healthy adults in a hospital environment constitute an important step toward the implementation of chronotherapeutic interventions in the hospital setting.

In the current study, the two units had identical but mirrored layouts and similar levels of photopic lux and irradiance, whereas levels of melanopic, cyanopic, and rhodopic lux were lower in the blue-depleted LE [28]. A challenge in hospital settings is to create an LE that has meaningful physiological effects without major side effects but is also sufficiently bright to allow hospital staff to perform necessary tasks. Based on previously published work regarding the dose–response relationship between melanopic illuminance and melatonin suppression, we decided to maintain melanopic lux below approximately 20 in the blue-depleted LE [10, 17, 45, 46]. Consistent with this, our findings regarding melatonin suppression are in line with previous work, although one recent study found that suppression can occur at lower levels of melanopic lux under optimal laboratory conditions [47]. Recent research has also shown that large differences exist between individuals with regard to the response of the circadian system to light [48]. Individual differences were also observed in our data on individual participants; however, 11 out of 12 participants exhibited larger circadian effects in the blue-depleted than in the normal LE (see Supplementary Figures S1 and S2). It

has also been shown that certain patient groups, such as those with bipolar disorders [27], seasonal affective disorder [49], and circadian rhythm disorders [50, 51] display greater circadian responses to light than nonpatient groups. Additionally, some of the most widely used medications in psychiatric disorders, selective serotonin reuptake inhibitors, appear to increase the sensitivity of the circadian system to light [52, 53], and some evidence exists of decreased retinal sensitivity in individuals with depressive disorder [54]. Thus, it is likely that a blue-depleted LE may exert differential effects on melatonin suppression in particular patient groups or those taking certain medications compared with healthy control populations, highlighting the need to evaluate how different patient groups will respond to changes in the LE in clinical trials [55].

Notably, a longer TST was observed following residence in the blue-depleted LE. In particular, the 8 min difference was similar to that reported in a meta-analysis of PSG data from treatment trials of cognitive-behavioral therapy for insomnia, which is considered the gold standard of insomnia treatment [56]. This suggests the potential of more pronounced effects in psychiatric inpatient populations, among whom levels of disrupted sleep are higher [43, 44, 57], in turn implying that the blue-depleted LE may be sufficient to meaningfully improve sleep for inpatients. Furthermore, we also observed increased duration of REM sleep. REM sleep propensity has been shown to be influenced by circadian rhythms [58] and reductions in REM sleep have been observed in the first sleep cycle following blue-light exposure concomitant with phase-delay of circadian rhythms [6, 59]. These findings are complimented by REM sleep increases in the first sleep cycle following administration of melatonin [60]. REM sleep has also been implicated in emotional brain processing [61], which may be relevant in mental illness. However, findings from clinical samples are ambiguous and REM dysregulation has been observed in affective disorders [62, 63]. Thus, the effect of a blue-depleted LE on REM sleep may have clinical implications that need to be addressed in future trials.

Nevertheless, although we observed an effect on objective markers of circadian rhythms and sleep, no differences were detected in subjective sleepiness between conditions in the evening or morning. This is similar to prior reports indicating a lack of differences in subjective sleepiness following exposure to blue-depleted light in the evening [13]. This finding may be important for hospital staff working evening or night shifts in a blue-depleted LE. However, we did observe that participants in the blue-depleted LE exhibited higher variability in response-times during the continuous performance of a neurocognitive test, indicating that levels of neurocognitive arousal were lower in the blue-depleted LE. Interestingly, this discrepancy between subjective sleepiness and objective arousal was also observed in the above-cited study of blue-depleted lighting [13]. The decreased arousal may be explained in part by a lower circadian drive for alertness resulting from circadian phase-advancement in the blue-depleted LE [64] but also from a reduction in the direct alerting effects of short-wavelength light [65, 66]. Notably, decreased pre-sleep arousal may be beneficial for agitated inpatients in a psychiatric unit and may also facilitate sleep onset.

Participants reported very low numbers of side effects in both LEs in the current study. No overall difference was detected in side effect scores between the LEs, suggesting that the blue-depleted LE did not have an obvious adverse impact on participants. The most frequently reported side effect in the blue-depleted LE compared with the standard LE was increased fatigue/tiredness. Participants were also less adept at discrimination of color hues in the blue-depleted LE, scoring in the low-ability range compared with the normal-ability range in the standard LE. This finding may be of practical consequence when designing hospital units with changes in LE; for example, not using amber colors for signs or markers in medical charts.

As exploratory analyses, we also tested potential order effects in the trial. First, we did not find significant suppression of melatonin in the blue-depleted LE irrespective of the order of exposure. Second, we found an effect of the order on the difference in DLMO phase-shifts between conditions, with the largest effect of the blue-depleted LE when it was received as the second condition. However, there may be an additional effect of going from a home environment to a highly regularized inpatient environment with fixed bedtimes, rise times, and mealtimes, which may also have impacted the results. Participants were going to bed about 35 min earlier, rising on average 1.5 h earlier, and had higher sleep regularity in condition 1 compared with that during the pre-randomization monitoring. They therefore regularly woke and were exposed to light earlier in the morning. Advancing bedtime, rise time, and exposure to daylight in the morning have a strong phase-advancing effect [67]; thus, any additional effect of the evening blue-depleted LE may be masked by these factors. In contrast, rise times and sleep regularity did not differ between condition 1 and condition 2. In support of this, we also found that the change in bedtimes from the pre-randomization period to condition 1 correlated with the change in DLMO, but this was not the case between condition 1 and condition 2. This may indicate that when adjusted to the sleep–wake schedule, the effect of the evening blue-depleted compared with standard LE is more prominent.

