Management of Shift Work Disorder

An American Academy of Sleep Medicine Clinical Practice Guideline

[Chair][1]; [TF Member][2]; [TF Member][3]; [TF Member][4]; [TF Member][5]; [AASM Staff][#]

[1][Chair Institution]; [2][TF Member Institution]; [3][TF Member Institution]; [4][TF Member Institution]; [5][TF Member Institution]; [#]American Academy of Sleep Medicine, Darien, IL

Introduction: This guideline establishes recommendations for the treatment of shift work disorder (SWD).
Methods: The American Academy of Sleep Medicine (AASM) commissioned a task force of experts in sleep and circadian medicine to develop recommendations and assign strengths based on a systematic review of the literature and an assessment of the evidence using the GRADE process. The task force summarized the relevant literature and the quality of evidence, the balance of benefits and harms, patient values and preferences, and resource use considerations supporting the recommendations. The AASM Board of Directors approved the final recommendations.

Recommendations: The following recommendations are intended as a guide for clinicians in choosing specific treatment(s) for symptoms of excessive sleepiness and/or insomnia, and for circadian adaptation in adults with SWD. Each recommendation statement is assigned a strength (e.g., "Strong" or "Conditional"). For SWD, there were only "conditional" recommendations for or against (i.e., "We suggest…") and those requiring the clinician to use clinical knowledge and experience and consider the individual patient's values and preferences to determine the best course of action. Interventions in recommendation statements were compared to no treatment.

Adults with SWD with symptoms of excessive sleepiness:

1. In adults with SWD with excessive sleepiness, the AASM suggests the use of armodafinil or modafinil over no armodafinil or modafinil (Conditional recommendation, moderate certainty evidence).
2. In adults with SWD with excessive sleepiness, the AASM suggests the use of bright light over no bright light during the night shift (Conditional recommendation, very low certainty evidence).
   Remark: Individuals with SWD who exhibit insomnia and daytime function impairments may also benefit from using bright light during their night shift.
3. In adults with SWD with excessive sleepiness, the AASM suggests the use of caffeine over no caffeine (Conditional recommendation, very low certainty evidence).
   Remark: Caffeine intake close to bedtime can disrupt sleep onset and quality, which may exacerbate symptoms of shift work disorder.
4. In adults with SWD with excessive sleepiness, the AASM suggests the use of a clockwise rotating shift schedule over a counterclockwise rotating shift schedule (Conditional recommendation, very low certainty evidence).
5. In adults with SWD with excessive sleepiness, the AASM suggests taking a nap over no nap prior to the night shift (Conditional recommendation, very low certainty evidence).
   Remarks: Sleep inertia occurring soon after the nap may temporarily increase sleepiness, decrease cognitive performance, and increase accident risk. Allowing adequate time for resolution of sleep inertia prior to driving or performing other safety-sensitive behaviors may be needed to reduce these risks.
6. In adults with SWD with excessive sleepiness, the AASM suggests not eating or eating a snack rather than eating a full meal during the night shift (Conditional recommendation, low certainty evidence).
7. In adults with SWD with excessive sleepiness, the AASM suggests the combination of caffeine and bright light over the combination of no caffeine and no bright light (Conditional recommendation, very low certainty evidence).
   Remark: Caffeine intake close to bedtime can disrupt sleep onset and quality, which may exacerbate symptoms of shift work disorder.

8. In adults with SWD with excessive sleepiness, the AASM suggests the combination of taking a nap and caffeine over the combination of no nap and no caffeine prior to the night shift (Conditional recommendation, very low certainty evidence).
9. In adults with SWD who are working either an 8-hour or 12-hour shift, the AASM **does not** suggest working one shift duration over the other (Conditional recommendation, very low certainty evidence).
   Remark: This recommendation does not consider other shift durations, rotation, or the number of consecutive shifts. This guideline did not look at shifts over 12 hours. The total number of hours worked per week ranged from 36 to 52.

Adults with SWD with sleep disturbance/insomnia:

10. In adults with SWD with daytime sleep disturbance/insomnia the AASM suggests the use of CBT-I over no CBT-I (Conditional recommendation, very low certainty evidence).
11. In adults with SWD with daytime sleep disturbance/insomnia following the night shift, the AASM suggests the use of melatonin over no melatonin (Conditional recommendation, very low certainty evidence).
12. In adults with SWD with sleep disturbance/insomnia, when transitioning from daytime to nighttime sleep, the AASM suggests the use of melatonin over no melatonin for night sleep following shift work (Conditional recommendation, low certainty evidence).
13. In adults with SWD who desire to take a nap prior to the first night shift, the AASM suggests the use of melatonin over no melatonin prior to the nap (Conditional recommendation, very low certainty evidence).
    Remarks: Melatonin may temporarily increase sleepiness, decrease cognitive performance, and increase accident risk. Allowing adequate time for resolution of sleepiness prior to driving, returning to work or performing other safety-sensitive behaviors may be needed to reduce these risks.
14. In adults with SWD with daytime sleep disturbance/insomnia, the AASM suggests the use of ramelteon and other melatonin receptor agonists over no ramelteon (Conditional recommendation, low certainty evidence).
15. In adults with SWD with daytime sleep disturbance/insomnia, the AASM suggests the use of suvorexant and other dual orexin receptor antagonists over no suvorexant (Conditional recommendation, low certainty evidence).
16. In adults with SWD with daytime sleep disturbance/insomnia, the AASM suggests **against** the use of triazolam and other benzodiazepines (conditional recommendation, very low certainty evidence).

Adults with SWD seeking circadian adaptation

17. In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the use of bright light over no bright light during the night shift (Conditional recommendation, very low certainty).
    Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.
18. In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the combination of bright light at night and fixed daytime sleep timing over the combination of no bright light and no fixed sleep timing (Conditional recommendation, very low certainty evidence).
    Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.
19. In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the combination of bright light at night, fixed daytime sleep timing, and reduced-light-transmittance glasses in the morning

over the combination of no bright light, no fixed sleep timing, and no reduced-light-transmittance glasses (Conditional recommendation, very low certainty evidence).

Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.

INTRODUCTION

This clinical practice guideline is intended to update the previously published American Academy of Sleep Medicine (AASM) guidelines on the treatment of shift work disorder (SWD)[1] and reflects the current recommendations of the AASM. SWD results when individuals are required to follow a work schedule that routinely overlaps with their usual sleep timing, for a period of at least 3 months. Patients with SWD may present with symptoms of excessive sleepiness and/or with sleep disturbance/insomnia, which are often caused by misalignment between the endogenous circadian system and the required shift work schedule, although the pathophysiology of SWD is incompletely understood. Of note, not all individuals who are shift workers develop symptoms of SWD. Shift work disorder is present in ~27% (95% confidence interval = 21-33%) of adult shift workers. [2] It should also be noted that the circadian rhythms of the majority of shift workers do not adapt to shift work schedules and circadian adaptation to the shift work schedule is not a common goal of treatment for patients with SWD. As such the majority of the recommendations provided in this guideline will focus on the management of excessive sleepiness or sleep disturbance/insomnia symptoms, rather than on circadian adaptation.

Exposure to shift work is recognized to increase risk for numerous poor health outcomes, including poor quality of life, unwanted weight gain, cardiometabolic disorders, neurological disorders, mood disorders, and malignancy. It should be noted that while the ultimate treatment goal will be to also mitigate these long-term health outcomes in shift workers, studies to date primarily look at the outcomes of symptom management. As the longer-term health impacts of interventions for SWD were not evaluated in the studies reviewed for this guideline, we are only able to address the efficacy of interventions in the context of more immediate symptom management.