Chronotherapeutic interventions that remove all light in the evening or block blue light with orange-tinted glasses [27] have demonstrated efficacy in reducing symptoms of mania in acutely admitted inpatients. These effects may be mediated by circadian or sleep pathways or may be the result of direct pathways influencing mood-centers in the brain, which have recently been identified in rodents [68]. Conversely, a recent exploratory study found no effects of blue-depleted light emitting diode (LED)-lighting on psychiatric symptoms in an inpatient psychiatric unit for affective disorders [69]. However, in this study incident or ambient light sources, such as TVs, mobile phones, or windows, were not controlled; moreover, the experimental light system was only installed in patient rooms, not corridors and common areas, and participants were thus free to enter and exit the experimental condition. This is problematic as the circadian system has recently been shown to be sensitive to very low levels of melanopic lux [47] or brief light exposures at night [17], and because increased sensitivity has been reported in several relevant patient groups [27, 49]. In contrast, the hospital unit in the current study is designed to allow a high level of control over both incident and ambient light. However, some extra effort may be needed from hospital staff to ensure adequate control over light in a psychiatric hospital unit, such as making blue-blocking filters available for mobile devices. In addition, these findings may be relevant across a variety of hospital units and might also possibly extend to other settings where control over ambient and incident light may be feasible such as trains, planes, and hotels.

Several limitations should be considered when interpreting the results from this study. First, an apparent effect was detected from residing in the hospital unit for the first week regardless of LE, suggesting that some degree of stabilization of sleep–wake rhythms could be achieved via a more regular routine. However, we did not design this study to investigate effects by condition order and these analyses, therefore, had limited statistical power. Second, researchers were given permission to access the hospital unit for only a limited time period (before it opened to acute admissions); thus, the study design had to consider such practicalities. Ultimately, as only a one-day washout phase was possible between the LEs, carryover effects cannot be excluded. However, this intermission is similar to that in other studies of the effects of light on evening melatonin and sleep [6, 13]. Third, participants resided in the unit from 05:00 pm until 08:00 am. During the day, they had to leave the unit owing to construction work. Participants in the current study thus may have been exposed to higher levels of light during daytime than the average patient housed in the hospital unit. Given that prior light history may exert protective effects against light exposure at night [70], the effects of a blue-depleted LE may be larger for an inpatient remaining indoors for most of the day. Fourth, 20 out of 48 PSG recordings were stopped at the designated wakeup time at 07:00 am. Therefore, when analyzing the data, the 07:00 am endpoint was applied to all recordings to minimize the influence of these events. Fifth, owing to the color of the light it was impossible to blind participants with regard to the specific LE in which they were residing. However, we did not observe a difference in subjective sleepiness scores, suggesting that expectancy effects were limited. Sixth, as we focused on a group of healthy young adults and the degree of some effects may differ in older adults with psychiatric disorders, some of our findings may not generalize across these populations. Seventh, we did not perform continuous measurements of light exposure at the eye level of the participants. Thus, we cannot control for the light exposure each participant was subjected to. Nevertheless, the current proof-of-concept study offered important insights regarding the effect of the modified hospital lighting system and provided a unique opportunity to apply physiological measurements such as melatonin assays and PSG, which are not always feasible for use with inpatients with severe mental disorders.

In conclusion, we have shown that the evening LE in a naturalistic setting can be modified according to chronobiological principles to have beneficial effects on the circadian system and sleep, without side effects. This offers translational relevance as it could readily be provided as a potential therapeutic intervention to large numbers of hospitalized patients with little increase in staff or patient burden.

Supplementary material

Supplementary material is available at *SLEEP* online.

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Author contributions

H.K. and K.L. conceived the study idea. D.V., K.L., and H.K. designed the study, with support from T.S., M.E., and A.O. D.V. and H.S.H. performed the data collection. D.V., H.K., and Ø.S. planned and performed the statistical analyses, with support from A.O. M.E. scored the PSG recordings. D.V., J.S., and H.K. wrote the initial draft with critical revisions from K.L., C.L.V., K.K., P.M.F., H.S.H., Ø.S., A.O., G.M., T.S., and M.E.

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Paper 4

Sleep and Work Functioning in Nurses Undertaking Inpatient Shifts in a Blue-Depleted Light Environment

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Abstract

Background: Blue-depleted light environments (BDLEs) may result in beneficial health outcomes for hospital inpatients. However, less is known about the effects on hospital staff. This study aimed to explore the effects of a BDLE compared with a standard hospital light environment (STLE) in a naturalistic setting on nurses' functioning during shifts and sleep patterns between shifts. **Methods:** Twenty-five nurses recruited from St. Olavs Hospital in Trondheim, Norway, completed 14 days of actigraphy recordings and self-reported assessments of sleep (e.g., total sleep time/sleep efficiency) and functioning while at work (e.g., mood, stress levels/caffeine use) in two different light conditions. Additionally, participants were asked to complete several validated scales and questionnaires to assess the symptoms of medical conditions and mental health conditions and the side effects associated with light conditions. **Results:** A multilevel fixed-effects regression model showed a within-subject increase in subjective sleepiness (by 17%) during evening shifts in the BDLE compared with the STLE ($p = .034$; Cohen's $d = 0.49$) and an 0.2 increase in number of caffeinated beverages during night shifts in the STLE compared with the BDLE ($p = .027$; Cohen's $d = 0.37$). There were no significant differences on either subjective or objective sleep measures nor on self-reported levels of stress or mood across the two conditions. Exploratory between-group analyses of questionnaire data showed that there were no significant differences except that nurses working in the BDLE reported perceiving the lighting as warmer ($p = .009$) and more relaxing ($p = .023$) than nurses working in the STLE. **Conclusions:** Overall, there was little evidence that the change in light conditions had any negative impact on nurses' sleep and function, despite some indication of increased evening sleepiness in the BDLE. We recommend further investigations on this topic before BDLEs are implemented as standard solutions in healthcare institutions and propose specific suggestions

for designing future large-scale trials and cohort studies. **Trial registration:** The study was registered before data collection was completed on the ISRCTN website (ISRCTN21603406).