This guideline, in conjunction with the accompanying systematic review [3], provides a comprehensive update of the available evidence and a synthesis of clinical practice recommendations for the treatment of symptoms of excessive sleepiness and/or insomnia, and for circadian adaptation in adults with SWD. Evidence for the recommendations is based largely on laboratory studies of simulated shift work in healthy adults and from real life field studies of shift workers who were not formally diagnosed with SWD, as well as from a small number of randomized, multicenter clinical trials in patients with SWD. It is intended to optimize patient-centric care by broadly informing clinicians who care for patients with SWD. The order of the recommendations is not intended to convey prioritization but is listed in alphabetical order for each of the targeted treatment categories: symptoms of excessive sleepiness, sleep disturbance/insomnia, and for circadian adaptation.

Clinical practice recommendations reflect those interventions for which there was sufficient evidence to make a recommendation. The absence of a particular intervention in this clinical practice guideline should not be interpreted as a statement against its clinical use. Interventions for which literature was reviewed but it was determined that insufficient evidence existed to make recommendations are discussed in the systematic review. “Insufficient evidence” to determine the effectiveness of a particular intervention does not mean that the intervention does not

work, but that evidence is lacking to guide decision-making. Additional research is needed to determine the effectiveness of the intervention and thus reflects a knowledge gap and future direction for research.

METHODS

The AASM commissioned a task force (TF) of sleep and circadian medicine researchers and clinicians with expertise in circadian rhythm disorders and shift work, and the treatment of shiftwork disorder (SWD). The TF was required to disclose all potential conflicts of interest (COI), per the AASM's COI policy, prior to being appointed to the TF and throughout the research and writing of these documents. In accordance with the AASM's conflicts of interest policy, TF members with a Level 1 conflict were not allowed to participate. TF members with a Level 2 conflict were required to recuse themselves from any related discussion or writing responsibilities. All relevant conflicts of interest are listed in the Disclosures section.

The TF conducted a systematic review of the published scientific literature, focusing on patient-oriented, clinically relevant outcomes. The key terms, search limits, and inclusion/exclusion criteria specified by the TF are detailed in the supplemental material of the accompanying systematic review [3]. This guideline focuses on the following critical outcomes: excessive sleepiness/alertness, accident risk, sleep quality, and cognitive performance/work performance. When there was not a clinically meaningful difference between the intervention and the comparator on the critical outcomes, decisions were informed by the important outcomes including circadian alignment, quality of life, mental health, sleep outcomes other than quality (sleep latency, total sleep time, sleep efficiency, wakefulness after sleep onset), as well as disease severity. It should be noted that for all data presented, due to the limited evidence investigating the use of these interventions in patients with SWD, the TF included evidence from individuals without a diagnosis of SWD. The studies were grouped into three separate categories based on the participants: patients with SWD, shift workers without a formal diagnosis of SWD, and healthy individuals who did not participate in shift work and were put in a lab simulated setting. The totality of this evidence was used in the evidence-to-decision-making framework outlined in the accompanying systematic review [3].

The purpose of the review was to determine whether the interventions provided clinically meaningful improvements in the relevant outcomes in comparison to no treatment. The clinical practice recommendations were then developed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process. The TF assessed the following four components to determine the direction and strength of a recommendation: certainty of evidence, balance of beneficial and harmful effects, patient values and preferences, and resource use. When determining the certainty of evidence, the TF considered the overall risk of bias (randomization, blinding, allocation concealment, selective reporting), imprecision (95% confidence interval crosses the clinically meaningful threshold or the null, and/or sample size < 200 participants), inconsistency ($I2 \geq 50\%$), indirectness (study population vs target patient population). Details of these assessments can be found in the accompanying systematic review[3]. Taking these major factors into consideration, each recommendation statement was assigned a strength ("Strong" or "Conditional"). Additional information is provided in the form of "Remarks" immediately following the recommendation statements, when deemed necessary by the TF. Remarks are based on the evidence evaluated during the systematic review and are intended to provide context for the recommendations and to guide clinicians in the implementation of the recommendations in daily practice.

The recommendations in this guideline define principles of practice that should meet the needs of most patients in most situations. A "Strong" recommendation is one that clinicians should follow for almost all patients (i.e.,

something that might qualify as a Quality Measure). A "Conditional" recommendation reflects a lower degree of certainty in the appropriateness of the patient-care strategy for all patients. It requires that the clinician use clinical knowledge and experience and strongly considers the individual patient's values and preferences to determine the best course of action. The ultimate judgment regarding any specific care must be made by the treating clinician and the patient, taking into consideration the individual circumstances of the patient, available treatment options, and resources. The AASM expects this guideline to have an impact on professional behavior, patient outcomes, and—possibly—health care costs. This clinical practice guideline reflects the state of knowledge at the time of publication and will be reviewed and updated as new information becomes available.

RECOMMENDATIONS

The following clinical practice recommendations are based on a systematic review and evaluation of evidence using the GRADE process. The implications of the strength of recommendations for guideline users are summarized in **Table 1**. Remarks are provided to guide clinicians in the implementation of these recommendations.

TABLE 1 – Implications of Strong and Conditional Recommendations for Users of AASM Clinical Practice Guidelines

User	**Strong Recommendations** *"We recommend…"*	**Conditional Recommendations** *"We suggest…"*
Clinicians	Almost all patients should be offered the recommended course of action. Adherence to this recommendation could be used as a quality criterion or performance indicator.	Most patients should be offered the suggested course of action; however, different choices may be appropriate for different patients. The clinician must help each patient determine if the suggested course of action is clinically appropriate and consistent with their values and preferences.
Patients	Almost all patients should be offered the recommended course of action, although a small proportion of patients would not choose it.	Most patients should be offered the suggested course of action, though some may not choose it. Different choices may be appropriate for different patients. The patient should work with their clinician to determine if the suggested course of action is clinically appropriate and consistent with their values and preferences.
Policy Makers	The recommended course of action can be adopted as policy for most situations. Adherence to the recommended course of action could be used as a quality criterion or performance indicator.	The ultimate judgment regarding the suitability of the suggested course of action must be made by the clinician and patient together, based on what is best for the patient. This decision-making flexibility should be accounted for when establishing policies.

TABLE 2 – Summary of Recommended Interventions

ADULTS WITH SWD

Intervention	Strength of recommendation	Overall Certainty of Evidence
Patients with symptoms of excessive sleepiness		
Armodafinil	Conditional for	⨁⨁⨁◯
Modafinil	Conditional for	⨁⨁⨁◯
Bright light during the night shift	Conditional for	⨁◯◯◯
Caffeine prior to or during the night shift	Conditional for	⨁◯◯◯
Clockwise rotating shift schedule	Conditional for	⨁◯◯◯
Nap prior to the first night shift	Conditional for	⨁◯◯◯
Not eating or eating a snack during the night shift	Conditional for	⨁⨁◯◯
Bright light and caffeine during the night shift	Conditional for	⨁◯◯◯
Nap and caffeine prior to the night shift	Conditional for	⨁◯◯◯
8-hour shift or 12-hour shift[1]	Conditional for	⨁◯◯◯
Patients with symptoms of insomnia		
CBT-I	Conditional for	⨁◯◯◯
Melatonin for day sleep after the night shift	Conditional for	⨁◯◯◯
Melatonin for night sleep following night shift work	Conditional for	⨁⨁◯◯
Melatonin prior to a nap prior to the night shift	Conditional for	⨁⨁◯◯
Ramelteon and other melatonin receptor agonists for daytime sleep	Conditional for	⨁⨁◯◯
Suvorexant and other dual orexin receptor antagonists for daytime sleep	Conditional for	⨁⨁◯◯
Triazolam and other benzodiazepines for daytime sleep	Conditional against	⨁◯◯◯
Patients addressing circadian adaptation		
Bright light during the night shift	Conditional for	⨁◯◯◯
Bright light during the night shift and fixed sleep timing	Conditional for	⨁◯◯◯
Bright light during the night shift, fixed daytime sleep timing, and reduced light-transmittance glasses in the morning	Conditional for	⨁◯◯◯
GRADE certainty of evidence: Very low ⨁◯◯◯; Low ⨁⨁◯◯; Moderate ⨁⨁⨁◯ [1]There was no evidence to favor 8-hour vs. 12-hour shift length		

Adults with Shift Work Disorder

Recommendations with sufficient evidence for specific interventions for the treatment of adults with SWD are presented below. Remarks are provided to guide clinicians in the implementation of these recommendations.

CONDITIONAL Recommendations For Use

Symptoms of excessive sleepiness

Recommendation 1: In adults with SWD with excessive sleepiness, the AASM suggests the use of armodafinil or modafinil over no armodafinil or modafinil. (Conditional recommendation, moderate certainty evidence)

The TF identified 5 RCTs and 2 observational studies for armodafinil in which the pooled estimates demonstrated clinically meaningful decreases in excessive sleepiness and accident risk. Performance on cognitive outcomes was also improved by armodafinil, but clinically meaningful thresholds were not set by the TF for these performance outcomes assessed. The TF's judgement of moderate benefits was driven by the clinically meaningful increase in sleep latency on the multiple sleep latency test (MSLT), indicating a decrease in objective levels of sleepiness, decrease in self-reported sleepiness on the Karolinska Sleepiness Scale (KSS), and a decrease in clinician-rated sleepiness, all in patients with SWD. Findings for armodafinil demonstrate moderate to high certainty of evidence for decreases in excessive sleepiness, low to moderate certainty of evidence for decreases in accident risk, and moderate certainty of evidence for increases in cognitive performance.

The TF identified 3 RCTs for modafinil in which the pooled estimates demonstrated a clinically meaningful decrease in excessive sleepiness and accident risk and a clinically meaningful increase in cognitive performance on the psychomotor vigilance task (PVT). Performance on other cognitive outcomes was also improved by modafinil, but clinically meaningful thresholds were not set by the TF for these outcomes. clinically meaningful increase in sleep latency on the MSLT in patients with SWD, indicating a decrease in objective levels of sleepiness, a potentially clinically meaningful increase in sleep latency on the maintenance of wakefulness test (MWT) in healthy participants, indicating an increase in objective levels of alertness, a potentially clinically meaningful decrease in self-reported sleepiness on the KSS in patients with SWD, and clinically meaningful decrease in lapses of attention on the PVT in patients with SWD drove the TF's judgment of moderate benefits. Findings for modafinil demonstrate very low to moderate certainty of evidence for decreases in excessive sleepiness, low to moderate certainty of evidence for decreases in accident risk, and low certainty of evidence for increases in cognitive performance.

Rare, but serious adverse events associated with the use of armodafinil/modafinil have been reported including suicidal ideation (in a patient on armodafinil with a history of depression), rare cases of serious or life-threatening rash and multi-organ hypersensitivity reactions. Armodafinil had more adverse events than placebo that resulted in withdrawal from the study, with headache and nausea being the most common. The undesirable effects for armodafinil/modafinil are similar, with the most common side effects including headache, nausea, dizziness, sleep disturbance, and anxiety[3, 4]. The risk of abuse and/or dependence have also been reported in association with the use of modafinil/armodafinil[3, 4]. The TF judged the undesirable effects as small.

The overall certainty of evidence for armodafinil/modafinil was moderate due to imprecision. [3, 4] The cost of the medications was considered low. The TF judged the treatment could have a variable effect on health equity; because those who work shift work may already be disadvantaged, symptom improvements from the use of armodafinil/modafinil could help them, increasing equity. [3, 4] The intervention was judged to be feasible based on low generic cost and high availability of these medications. Moreover, there is a long history of successful use in widely varying populations.

Recommendation 2: In adults with SWD with excessive sleepiness, the AASM suggests the use of bright light over no bright light during the night shift. (Conditional recommendation, very low certainty)

Remark: Individuals with SWD who exhibit insomnia and daytime function impairments may also benefit from using bright light during their night shift.

The TF identified 18 RCTs and 6 observational studies that used various intensities and durations of acute exposure to bright light during the night shift in which the pooled estimates demonstrated clinically meaningful decreases in excessive sleepiness and improvement in cognitive performance on the PVT. There were also improvements in many other cognitive performance measures, but clinically meaningful thresholds were not set by the TF for the other performance outcomes assessed. A potentially clinically meaningful increase in sleep latency on the maintenance of wakefulness test (MWT), indicating an increase in objective levels of alertness, and a potentially clinically meaningful decrease in lapses of attention on the PVT were seen in studies of healthy adults tested in the laboratory and this drove the TF's judgment of small benefits. The studies in which cognitive performance was assessed were nearly split between laboratory and field-based research testing healthy participants or shift workers with no diagnosis of SWD. Findings for acute exposure to bright light demonstrate very low to low certainty of evidence for decreases in excessive sleepiness, very low certainty of evidence for decreases in accident risk, and very low certainty of evidence for increases in cognitive performance.

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. Potential desirable effects are small. There was no mention of adverse events though undesirable effects may include headache and eye strain from bright light. Resources required are negligible. The intervention is probably feasible to implement, likely has no impact on equity, and its acceptability to key interest holders most likely varies.

Recommendation 3: In adults with SWD with excessive sleepiness, the AASM suggests the use of caffeine over no caffeine. (Conditional recommendation, very low certainty evidence)

Remarks: Caffeine intake close to bedtime can disrupt sleep onset and quality, which may exacerbate symptoms of shift work disorder.

The TF identified 8 RCT studies for varying doses of caffeine either prior to night shift or within the first few hours of the start of the night shift in which the pooled estimates demonstrated that there may be a clinically meaningful decrease in excessive sleepiness and an improvement in cognitive performance on the PVT. There were also improvements in other cognitive performance measures, but clinically meaningful thresholds were not set by the TF. A potential clinically meaningful increase in sleep latency on the MSLT, indicating a decrease in objective levels of sleepiness, a potential clinically meaningful decrease in self-reported sleepiness on the Karolinska Sleepiness Scale (KSS), and a potential clinically meaningful decrease in lapses of attention on the PVT were seen in studies of healthy adults tested in the laboratory or shift workers with no diagnosis of SWD and this drove the TF's judgment of small benefits. Findings for caffeine demonstrate very low to low certainty of evidence for decreases in excessive sleepiness, and low certainty of evidence for improvements in cognitive performance.