Keywords: Blue-depleted Light Environment; Hospital Lighting; Shift Work; Sleep; Work Function

Background

Exposure to light and darkness over the course of a day is the major cue for entrainment of sleep and wakefulness in humans (1). However, in modern societies, humans are frequently exposed to artificial light sources during the dark period (evenings and nights) of the day. Artificial or polychromatic white light has been found to aid vision and enhance alertness and performance at night (2,3). It is also well established that exposure to artificial light can compromise the rhythmicity and timing of individual sleep and wakefulness patterns and thus cause, e.g., sleep problems, medical problems, and mental health problems (4). This is especially important for shift workers, who are regularly required to be awake and active during the dark period of the day and to subsequently sleep or rest during the light part of the day. Such rest–activity patterns are associated with an increased risk of, e.g., insomnia or shift work disorder (5–7), cardiovascular disease (8,9), cancer (10–13), gastrointestinal disorders (14), metabolic disturbances (15), diabetes (16–18), and impaired reproductive health (19–21) as well having adverse effects on mental health (4,22,23) and work–life balance (24).

Shift work is particularly common in the healthcare sector, where 24-hour services are necessary to provide required health services (25). Given the critical need to provide medical care around the clock, it is not surprising that hospital inpatients experience disruptions in their sleep–wake cycles and, thus, typically sleep poorly, e.g., due to elevated levels of light and noise (26,27). In recent years, several clinical and research groups have advocated the installation of blue-depleted light environments (BDLEs; indoor lighting blocking short-frequency, blue light < 530 nm) to counteract the effects of artificial light exposure at night and help stabilize the sleep–wake patterns of hospital inpatients, with positive effects being reported following such interventions (28,29). Likewise, a study on healthy adults residing in a BDLE found positive effects on sleep without any adverse effects or side effects (30).

Recently, a new acute psychiatric unit was built at St. Olavs Hospital, Østmarka, in Trondheim, Norway (latitude ~63°N) in which new lighting systems were installed. The unit consists of two inpatient wards: one allows for the introduction of a BDLE during evenings and nights, whereas the other has a standard hospital lighting environment (STLE). This setup was primarily established to investigate the effects of evening and night BDLE on sleep and recovery time for patients admitted to the hospital (31). However, in this regard, investigating whether exposure to a BDLE represents any benefits or harm to the nurses engaged in shift work under such conditions is also highly warranted. To the best of our knowledge, no previous studies have explored whether working in a BDLE compared with a STLE impacts the work performance and/or well-being of nurses in a naturalistic setting. The main aim of the present study was, therefore, to use subjective (work and sleep diaries) and objective (actigraphy) recordings to investigate nurses' sleep patterns, work functioning, levels of stress, and mood state over a 2-week period during which they undertook shifts in either a BDLE or a STLE. Additionally, we explored nurses' self-reported physical and mental health when working in each light condition.

Methods

Study Design and Participants

The present study was originally designed as a non-randomized 12-week cross-over trial (ISRCTN21603406). The aim was to investigate the effects of evening and night BDLE compared with those of STLE in a sample of nursing staff (nurses and nurse assistants – referred to as nurses hereafter) working shifts in an acute psychiatric unit at St. Olavs Hospital. The unit was built as two separate wards with mirror-image layouts each consisting of 20 patient rooms and common areas. In one of the wards, both light fixtures and incident

light were depleted of blue light frequencies (<530 nm) from 18:30 to 07:00, whereas the other ward had standard hospital lighting. Light measurements demonstrated that the lighting in the two wards had similar levels of photopic lux but that the levels of melanopic lux were lower in the BDLE than in the STLE. Details of the layout, light system, and light measurement methods are thoroughly described elsewhere (30). The nurses could not manually change the lighting in any of the light conditions, and both units had similar light environments during daytime.

Nurses employed at the acute psychiatric unit at St. Olavs Hospital when the study started in November 2018 were invited to participate if they currently worked at least 50% of fulltime equivalent. Based on this criterion, 25 of 106 employees were excluded from participation because they were on leave (e.g., maternity or sick leave). As such, the sample comprised a convenience sample of nurses (n = 86) studied in their natural work setting. Study participation was voluntary. When data collection began, one-half of the nursing staff initially worked in the unit with BDLE and the other half in the unit with STLE. The order of the conditions was not randomized due to a preset work schedule. Some nurses were permanently assigned to work night shifts, whereas others rotated between day and evening shifts or only worked on weekends.

Of the 86 nurses who met the inclusion criteria, 25 (29.1%) agreed to participate and signed an informed consent form before participating in the study and provided data for the first 6 weeks of data collection (working either in the BDLE or STLE). After 3 weeks of working in each light condition, participants were asked to complete questionnaires and to keep a work and sleep diary for 2 weeks. After the cross-over (week 6 to 12 of the study), 10 (11.7%) participants provided data for the other light condition (either BDLE or STLE). Actigraphy data were collected from 23 of 25 participants during the first 6 weeks of data collection and from 8 of 10 participants in the last 6 weeks of data collection.

The study was designed and implemented by external researchers (i.e., not employed at the acute psychiatric unit at St. Olavs Hospital) in response to concerns raised by nurses and safety representatives about the possible negative side effects of working in a BDLE. The topic was generally discussed with employees in the acute psychiatric unit through informational meetings and one-on-one meetings (e.g., between a nurse and a safety representative or a nurse and management) throughout the planning period, and both nurses and safety representatives were closely involved in the development of the present study. Anonymity was strictly implemented to protect the privacy of those who chose to participate. Given these precautions, it is not clear why the participation rate was not higher. Due to the comparatively small sample size, we were limited in the analyses we were able to conduct, and we were not able to carry out the investigation based on a cross-over design.