The overall certainty of evidence was very low due to indirectness and imprecision. The TF judged the benefits to be small and the harms to be variable, as there are unknowns about caffeine consumption. The potential benefits

of caffeine should be evaluated within the context of possible undesirable effects including sleep disruption, as reported under important outcomes in the systematic review[3] In addition, the TF considered the side effects of palpitations, tremor, agitation and gastrointestinal upset that are frequently reported with caffeine use,[5] along with the potential for caffeine withdrawal symptoms when making these recommendations [6, 7] Caffeine is low in cost and widely available in different forms, however, there remains a question of optimal dose and timing of caffeine. Overall, the TF decided that most patients would use caffeine over no treatment for SWD.

Recommendation 4: In adults with SWD with excessive sleepiness, the AASM suggests the use of a clockwise rotating shift schedule over a counterclockwise rotating shift schedule. (Conditional recommendation, very low certainty evidence)

The TF identified 10 observational planned work schedule studies in which pooled estimates demonstrated potentially clinically meaningful improvements in excessive sleepiness in those individuals following a clockwise rotating schedule, when compared to a counterclockwise rotating schedule. Cognitive performance was also improved by a clockwise rotating schedule, when compared to a counterclockwise rotating schedule, but clinically meaningful thresholds were not set by the TF for the performance outcomes assessed. A potential clinically meaningful decreases in self-reported sleepiness on the KSS were seen in observational studies of shift workers without a diagnosis of SWD and this drove the TF's judgment of small benefits. Findings for the planned clockwise rotating work schedule demonstrate very low certainty of evidence for decreases in excessive sleepiness and improvements in cognitive performance compared to a counterclockwise rotating schedule.

The overall certainty of evidence was very low due to indirectness and imprecision. All included studies were observational, and one study allowed participants to select their shift. No adverse effects were reported in any of the included studies, however rapid shift rotation in either direction may be a challenge for workers to adapt to. It was noted that the feasibility and resources required for implementing this intervention fall primarily at the level of the institution in terms of implementing appropriate scheduling and staffing and would be challenging to implement at the individual level. However, equity could be improved by allowing employees some degree of choice in terms of which shifts they are scheduled to work.

Recommendation 5: In adults with SWD with excessive sleepiness, the AASM suggests taking a nap over no nap prior to the night shift. (Conditional recommendation, very low certainty evidence)

Remarks: Sleep inertia occurring soon after the nap may temporarily increase sleepiness, decrease cognitive performance, and increase accident risk. Allowing adequate time for resolution of sleep inertia prior to driving or performing other safety-sensitive behaviors may be needed to reduce these risks.

The TF identified 3 studies for taking a nap prior to the night shift in which the pooled estimates demonstrated potentially clinically meaningful decrease in excessive sleepiness and improvement in cognitive performance on the PVT. However, performance on other outcomes and daytime sleep quality were not meaningfully improved by taking a nap prior to the night shift. A potential clinically meaningful increase in sleep latency on the MWT, indicating an increase in objective levels of alertness, and a potential clinically meaningful decrease in lapses of attention on the PVT were seen in studies of healthy adults tested in the laboratory and this drove the TF's judgment of moderate benefits. Findings for taking a nap prior to the night shift demonstrate very low certainty of evidence

for decreases in excessive sleepiness and improvements in cognitive performance compared to not taking a nap prior to the night shift.

The overall certainty of evidence was very low due to indirectness and imprecision. The included studies demonstrated variability in the duration and timing of naps, shifts, and outcome measures. Potential undesirable effects that were not reported in these studies include the risk of sleep inertia occurring soon after naps, which may incur safety risk for driving, cognitive performance or other activities. Taking a nap is widely accessible and incurs low cost, and is thus an acceptable intervention for most individuals. However, it does require an appropriate sleep environment and time for a nap outside the main sleep period.

Recommendation 6: In adults with SWD with excessive sleepiness, the AASM suggests not eating or eating a snack rather than eating a full meal during the night shift. (Conditional recommendation, low certainty evidence)

The TF identified 4 RCTs studies for not eating or only eating a snack during the night shift in which the pooled estimates demonstrated a potentially clinically meaningful improvement in excessive sleepiness and cognitive performance on the PVT and reduction in accident risk versus eating a meal during the night shift. Other cognitive performance outcomes were also improved by not eating or only eating a snack on the night shift, when compared to eating a full meal on the night shift, but clinically meaningful thresholds were not set by the TF . The potentially clinically meaningful decreases in lapses of attention on the PVT and decreases in accident risk on a driving simulator were seen in studies of healthy adults tested in the laboratory and this drove the TF's judgment of small benefits. Findings for not eating or only eating a snack on the night shift demonstrate low certainty of evidence for decreases in excessive sleepiness and improvements in cognitive performance, and very low certainty of evidence for decreases in accident risk compared to eating a full meal during the night shift.

The overall certainty of evidence was low. The certainty of evidence was downgraded due to inconsistency, indirectness, and imprecision. There was an increase in reports of hunger and stomach upset in the group that did not eat at night, particularly on the first night of the intervention, otherwise no significant adverse events were noted.

The TF determined that for most individuals the benefits of not eating or only eating a snack during the night shift outweighed any risks or undesirable effects. However, special consideration would be needed for individuals in which extended fasting may be contraindicated, for example in those individuals with type-I diabetes.

Recommendation 7: In adults with SWD with excessive sleepiness, the AASM suggests the combination of caffeine and bright light over the combination of no caffeine and no bright light. (Conditional recommendation, very low certainty evidence)

Remark: Caffeine intake close to bedtime can disrupt sleep onset and quality, which may exacerbate symptoms of shift work disorder.

The TF identified 2 RCTs for the combination of caffeine and bright light compared to no treatment during the night shift in which the pooled estimates demonstrated potentially clinically meaningful improvements in excessive sleepiness and improvement in cognitive performance on the PVT. Other cognitive performance

outcomes were also improved by the combination of caffeine and bright light during the night shift, but clinically meaningful thresholds were not set by the TF. A potentially clinically meaningful reduction in self-reported sleepiness on the SSS and a potentially clinically meaningful increase in sleep latency on the MWT, indicating an increase in objective levels of alertness were seen in studies of healthy adults tested in the laboratory, and this drove the TF's judgment of small benefits. Findings for the combination of caffeine and bright light during the night shift demonstrate very low to low certainty of evidence for decreases in excessive sleepiness and very low certainty of evidence for increases in cognitive performance compared to no caffeine and no bright light.

The overall certainty of the evidence was very low due to the risk of bias, indirectness and imprecision. Potential desirable effects are likely small. Potential undesirable effects include disturbed sleep following caffeine use too close to daytime sleep, in addition to the previously noted common side effects of caffeine, including palpitations, tremor, agitation and gastrointestinal upset. Bright light may cause headaches and eye strain in susceptible individuals. The TF determined there is probably no important uncertainty or variability in the value placed on reducing sleepiness and improving cognitive performance. Resources required overall are negligible. However, implementation of the bright light component of the intervention may be limited by work environment and employer acceptance. Overall, the intervention probably has no impact on equity, is probably acceptable to key interest holders, and is probably feasible to implement.