Ethics

The study protocol was approved by the Regional Ethical Committee of Central Norway (REK reference number: 2018/1516). The study was registered on 28/12/2018 through the ISRCTN website (ISRCTN21603406).

Assessments

- Demographic and background variables – Information was collected regarding sex, age, height and weight, cohabitation status, whether the nurses had children living at home, number of years worked as nursing staff, and percentage of fulltime equivalent.
- Work diary – The work diary comprised 10 questions to gather data on the day-to-day shift schedule of the participants for 14 consecutive days: the date of the shift and work hours. They were also asked to report the number of caffeinated beverages consumed during each shift (e.g., coffee, tea, energy drinks), levels of sleepiness (from

not at all sleepy (1) to very sleepy (5)), stress (from not at all stressed (1) to very stressed (5)), and mood, i.e., positive feelings (from not at all positive (1) to very positive (5)) and negative feelings (from not at all negative (1) to very negative (5)).

- Sleep diary – Sleep was assessed by a sleep diary (32) to provide subjective, daily estimates of sleep episodes for 14 consecutive days (in parallel with the work diary). The following measures were derived from the diary: Time in Bed (TIB), Sleep Period Time (SPT; duration of the sleep period); Total Sleep Time (TST), Sleep Onset Latency (SOL), Wake After Sleep Onset (WASO), Early Morning Awakening (EMA; time spent in bed after final rise time), Sleep Efficiency (SE; total sleep time as a percentage of time in bed), number of awakenings, and an overall rating of the sleep quality (from very restless (1) to very sound (5)).
- Actigraphy – Motor activity was assessed using actigraphy data collected with GENEActive® actiwatches for 14 consecutive days to derive the following estimates: Wake After Sleep Onset (WASO), Total Sleep Time (TST), Sleep Period Time (SPT; time between falling asleep and the final awakening), and number of sleep periods (SIBS). The actiwatch data were processed and scored using the GGIR package (version 2.2-1) (33–35) for R (version 3.6.2). The GGIR sleep-detection algorithm was used to identify sleep onset and rise times and to score sleep and wakefulness between these timepoints. Due to a high proportion of daytime sleep in the shift-working participants and frequent, multiple sleep periods within 24 hours, the scored actigraphy output was manually compared with participants' sleep diaries to correct obvious error estimates by the software. Where obvious discrepancies between sleep diaries and actigraphy appeared, the sleep diary data were consulted.
- Questionnaire data – Participants were asked to complete several validated scales and questionnaires to assess symptoms on medical conditions, mental health conditions,

and side effects associated with the light conditions. Specifically, the Kessler Psychological Distress Scale (K10; used to identify adults with varying levels of psychological distress) (36), a short version of the Psychological Health Questionnaire (PHQ; to assess sleep disturbances, headaches, respiratory infections, and gastrointestinal problems) (37), the Headache and Eyestrain Scale (H&ES; to assess eye strain and headache) (38), an evaluation of beliefs about the light condition (BAL; rating pleasantness and color of the lighting) (39), one additional item probing the experienced adequacy of the lighting in a work setting ('unsuitable for work/suitable for work'), one item assessing work strain and three items assessing performance and effort from the Psychological Variables Questionnaire (40), 12 items assessing negative side effects of the light conditions (31), and the Brief Horne–Östberg Morningness–Eveningness Questionnaire (MEQ; to assess chronotype) (41).

Statistical Analysis

Fixed-effects regression models were fitted to capture the within-subject effects using methods of maximum likelihood estimation in STATA version 17. Sleep and work diary data and actigraphy data were structured so that each participant was compared with themselves in terms of how they slept and functioned across the two different light conditions. Sleep periods that started within 15 hours after a shift ended were included in the analyses. As previously mentioned, the participants kept diaries and wore an actiwatch for approximately 14 days in each light condition and typically had ~5 shifts during this time. By structuring the data this way, each participant contributed multiple observations across the two light conditions (168 shifts in total), giving the study an acceptable statistical power. Results are shown separately for comparisons of evening BDLE with evening STLE, of night BDLE with night STLE, and of combined evening and night BDLE with combined evening and night STLE. Additionally,

mean values for each light condition, estimated mean difference, confidence intervals (CI; 95%), and effects sized in terms of Cohen's *d* are shown. Cohen's *d* was calculated in line with recognized guidelines (42,43). As a benchmark for interpreting Cohen's *d*, 0.80 is regarded as large, 0.50 as moderate, and 0.20 as small (44).

Due to the limited sample size of the present study, analyses performed on outcome variables from the questionnaires (i.e., outcomes without multiple observations) should be regarded as exploratory. One-way between-group ANOVAs were performed using IBM SPSS Statistics version 25 to examine differences in the medical and mental health of participants working in the BDLE compared with the STLE during the first round of data collection (data from the second round were excluded in this analysis due to the inadequate sample size).

Results

Sample characteristics

The nurses included in the study had a mean age of 39.9 years (SD = 12.3 years), were predominantly female (83.3%), and married/cohabitating (54.1%) and/or had children living at home (54.1%) in about half of cases. On average, they worked 89.2% (SD = 14.4%) of fulltime equivalent and had nearly ten years of work experience as nurses (mean = 9.4 years; SD = 7.7 years).

Differences between blue-depleted and standard hospital light environments

Table 1 shows the results from the fixed-effects linear models comparing the effect of BDLE with that of the STLE on the outcome variables. Analyses of the work diaries showed within-subject differences of increased subjective sleepiness (by 17%) during evening shifts in the BDLE compared with the STLE ($p = .034$; Cohen's $d = 0.49$) and a 0.2 increase in number of

caffeinated beverages consumed during nights in the STLE compared with the BDLE (p = .027; Cohen's *d* = 0.37). There were no differences in terms of stress levels or positive and negative feelings during shifts (p-values ranging from .246 to .943). Sleep diary data indicated no differences on any of the outcome variables (TIB, TST, SOL, WASO, EMA, SE, number of awakenings, or sleep quality; p-values ranging from .206 to .991). On actigraphy data, we found no differences on any of the outcome variables (TST, WASO, SPT or SIBS; p-values ranging from .129 to .949) between conditions.

[Table 1 about here.]

Exploratory analyses of questionnaire data

Given the limited sample size available, exploratory one-way between-group ANOVAs were performed on items extracted from the self-rated questionnaires (i.e., outcomes without multiple observations). Supplementary Table 1 shows the means and standard deviations for these variables for all participants and then categorized according to light condition. There were no significant differences between the groups except that nurses working in the BDLE reported perceiving the lighting as warmer (p = .009) and more relaxing (p = .023) than nurses in the STLE.

Discussion

The main aim of the present study was to investigate the effects of a BDLE compared with a STLE in an acute psychiatric unit at St. Olavs Hospital on shift working nurses' sleep, mood, levels of stress, and caffeine use. To the best of our knowledge, this is the first study to examine how nurses experience working in a BDLE compared with a STLE. Overall, the results showed that most aspects of the nurses' sleep and functioning were unchanged by

exposure to the two light conditions. However, the nurses reported higher levels of sleepiness during evening shifts in the BDLE than in the STLE. In addition, nurses reported consuming a slightly higher number of caffeinated beverages during night shifts in the STLE than in the BDLE.

The fact that subjective sleepiness was higher during evening shifts in the BDLE makes sense considering that lower levels of white light exposure during the evening (when it is becoming gradually darker outside) are associated with lower levels of melatonin suppression (45). Melatonin is a hormone that helps the body to know when it is time to sleep and wake up, and melatonin suppression is associated with shifting of the circadian phase so that sleepiness and sleep occur later in the day (46,47). An at least partial circadian adaptation to night shifts might be desirable, since it could potentially increase job performance and reduce the risk of accidents at work or during commute as well as improve daytime sleep during days off work, when nurses must re-adapt to a daytime schedule (48–50). We did not find support for differences in adaptation to shift work between the light conditions, but the lower levels of evening sleepiness in the STLE are likely a reflection of white light having a direct activating effect, e.g., by increasing alertness (3,38,39). As such, increased sleepiness in the BDLE may compromise nurses' safety, e.g., if they need to react instantly to adverse events. Further, it is comparably surprising that we did not find the same increase in sleepiness during night shifts in the BDLE. One explanation may be that the study does not have statistical power to detect, e.g., small within-subject effects of BDLE compared with STLE. Another possible explanation is the ceiling effect, whereby the level of sleepiness during the night shift was high in both light conditions and the measurement for sleepiness used in this study is not sufficiently suited to distinguish between nuances in the levels of sleepiness.

Our research group previously conducted a pilot study with 12 healthy adults using a randomized cross-over design comparing the effects of a BDLE with a STLE on, e.g., sleep, subjective sleepiness, and the experience of side effects (30). In that study, the effects of the BDLE were generally positive. Participants did not report higher levels of sleepiness or negative side effects, the participants' sleep–wake cycle was phase-advanced (i.e., higher levels of melatonin earlier at night), and they slept marginally longer (8.1 minutes) after residing in the BDLE. One explanation for the conflict with our finding of increased sleepiness during evening shifts in the BDLE could be the difference between assessments, i.e., hourly ratings of sleepiness from 19:00 to 23:00 versus retrospective global assessment of sleepiness during whole shifts. Alternatively, differences in the demands made on participants simply residing in the building compared with nurses performing work-related tasks could further impact the extent to which an individual experiences fatigue and sleepiness. Additionally, in the present study, we did not find significant differences on any sleep outcomes after working in the BDLE compared with the STLE, which might also be explained by the difference between assessments (i.e., polysomnography data versus diary and actigraphy data) or that artificial light exposure when commuting home from work and at home before bedtime is sufficient to reverse the subtle effects of a BDLE at work (51–53).

We also found a small (0.2) increase in the number of caffeinated beverages consumed when undertaking night shifts in the STLE compared with the BDLE. While interesting, the available data do not allow us to determine whether this is best explained by differences in energy levels or perceived alertness during night shifts in different light conditions or individual fluctuation in caffeine intake (related to spurious factors), etc. Interestingly, we found no differences between BDLE and STLE on nurses' reported levels of stress, positive or negative mood during shifts, or sleep patterns after each shift was completed. This was unexpected given that shift work is a known risk factor for, e.g., poor sleep (5), medical or

mental health problems (4), and impaired attention and alertness during waking hours (54). Some of the negative effects of shift work can generally be attributed to suboptimal shifting of the circadian phase (55). However, as light can be used to shift the circadian phase to better adapt to night work (56), we might expect BDLE, or 'virtual darkness' (57,58), to have a different effect on nurses' sleep and functioning in a naturalistic setting than STLE. In many respects, the limited number of macro-level differences between the light conditions is encouraging, as it indicates that a BDLE is not associated with major side effects or harmful effects. However, these findings need to be confirmed in further studies before BDLEs can be clearly established as beneficial to patients and not harmful to clinical staff working in inpatient units.