Recommendation 8: In adults with SWD with excessive sleepiness, the AASM suggests the combination of taking a nap and caffeine over the combination of no nap and no caffeine prior to the night shift. (Conditional recommendation, very low certainty evidence)

The TF identified a single RCT with two experimental conditions (lab and field) combining a nap and caffeine prior to the night shift, compared to no treatment, in which the estimates demonstrated potentially clinically meaningful decreases in excessive sleepiness and improvement in cognitive performance on the PVT. Other cognitive performance outcomes were also improved by the combination of taking a nap and caffeine prior to the night shift, but a clinically meaningful threshold was not set by the TF. The potentially clinically meaningful reduction in subjective sleepiness on the KSS, a potentially clinically meaningful increase in sleep latency on the MWT, indicating an increase in objective levels of alertness, and the potentially clinically meaningful decrease in lapses of attention on the PVT were seen in a study of healthy adults in the laboratory and a field study of shift workers, and this drove the TF's judgment of moderate benefits. Findings for the combination of taking a nap and caffeine prior to the night shift demonstrate very low certainty of evidence for decreases in excessive sleepiness and improvements in cognitive performance compared to no nap and no caffeine.

The overall certainty of evidence was very low due to risk of bias, indirectness, and imprecision. Potential desirable effects are likely moderate. Potential undesirable effects include disturbed sleep following caffeine too close to daytime sleep in addition to the previously noted common side effects of caffeine, including palpitation, tremor, agitation and gastrointestinal upset; severity of this varies by timing and dose of caffeine administration and between individuals. Taking a nap and caffeine are widely accessible and thus an acceptable intervention for most, however obligations prior to a shift and lack of time to nap prior to a shift may limit feasibility. There is probably no impact on equity.

Recommendation 9: In adults with SWD who are working either an 8-hour or 12-hour shift, the AASM does not suggest working one shift duration over the other. (Conditional recommendation, very low certainty evidence)

Remark: This recommendation does not consider other shift durations, rotation, or the number of consecutive shifts. This guideline did not look at shifts over 12 hours. The total number of hours worked per week ranged from 36 to 52.

The TF identified 5 non-randomized studies for working 8-hour versus 12-hour shift in which pooled estimates did not demonstrate differences in excessive sleepiness, sleep quality or cognitive performance between the two shift durations. Findings did not support one shift duration over the other.

The overall certainty of evidence was very low due to imprecision and indirectness. All studies were observational, typically comparing performance between two similar sites with different shift schedules, or within a single site before and after a schedule change. The value and acceptability of an 8-hour shift versus a 12-hour shift is expected to vary, depending on whether a participant prefers to work more days each week with shorter hours per shift, or fewer days each week with longer hours per shift. The feasibility of implementation of either intervention is variable, depending on the required shift coverage needed by the employer.

Symptoms of sleep disturbance/insomnia

Recommendation 10: In adults with SWD with daytime sleep disturbance/insomnia, the AASM suggests the use of CBT-I over no CBT-I. (Conditional recommendation, very low certainty evidence)

The TF identified 1 RCT and 3 non-RCT studies for in-person, self-directed, and group-based cognitive-behavioral therapy for insomnia (CBT-I) to improve daytime sleep in which the pooled estimates demonstrated improved sleep quality, but clinically meaningful thresholds were not set by the TF for the sleep quality outcomes assessed. Findings for CBT-I demonstrate very low certainty of evidence for improvements in daytime sleep quality compared to no CBT-I.

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. It should be noted that CBT-I is a therapy developed and validated for the treatment of chronic insomnia. The CBT-I protocols described in these studies were modified to treat shift workers; details of the protocols and modifications were not included in the published studies.

Adverse effects were not reported. The TF noted that potential undesirable effects may include a short-term reduction in total sleep time due to sleep restriction. Access to treatment may be limited due to an insufficient number of trained providers, financial constraints, access to and ability to use self-directed programs, and time needed to complete a full course of treatment. Some patients may not wish to invest the time, cost, and effort needed for effective treatment; however, patients desiring improvement of insomnia without medication may find this acceptable. Overall, the TF decided that most patients would prefer CBT-I over no treatment for SWD occurring with insomnia.

Recommendation 11: In adults with SWD with daytime sleep disturbance/insomnia following the night shift, the AASM suggests the use of melatonin over no melatonin. (Conditional recommendation, very low certainty evidence)

The TF identified 10 RCTs for the use of melatonin for improving daytime sleep following the night shift in which the pooled estimates demonstrated improved sleep quality, but clinically meaningful thresholds were not set by the TF for the sleep quality outcomes assessed. Pooled estimates also demonstrated a potentially clinically meaningful improvement in important outcomes of self-reported and objectively measured sleep duration. Findings for melatonin demonstrate very low certainty of evidence for improvements in daytime sleep quality and decreases in excessive sleepiness compared to placebo.

The overall certainty of evidence was low due to indirectness, imprecision, and risk of bias. The TF judged the beneficial effects of melatonin for sleep after a night shift to be trivial. Undesirable effects of melatonin were judged to be trivial and include headaches, dizziness, nausea, and drowsiness. The TF deemed that melatonin would be feasible and acceptable for most shift workers and did not find any impact on equity and found negligible costs and savings.

Recommendation 12: In adults with SWD with sleep disturbance/insomnia, when transitioning from daytime to nighttime sleep, the AASM suggests the use of melatonin over no melatonin for night sleep following shift work. (Conditional recommendation, low certainty evidence)

The TF identified 3 RCTs for the use of melatonin to improve nighttime sleep during the transition from daytime to nighttime sleep in which the pooled estimates demonstrated potentially clinically meaningful improvements in important outcomes of increased self-reported and objectively measured sleep duration and a clinically meaningful decrease in sleep latency. Findings for melatonin demonstrate low to moderate certainty of evidence for improvements in nighttime sleep quality when transitioning from daytime to nighttime sleep compared to placebo.

The overall certainty of evidence was low due to imprecision and indirectness. The TF judged the beneficial effects of melatonin for transitioning to nighttime sleep after daytime sleep to be small. Undesirable effects of melatonin were judged to be trivial and include headaches, dizziness, nausea, and drowsiness. The TF deemed that melatonin would be feasible and acceptable for most shift workers and did not find any impact on equity and found negligible costs and savings.

Recommendation 13: In adults with SWD who have difficulty taking a nap prior to the first night shift, the AASM suggests the use of melatonin over no melatonin prior to the nap. (Conditional recommendation, very low certainty evidence)

Remarks: Melatonin may temporarily increase sleepiness, decrease cognitive performance, and increase accident risk. Allowing adequate time for resolution of sleepiness prior to driving, returning to work or performing other safety-sensitive behaviors may be needed to reduce these risks.

The TF identified 4 RCTs for the use of melatonin to improve a nap prior to the first night shift in which the pooled estimates demonstrated potentially clinically meaningful increase in important sleep outcomes, including increases in total sleep time and a clinically meaningful reduced wakefulness after sleep onset. In the included RCTs, the

timing of melatonin administration ranged from 30 min to 2 hours prior to a 3-hour or 4-hour sleep opportunity (1 RCT only examined sleep onset latency), to facilitate napping during the daytime, prior to the night shift. The exact timing of the implementation at an individual level may vary depending on their work schedule and desired timing of the nap. Findings for melatonin demonstrate very low certainty of evidence for improvements in daytime nap sleep prior to the first night shift compared to placebo.

The overall certainty of evidence was very low due to indirectness and imprecision. The TF judged the beneficial effects of melatonin to improve a nap prior to the first night shift to be small. Undesirable effects of melatonin were judged to be trivial and include headaches, dizziness, nausea, and drowsiness. Caution should be exercised when using melatonin to allow adequate time for resolution of sleepiness prior to engaging in safety-sensitive behaviors. The TF found that melatonin would be feasible and acceptable for most shift workers and did not find any impact on equity and found negligible costs and savings.