Limitations and future directions

There are some important limitations of the present study that should be considered. Due to the comparatively small sample size, we were limited in the types of analyses we were able to conduct. Further, we did not perform any correction for multiple comparisons (e.g., by adjusting for false discovery rate (59)) as this, given our limited sample size, would have increased the risk of false negatives. Failure to detect, e.g., side effects of the light conditions would be potentially harmful to the nurses. A larger sample size is important for, e.g., reliable, and meaningful multivariable analysis of the effects of a BDLE compared with a STLE on nurses' sleep, health, and functioning or effects of switching between light conditions. A larger sample size would also facilitate analysis of whether the BDLE directly affects the nurses' circadian rhythms and the impact of possible confounding factors (e.g., if patients exposed to BDLE were calmer and, as such, influenced the nurses). The within-subject design in a naturalistic setting is a strength of the present study, but due to the low participation rate (29.1%), we cannot ascertain whether our findings are representative of all

nurses working at the acute psychiatric unit at St. Olavs Hospital. Although other single-site studies in small workplaces (less than ~100 employees) will also necessarily be bound by an upper limit of available participants, having high participation rates would ensure that any drawn conclusions will be representative of all employees. Additionally, use of employer or registry data in future studies, as opposed to self-reporting, could ease time demands on the participants in addition to serving as a source of objective, high-quality information on how shift working nurses are affected by a BDLE. Such sources could be used to collect information on, e.g., sickness absence, other types of leave, healthcare resource use, and medical or mental health diagnoses. They will not, however, be suitable to investigate individual experiences of day-to-day life, and important information on, e.g., personal experiences in and of the work environment, levels of presenteeism (i.e., reduced productivity while at work), impairment in general activities outside of work, or subclinical symptoms of medical or mental health conditions.

Conclusions

Our study suggests that working in a BDLE does not considerably impact the nurses' sleep, levels of stress, or mood in a naturalistic setting. There was some indication that the light environments may affect the nurses' functioning during shifts. Limitations of the present study placed restrictions on the analyses that were able to be conducted and the conclusions that could be drawn. We are, however, optimistic that BDLEs in hospitals are acceptable to the nurses. We recommend further investigations on this topic before BDLEs are implemented as standard solutions in healthcare institutions, and we have proposed specific suggestions for designing future large-scale trials and cohort studies.

List of abbreviations

BAL – Evaluation of beliefs about the light condition

BDLE – Blue-depleted light environment

EMA – Early Morning Awakening

H&ES – Headache and Eyestrain Scale

K10 – Kessler Psychological Distress Scale

MEQ – Morningness–Eveningness Questionnaire

PHQ – Psychological Health Questionnaire

REK – Regional Ethical Committee of Central Norway

SE – Sleep Efficiency

SIBS – Number of sleep periods

SOL – Sleep Onset Latency

SPT – Sleep Period Time

STLE – Standard hospital light environment

TIB – Time in Bed

TST – Total Sleep Time

WASO – Wake After Sleep Onset

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Regional Ethical Committee of Central Norway (REK reference number: 2018/516). Written informed consent was obtained from all subjects involved in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available as we do not have ethical approval for this type of data sharing.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization, K.K, H.K., K.L. and Ø.V.; methodology, K.K., A.H., S.P. and Ø.V.; formal analysis, K.K. and Ø.V.; investigation, K.K. and P.F.; data curation, K.K., P.F. and D.V.; writing—original draft preparation, K.K.; writing—review and editing, P.F., B.S., K.L., D.V., C.V., A.H., S.P., J.S. and Ø.V.; project administration, K.L. and Ø.V.; funding acquisition, K.K. All authors have read and agreed to the published version of the manuscript.

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Table 1. Results from fixed effects linear models comparing the effects of BDLE with STLE.

	Mean STLE	Mean BDLE	Estimated mean Difference	95% CI	P Value	Cohen's *d*
Work Diary						
Number of Caffeinated drinks						
E vs E	2.15	1.19	0.21	-0.42 to 0.84	0.508	0.636
N vs N	2.11	1.73	-0.37	-0.70 to -0.04	**0.027***	0.367
E.N. vs E.N.	2.14	1.49	-0.09	-0.42 to 0.24	0.582	0.490
How stressful was your shift? *(range 1-5)* [a]						
E vs E	2.56	2.31	-0.32	-0.92 to 0.27	0.277	0.225
N vs N	2.95	2.70	-0.30	-0.88 to 0.28	0.312	0.248
E.N. vs E.N.	2.74	2.53	-0.24	-0.65 to 0.17	0.246	0.202
How sleepy were you during the shift? *(range 1-5)* [a]						
E vs E	2.46	3.03	0.74	0.06 to 1.42	**0.034***	0.486
N vs N	2.86	3.07	0.22	-0.34 to 0.77	0.440	0.204
E.N. vs E.N.	2.65	3.06	0.42	0.002 to 0.05	0.048	0.372
How positive did you feel during the shift? *(range 1-5)* [a]						
E vs E	3.81	3.84	0.10	-0.33 to 0.53	0.654	-0.037
N vs N	3.25	3.53	-0.13	-0.49 to 0.23	0.486	-0.382
E.N. vs E.N.	3.55	3.67	-0.34	-0.30 to 0.24	0.804	-0.150
How negative did you feel during the shift? *(range 1-5)* [a]						
E vs E	1.62	1.63	0.10	-0.45 to 0.65	0.723	-0.011
N vs N	1.70	1.57	-0.09	-0.46 to 0.28	0.619	0.194
E.N. vs E.N.	1.66	1.60	-0.01	-0.32 to 0.30	0.943	0.076
Sleep Diary						
Time in Bed, min						
E vs E	507.00	481.00	31.47	-198.37 to 261.30	0.785	0.088
N vs N	488.00	529.00	98.99	-177.39 to 375.37	0.476	-0.104
E.N. vs E.N.	499.00	508.00	73.34	-102.50 to 249.17	0.410	-0.025
Sleep Period Time, min						
E vs E	410.00	405.00	-18.19	-70.74 to 34.37	0.491	0.074
N vs N	361.00	399.00	65.30	-45.14 to 175.73	0.241	-0.238
E.N. vs E.N.	390.00	401.00	34.18	-28.13 to 96.48	0.279	-0.093
Total Sleep Time, min						
E vs E	356.00	371.00	-7.57	-61.88 to 46.74	0.781	-0.203
N vs N	328.00	376.00	6.11	-41.30 to 173.52	0.223	-0.314
E.N. vs E.N.	344.00	374.00	39.25	-21.84 to 100.33	0.206	-0.239
Sleep Onset Latency, min						
E vs E	23.31	24.54	-3.09	-20.29 to 14.11	0.720	-0.046
N vs N	14.68	8.85	-2.25	-13.15 to 8.65	0.680	0.334
E.N. vs E.N.	19.64	15.94	-2.82	-12.32 to 6.67	0.557	0.162
Wake After Sleep Onset, min						
E vs E	34.07	9.11	-10.80	-34.95 to 13.36	0.374	0.804
N vs N	18.65	13.62	1.43	-14.32 to 17.19	0.856	0.194
E.N. vs E.N.	27.43	11.58	-3.58	-17.08 to 9.92	0.600	0.537

Early Morning Awakening, min						
E vs E	15.74	11.04	-5.02	-16.61 to 6.57	0.389	0.287
N vs N	67.68	114.00	54.63	-129.70 to 238.96	0.555	-0.172
E.N. vs E.N.	37.50	67.68	28.12	67.21 to 123.45	0.560	-0.156
Sleep Efficiency, %						
E vs E	77.84	83.83	0.66	11.48 to 12.80	0.913	-0.378
N vs N	78.31	79.79	0.09	-11.44 to 11.63	0.987	-0.083
E.N. vs E.N.	78.03	81.61	0.67	-7.39 to 8.73	0.870	-0.214
Nightly Awakenings, No.						
E vs E	1.60	1.39	-0.41	-1.26 to 0.44	0.336	0.152
N vs N	1.26	1.35	0.38	-0.37 to 1.12	0.313	-0.068
E.N. vs E.N.	1.45	1.37	0.05	-0.50 to 0.59	0.864	0.060
Sleep Quality [a]						
E vs E	3.05	3.48	0.23	-0.65 to 1.11	0.601	-0.397
N vs N	3.29	3.29	<0.00	-0.52 to 0.52	0.991	0.000
E.N. vs E.N.	3.15	3.38	0.10	-0.37 to 0.57	0.671	-0.243
Actigraphy						
Sleep Period Time, min						
E vs E	410.00	402.00	11.65	-48.65 to 71.95	0.698	0.123
N vs N	369.00	389.00	67.18	-53.89 to 188.26	0.269	-0.135
E.N. vs E.N.	393.00	395.00	53.19	-15.89 to 122.28	0.129	-0.020
Total Sleep Time, min						
E vs E	362.00	345.00	1.86	-56.37 to 60.09	0.949	0.283
N vs N	342.00	366.00	68.88	-42.37 to 180.13	0.218	-0.329
E.N. vs E.N.	353.00	356.00	50.30	-14.77 to 115.37	0.128	-0.221
Wake After Sleep Onset, min						
E vs E	52.00	57.24	7.72	-16.28 to 31.70	0.518	-0.131
N vs N	26.55	22.89	-1.79	-22.26 to 18.67	0.860	0.126
E.N. vs E.N.	40.57	39.40	2.15	-12.57 to 16.86	0.772	0.031
Sleep Periods, No.						
E vs E	14.10	13.79	-2.23	-5.13 to 0.68	0.130	0.070
N vs N	11.67	11.76	1.64	-2.86 to 6.14	0.464	-0.017
E.N. vs E.N.	13.10	12.84	0.13	-2.45 to 2.71	0.919	0.053

BDLE = blue-depleted light environment, STLE = standard hospital light environment; E = evening shifts; N = night shifts; E.N. = evening/night shifts combined. Number of observations = 168; n = 25. [a] Rated on a 5-point scale from not at all stressed/sleepy/positive/negative/restless (1) to very stressed/sleepy/positive/negative/restless (5).

Supplementary Table 1. Results from one-way between groups ANOVAs of questionnaire data.