Recommendation 14: In adults with SWD with daytime sleep disturbance/insomnia symptoms, the AASM suggests the use of ramelteon and other melatonin receptor agonists over no ramelteon. (Conditional recommendation, low certainty evidence)

The TF identified 1 RCT for the use of an 8 mg dose of ramelteon to improve daytime sleep in which the estimates demonstrated clinically meaningful improvements in important sleep outcomes including a potentially clinically meaningful decrease in percent wakefulness during sleep time (inverse of sleep efficiency), clinically meaningful increases in self-reported and objective sleep duration, and potentially clinically meaningful decreases in wakefulness after sleep onset. Outcomes were seen in a study of healthy adults tested in the laboratory and this drove the TF's judgment of moderate benefits. Findings for ramelteon demonstrate low certainty of evidence for increases in daytime sleep quality compared to placebo.

The overall certainty of evidence was low due to indirectness and imprecision. The TF determined benefits to be moderate due to improvements in a number of sleep outcomes. There were no reports of adverse events in the study reviewed. Undesirable effects of ramelteon reported clinically include dizziness, somnolence and fatigue. The TF determined that there would probably be no important uncertainty in values and that the balance of desirable and undesirable effects favors the use of ramelteon. The TF judged that the use of ramelteon would likely be acceptable and feasible to most patients with SWD.

Recommendation 15: In adults with SWD with daytime sleep disturbance/insomnia symptoms, the AASM suggests the use of suvorexant and other dual orexin receptor antagonists over no suvorexant. (Conditional recommendation, low certainty evidence)

The TF identified 1 RCT for 10 and 20 mg doses of suvorexant to improve daytime sleep in which the estimates demonstrated improvements in sleep quality, but a clinically meaningful threshold was not set by the TF for the sleep quality outcome assessed. Estimates also demonstrated clinically meaningful improvements in important outcomes of self-reported and objectively measured sleep duration and sleep latency. The 20 mg dose demonstrated a stronger effect compared to the 10 mg dose. Clinically meaningful increases in self-reported and objective sleep duration were seen in studies of shift workers with daytime insomnia and this drove the TF's judgment of moderate benefits. Findings for suvorexant demonstrate moderate certainty of evidence for increases in daytime sleep

quality, moderate certainty of evidence for increases in total sleep time, and low certainty of evidence for decreases in sleep latency compared to placebo.

The overall certainty of evidence was low due to imprecision and indirectness. There were no adverse events reported among patients taking suvorexant among the study included in the assessment; however, clinically suvorexant has been shown to have the undesirable effects of drowsiness, dizziness, headache, unusual dreams, dry mouth, cough, and diarrhea in other evaluations.[8] In addition, a 30 mg dose has not been approved for use due to increased suicidal ideation[9]. The TF determined that there is probably no important uncertainty or variability in how much people value improvements in sleep quality. Suvorexant is likely to be acceptable and feasible for many patients. It is widely available but involves moderate costs to patients.

CONDITIONAL Recommendation Against Use

Recommendation 16: In adults with SWD with daytime sleep disturbance/insomnia, the AASM suggests <u>against</u> the use of triazolam and other benzodiazepines. (Conditional recommendation, very low certainty evidence)

The TF identified 4 RCTs for triazolam in which pooled estimates demonstrated clinically meaningful decreases in excessive sleepiness. Pooled estimates also demonstrated potentially clinically meaningful improvements in important sleep outcomes. There were clinically meaningful increases in self-reported and objective sleep duration and subsequently a potentially clinically meaningful increase in the latency to sleep on the MSLT during simulated nightshifts. Findings for triazolam demonstrate very low certainty of evidence for improvements in daytime sleep quality and low to moderate certainty of evidence for decreases in excessive sleepiness compared to placebo.

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. The TF noted that potential undesirable effects may include a safety concern with falls, abuse of the medication, dependence on the medication, and withdrawal symptoms.[10, 11] The magnitude of undesirable effects of the medication were determined to be moderate. The TF concluded that the potential undesirable effects associated with triazolam use outweighed the beneficial effects shown.

The TF determined that triazolam would not have an impact on health equity and that the costs of the medication are negligible. The TF concluded that triazolam would probably not be acceptable to key interest holders due to the shift in clinical practice away from long-term benzodiazepine use.

Circadian Adaptation

Recommendation 17: In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the use of bright light over no bright light during the night shift. (Conditional recommendation, very low certainty)

Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The majority of evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.

The TF identified 8 RCTs and 3 non-RCTs, laboratory and field-based studies, for bright light during the night shift for circadian adaptation in which the pooled estimates demonstrated partial or full circadian adaptation to the night shift. Pooled estimates also demonstrated potentially clinically meaningful decreases in excessive sleepiness with bright light induced circadian adaptation. There were also clinically meaningful increases in important sleep outcomes with bright light induced circadian adaptation. A potentially clinically meaningful increase in sleep latency on the repeated test of sustained wakefulness (RTSW), indicating increases in objective levels of alertness, was seen in a study of healthy adults in the laboratory, and this drove the TF's judgment of small benefits. Findings for circadian adaptation in response to bright light exposure demonstrate very low certainty of evidence for decreases in excessive sleepiness..

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. Potential desirable effects are small. There is no mention of adverse events though undesirable effects may include headache and eye strain from bright light in susceptible individuals. Resources required are negligible. Overall, the intervention probably has no impact on equity, acceptability to key interest holders probably varies, and is probably feasible to implement. Full circadian adaptation may not be a goal for treatment for most shift workers as then they would be circadian misaligned on days off work. Partial circadian adaptation may be a compromise to full circadian adaptation.

Recommendation 18: In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the combination of bright light at night and fixed daytime sleep timing over the combination of no bright light and no fixed sleep timing. (Conditional recommendation, very low certainty evidence)

Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.

The TF identified 1 RCT for the combination of bright light during the night shift and fixed daytime sleep timing in a dark environment for circadian adaptation in which the pooled estimates demonstrated partial circadian adaptation to the night shift. Pooled estimates also demonstrated decreases in excessive sleepiness with the combination of bright light and fixed sleep timing, but clinically meaningful thresholds were not set by the TF for excessive sleepiness outcome assessed. The treatment outcomes were seen in a study of healthy adults in the laboratory, and this drove the TF's judgment of moderate benefits. Findings for circadian adaptation in response to bright light exposure and fixed sleep timing demonstrate very low certainty of evidence for decreases in excessive sleepiness.

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. Potential desirable effects of circadian adaptation are likely moderate. Undesirable effects are trivial overall and may include headache and eye strain related to bright light exposure in those who are susceptible. Resources required are negligible. Overall, the intervention probably has no impact on equity, is probably acceptable to key interest holders, and is probably feasible to implement.

Recommendation 19: In adults with SWD seeking circadian adaptation to the night shift, the AASM suggests the combination of bright light at night, fixed daytime sleep timing, and reduced light-transmittance glasses in the morning over the combination of no bright light, no fixed sleep timing, and no reduced light-transmittance glasses. (Conditional recommendation, very low certainty evidence)

Remarks: For individuals who work rotating or frequently changing shifts, circadian adaptation is not a realistic goal of treatment and therefore they would not be expected to benefit from this intervention. The evidence supporting this recommendation came from studies in which individuals reached partial circadian adaptation to the night shift.