	Blue-depleted (n = 9)	**Standard (n = 15)**	**P value**	**Overall**
Kessler Psychological Distress Scale, total	18.00 (3.46)	16.20 (2.75)	.173	16.88 (3.10)
Tired *(range 1-5)* [a]	2.33 (.87)	2.07 (.88)	.479	2.17 (.87)
Nervous	1.56 (1.13)	1.60 (.51)	.895	1.58 (.78)
Nervous & unable to calm down	1.00 (.00)	1.00 (.00)	.	1.00 (.00)
Hopeless	1.33 (.50)	1.33 (.49)	1.00	1.34 (.48)
Restless	1.78 (.83)	1.60 (.74)	.591	1.67 (.76)
Restless & unable to sit still	1.44 (.73)	1.20 (.41)	.302	1.29 (.55)
Depressed	1.67 (.71)	1.27 (.46)	.105	1.42 (.58)
Fatigued	1.89 (.93)	1.67 (.62)	.487	1.75 (.74)
Sadness	1.11 (.33)	1.00 (.00)	.203	1.04 (.20)
Worthless	1.56 (.73)	1.13 (.35)	.067	1.29 (.55)
Psychological Health Questionnaire				
Trouble sleeping *(range 1-7)* [b]	3.33 (.2.18)	2.93 (1.22)	.568	3.08 (1.61)
Awake at night	4.33 (1.87)	4.07 (1.49)	.703	4.17 (1.61)
Nightmares or bad dreams	1.89 (.93)	1.87 (1.55)	.969	1.87 (1.33)
Restful sleep[bb]	4.00 (.50)	3.80 (.49)	.777	3.87 (1.62)
Headache	2.44 (1.42)	2.00 (.93)	362	2.17 (1.13)
Headache due to stress	2.33 (1.41)	2.33 (1.54)	1.00	2.33 (1.47)
Headache due to frustration	1.89 (1.45)	1.53 (.74)	.434	1.67 (1.05)
Upset stomach	2.22 (1.99)	1.93 (1.34)	.673	2.04 (1.57)
Careful with food to avoid upset stomach	2.44 (2.40)	1.87 (1.60)	.485	2.08 (1.91)
Nausea	1.67 (1.66)	1.40 (1.30)	.665	1.50 (1.41)
Constipation/diarrhea	2.00 (2.12)	2.00 (1.41)	1.00	2.00 (1.67)
Mild cold, times	2.33 (2.18)	1.27 (.46)	.077	1.67 (1.44)
Severe cold, times	1.00 (.00)	1.07 (.26)	.451	1.04 (.20)
Duration of cold	3.67 (3.01)	2.00 (1.27)	.125	2.59 (2.12)
Headache and Eyestrain Scale, total	15.56 (4.78)	14.40 (3.56)	.505	14.83 (4.00)
Irritability *(range 1-4)* [c]	2.11 (.79)	1.87 (.83)	.484	1.96 (.81)
Headache	1.89 (.93)	1.73 (.88)	.686	1.79 (.88)
Eye strain	2.22 (.97)	2.13 (.99)	.832	2.17 (.96)
Eye discomfort	2.11 (1.05)	1.73 (.80)	.330	1.87 (.90)
Eye fatigue	2.22 (.97)	2.00 (.85)	.561	2.08 (.88)
Difficulty focusing	1.89 (.93)	1.80 (.68)	.789	1.83 (.76)
Difficulty concentrating	1.89 (.78)	1.80 (.68)	.771	1.83 (.70)
Blurred vision	1.22 (.44)	1.33 (.49)	.582	1.29 (.46)
Evaluation about beliefs about the light condition				
Unpleasant - pleasant *(range 1-7)* [d]	4.56 (1.42)	4.33 (1.54)	.729	4.42 (1.47)
Uncomfortable - comfortable	4.00 (2.37)	4.40 (1.55)	.609	4.25 (1.80)
Disturbing - not disturbing	4.33 (2.50)	5.07 (1.87)	.421	4.79 (2.11)
Causing glare - not causing glare	4.89 (2.09)	4.80 (1.90)	.916	4.83 (1.92)
Uniform - non-uniform	4.56 (1.94)	5.67 (1.45)	.123	5.25 (1.70)
Warm - cold	2.89 (1.76)	4.87 (1.55)	**.009***	4.12 (1.87)
Dim - bright	3.33 (2.35)	4.67 (1.84)	.135	4.17 (2.10)
Relaxing - stimulating	2.56 (2.01)	4.47 (1.77)	**.023***	3.75 (2.05)
Unsuitable for work - suitable for work *(range 1-7)* [d]	3.78 (1.86)	4.93 (1.44)	.101	4.50 (1.67)
Work strain *(range 1-5)* [e]	2.22 (.97)	2.57 (.94)	.400	2.43 (.945)

Performance and Effort				
Concentration *(range 1-7)* [f]	5.22 (.83)	5.64 (.50)	.143	5.48 (.67)
Performance	5.11 (1.05)	5.50 (.52)	.249	5.35 (.78)
Effort	4.78 (.83)	4.43 (1.09)	.423	3.43 (.99)
Other side effects				
Dry eyes, mouth, or nose *(range 1-4)* [c]	2.11 (1.05)	1.93 (1.10)	.701	2.00 (1.06)
Sleepiness during the day	2.78 (1.09)	2.33 (.72)	.242	2.50 (.88)
Poor sleep quality	2.44 (1.33)	2.20 (.78)	.573	2.29 (.99)
Too much sleep	1.00 (.00)	1.27 (.46)	.097	1.17 (.38)
Tired during the day	3.11 (.93)	2.33 (.98)	.067	2.63 (1.01)
Restlessness	1.67 (.71)	1.47 (.74)	.523	1.54 (.72)
Dizziness	1.44 (1.01)	1.13 (.35)	.285	1.25 (.67)
Excessive sweat	1.22 (.44)	1.47 (.64)	.325	1.38 (.57)
Diarrhea	1.33 (1.00)	1.13 (.35)	.483	1.21 (.65)
Changed/poor appetite	1.11 (.33)	1.20 (.78)	.749	1.17 (.64)
Constipation	1.22 (.44)	1.40 (.91)	.591	1.33 (.76)
Nausea/upset stomach	1.44 (1.01)	1.20 (.56)	.452	1.29 (.75)
Morningness-Eveningness Questionnaire [g]	14.75 (2.38)	14.53 (6.10)	.925	14.61 (5.05)

Means, standard deviations are shown for the blue-depleted and standard hospital light environment separately, and for participants overall from the first round of data collection. [a] Rated on a 5-point scale from 'not at all' (1) to 'most of the time' (5); [b] Rated on a 7-point scale from 'not at all' (1) to 'all the time' (7); [bb] Scoring on this item has been reversed; [c] Rated on a 4-point scale from 'absent' (1) to 'severe' (4); [d] Rated on a 7-point scale with each word pair as anchoring; [e] Rated on a 5-point scale from 'not at all heavy' (1) to 'very heavy' (5); [f] Rated on a 7-point scale so that higher score reflect degree of each item; [g] Scores on average reflect neither morning or evening types, with higher degree of chronotype variance in the standard hospital light environment.