The TF identified 4 RCTs and 1 crossover study for the combination of bright light at night, fixed daytime sleep timing in a dark environment, and reduced light-transmittance glasses worn in the morning between the end of the night shift and daytime sleep for circadian adaptation in which the pooled estimates demonstrated partial circadian adaptation to the night shift. Pooled estimates also demonstrated clinically meaningful decreases in accident risk and improvements in important sleep outcomes including increased self-reported and objective sleep duration. The treatment outcomes were seen in studies of healthy adults in the laboratory, and this drove the TF's judgment of moderate benefits. Findings for circadian adaptation in response to bright light exposure, fixed sleep timing, and reduced light-transmittance glasses demonstrate very low certainty of evidence for decreases in excessive sleepiness, very low certainty of evidence for improvements in sleep quality, very low certainty of evidence for accident risk and low certainty of evidence for improvements in cognitive performance.

The overall certainty of evidence was very low due to indirectness, imprecision, and risk of bias. Potential desirable effects are likely moderate in amplitude. There is no mention of adverse events though undesirable effects may include headache and eye strain from bright light in those who are susceptible. Driving safety must be assessed when using reduced light-transmittance glasses. Resources required are negligible. Overall, the intervention probably has no impact on equity, is probably acceptable to key interest holders, and is probably feasible to implement.

No Recommendations

The TF used 'no recommendation' when there was value in the findings but thought further research and innovation for this intervention is needed. There was insufficient and inconclusive evidence to make recommendations for the following: light filtering glasses, planned work schedule, split sleep, and planned naps during the shift.

The evidence is reported in the accompanying systematic review and supplemental materials.[3, 4]

DISCUSSION

Shift work disorder can be challenging to manage, requiring individualized treatment recommendations based on shift schedule and rotation, non-work demands (e.g., family, social) and patient symptoms. It is not expected that all guidelines will be applicable for all patients, but instead the clinician can use these guidelines to craft an individualized treatment plan for each patient.

In addition to the limitations noted above, within the individual treatment options there are several implementation considerations to keep in mind, as detailed below.

Patients with Excessive Sleepiness

Medications

The wake-promoting medications armodafinil and modafinil are the only FDA-approved medications to treat excessive sleepiness in patients with SWD. Armodafinil has a longer duration of effect as compared to modafinil with regards to the clinically meaningful increase in sleep latency on the multiple sleep latency test. While there do appear to be some concerns with respect to more common side effects of armodafinil and modafinil, such as headache, nausea and some risk of insomnia/sleep disturbance, the risk of serious undesirable effects was judged to be low. Future studies are needed to determine the long-term effects of chronic armodafinil and modafinil use on excessive sleepiness in patients with SWD. In addition, the effects of these wake-promoting medications on actual accident rates in this population have not been studied. Finally, the impact of these medications on the long-term morbidity associated with shift work and/or SWD (e.g., cardiometabolic disease, malignancy) have not been studied.

Caffeine

Further research is needed to better determine the optimal dose and timing of caffeine to improve the symptoms of excessive daytime sleepiness in individuals with SWD. Important considerations include acute side effects of caffeine, as well as potential impact on sleep and recovery from shift work schedules. Caffeine has a negative impact on subsequent sleep, and acceptable proximity to subsequent sleep is not established and likely varies by dosage and individual. Caffeine within six hours prior to sleep reduces sleep duration and quality[12,13] and caffeine appears to be more disruptive to daytime compared to nighttime sleep[14]; whereas caffeine taken near the beginning of the nightshift appears to have less of an impact on daytime sleep[15]. While caffeine has been documented to increase sleep latency and reduce total sleep time, there is heterogeneity to this response, with adenosine receptor gene polymorphisms contributing to susceptibility to sleep disturbance.[16] In addition, while not directly evaluated in the studies included in this guideline, there is some evidence that individuals can develop tolerance to the central and peripheral effects of caffeine with regular use.[17]

Naps

While taking a nap prior to the night shift was found to improve subjective and objective alertness in the small number of studies included in this guideline, outcomes from studies evaluating naps during the night shift varied considerably with respect to the number, duration, and timing of naps, and benefits to excessive sleepiness and driving safety were not consistent across all studies. A potential concern with taking a nap includes the risk of sleep inertia occurring immediately after waking which may interfere with alertness during the commute or during work.[18] When making the decision to implement napping, particularly during the night shift, consideration must be made for whether the individual would have adequate time to recover from any potential sleep inertia prior to returning to work (e.g., >20 min). [19]Further strategies to address this are discussed under combination treatments. Future research is needed to optimize the timing and duration of naps, as well as recovery from naps, to improve sleepiness, cognition, and safety outcomes for shift workers.

Bright light

Exposure to bright light to acutely improve alertness during shift work schedules is based on the alerting effects of light on the brain and on other proposed mechanisms including reduction in melatonin levels and increases in body temperature levels at night. Bright light was primarily utilized for its acute effects on improving performance.

However bright light at night also has phase shifting properties. It is possible that bright light during the shift could contribute to improved circadian adaptation and thus improvement in symptoms of shift work disorder over the long term in individuals routinely working a stable nightshift. However, bright light also suppresses melatonin. Important considerations when implementing bright light include whether it may or may not be practical in the work environment (e.g., driving) and whether all employees would benefit from light exposure when working in a group, as it is difficult to limit the light exposure to a single individual unless individual light emitting glasses are used. Whether there are negative health consequences associated over the long term with bright light exposure at night is not clear and an area in need of further study.

Meal timing

Interventions targeted at meal timing are based upon the recognition that most shift workers do not fully adapt to a nocturnal schedule, so their metabolic processes may still be most active during the daytime. In that context, limiting food intake overnight by either not eating, or only eating a snack, rather than eating a full meal was shown to be beneficial in terms of alertness, accident reduction and cognitive performance.[20] When considering this type of intervention, it is important to take into account whether the individual is attempting to seek circadian adaptation with the night shift, in which case this intervention may not be as effective, or may actually cause harm due to promoting 'wrong time' eating. In addition, individual psychological and medical factors related to the ability to tolerate working while fasting must also be considered. Future research is needed to evaluate whether implementing specific types of eating schedules in shift workers may have longer term cardiometabolic health benefits.[20]

Combination treatments

The concept behind combination treatments is that they work on different brain/physiological mechanisms and/or different timings of use to promote alertness during the shift work schedule. The recommendation to combine a nap with caffeine is based on study conditions that are limited to a nap preceding night shift followed by caffeine administration. In addition to implementation prior to the shift, caffeine followed by taking a nap might be used during a shift to improve alertness, and caffeine can reduce the impact of sleep inertia from the nap. No studies utilizing this caffeine-nap strategy were eligible for inclusion in this analysis, therefore we cannot comment on the efficacy of this intervention for shift work and SWD. Similar to other recommendations involving caffeine, subsequent sleep quality and quantity can be negatively impacted, and this should be taken into consideration when selecting timing of caffeine administration. The combination of bright light with caffeine is found to be an effective way of reducing sleepiness and improving performance at night.. Future research is also needed to evaluate other combination treatment strategies such as armodafinil or modafinil combined with bright light or caffeine during the night shift; as well as the combination of sleep promoting medications during the daytime and wakefulness promoting strategies during the nightshift and the combination of naps prior to the night shift and wakefulness promoting strategies beyond caffeine.

Patients with Sleep Disturbance/Insomnia Symptoms

Medications

While triazolam was demonstrated to improve sleep outcomes and daytime sleepiness, there are significant safety concerns associated with chronic benzodiazepine use, including the risk for falls, abuse of the medication, dependence on the medication, and withdrawal symptoms. Weighing those risks against any potential benefits that could come from use of the medication, the task force determined that the potential for harm outweighed the

potential benefits, so did not recommend the use of triazolam for the treatment of SWD. Suvorexant and ramelteon did not have the same level of safety concerns, so were considered to be appropriate for use in SWD. However, it is important to keep in mind that many shift workers attempting to sleep during the day may still have other daytime responsibilities (e.g., childcare) so they may not have a full eight-hour time window that is protected for sleep. In those cases, the risks of potential residual sedating effects of medication must be weighed against the potential benefits of improving daytime sleep. Patients should be counseled on the importance of allowing adequate time for sleep if this intervention is implemented.

Cognitive Behavioral Therapy for Insomnia

CBT-I is considered to be the gold-standard treatment for chronic insomnia, a condition of chronic difficulty getting to sleep or staying asleep. Shift workers may experience insomnia symptoms due to a misalignment of their work hours with their circadian rhythm, but in some cases may also have chronic insomnia. In this review, at least one study acknowledged that while all of their participants had insomnia symptoms, not all met criteria for shift work disorder due to reporting improved insomnia symptoms on days off.[21, 22]

When recommending CBT-I for shift workers, there are several important considerations. First, at baseline there is a shortage of CBT-I providers, with further potential access limitations due to the atypical work schedules of many shift workers. Second, it should be noted that all of the studies reviewed for these guidelines included some form of modification of the CBT-I protocol tailored for shift workers, which not all CBT-I providers may be familiar with or trained to implement. For example, Jarnefelt et al's[21, 22] adapted CBT-I version specifically tailored sleep hygiene recommendations to shift work, such as scheduling sleep, wake, meals, and exercise appropriately around work shifts, avoiding light and noise exposure during sleep periods, and gaining social support from family members. Lee et al[23] also used a version of CBT-I that was tailored to shift workers; modifications were not specifically detailed. Peter et al[24] modified their protocol for shift workers to report daytime sleep, and their outpatient protocol included bright light treatment between two of the sessions. Future research on this topic should focus on evaluating the effectiveness of specific CBT-I adaptations for treating insomnia symptoms in shift workers.

Melatonin

As with most other treatments studied for shift work disorders, there is significant variability in the dose and timing of melatonin administration relative to daytime sleep with doses in the studies included for this analysis ranging from 0.1-40 mg taken prior to a daytime sleep opportunity. In part this comes from the dual role that melatonin can play, having both sleep promoting and phase resetting effects, depending on the dose and time at which it is received. In addition, it should be noted that there is significant variability in the amount of melatonin present in most over the counter supplements, with at least findings from one study demonstrating actual melatonin levels ranging from –83% to +478% of the labeled content.[25] Chewable and capsule formulations tended to exhibit the greatest variability. These factors should be taken into account when determining the overall efficacy of treatment with melatonin.

Patients Seeking Circadian Adaptation

Most individuals working nights do not align or entrain their circadian rhythm to night shift work[26]; studies show variation among shift workers' phase with many remaining aligned with nighttime sleep. This circadian misalignment leads to shorter sleep duration and less refreshing sleep, as well as eating and being active during the biological night when the body is not prepared, which may contribute to the long-term health effects associated

with shift work including increased rates of cardiovascular disease, obesity, and malignancy. Partial alignment with the night shift, compared to no alignment, has been shown to provide benefit to performance, alertness and mood.[27] As most shift workers return to nighttime sleep on days off, partial alignment is a reasonable goal and is expected to improve both insomnia and neurocognitive symptoms associated with shift work.

Combination treatments

Combination treatments utilize timed bright light + reduced light transmittance glasses + fixed sleep timing or bright light + fixed sleep timing to target circadian adaptation, i.e., assisting the patient's intrinsic rhythm to better align with the required shift work schedule. As a result, the intervention targets and is most effective for those working routine night shifts, and not individuals doing occasional shift work or rotating shifts. Implementation details vary between studies. Bright light was administered 40 minutes prior to the night shifts and in the first hour of typical sleep before starting night shift, or intermittently throughout the night shift. Light strength varied from 2500 to 5500 Lux or "full spectrum bright light via portable lamps".[28] Fixed sleep timing included a dark sleep environment and sleep mask, occurring within 90-120 minutes of the shift ending, and lasting 7-8 hours. Studies with reduced light transmittance glasses utilized these to minimize light during the morning commute home, requiring use from the end of the shift until the sleep period. It should be noted that there may be potential risks to wearing reduced light transmittance glasses while driving, due to concerns about decreased alertness. Future research is needed to assess whether treatments targeting circadian adaptation improve the long-term health concerns such as cardiovascular disease, obesity, and malignancy associated with shift work.

Other Considerations

When considering shift duration, the task force did not seek to comment on overall shift duration recommendations, as this was addressed in a separate paper.[29] For this guideline, we limited our analyses to studies looking at shifts of 12 hours or shorter. Within that context, the available data only compared outcomes from 8-hour shifts to 12-hour shifts and did not demonstrate a difference in outcomes between those specific shift durations. However, these guidelines are not meant to indicate that only shift durations of 8 or 12 hours are recommended as other shift durations were not included in the available studies. Many factors need to be taken into account when considering shift duration, as this will also impact the number of shifts per week, and time off between shifts.

Data regarding planned work schedules reflecting different distributions and rotations of day, evening and night shifts over the course of several work weeks was reviewed for these guidelines, however the studies were deemed to be too heterogeneous to be included in the metanalysis. Studies were primarily field based, often comparing outcomes across two sites within the same company that followed slightly different scheduling patterns. However, within that context, each company followed a slightly different rotation schedule in terms of shift duration, number of days following each shift prior to changing schedule, and number of days off between shifts, so results were not generalizable.

It should also be noted that overall planning of the timing, duration and rotation of work schedules usually requires implementation at an employer level and may not be practical or implementable at an individual patient level.

Future Research Needs

A primary challenge encountered in making treatment recommendations for SWD is that while shift work is common, and many individuals experience symptoms of SWD, very few clinical trials included individuals with a formal diagnosis of SWD. As a result, current treatment strategies have focused primarily on the short-term symptoms of SWD that may be associated with working a shift work schedule, but there are few studies looking at how to mitigate the long-term health consequences of shift work or circadian misalignment. In addition, most shift work studies and models focus on individuals working overnight or rotating shifts. A large segment of the population is required to work early morning shifts, which for most individuals also meet the criteria of having to work during times one would normally be sleeping, resulting in chronic sleep loss and morning circadian misalignment. However, research strategies focused on mitigating sleep loss and long-term health consequences of early morning shift workers are limited. Overall, future research studies should focus on clearly identifying individuals who are experiencing SWD when studying the impact of interventions. In addition, more research is needed into interventions that can both target acute symptoms and mitigate long-term health risks.

REFERENCES

1. Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. *Sleep*. 2007;30(11):1445-59.
2. Pallesen S, Bjorvatn B, Waage S, Harris A, Sagoe D. Prevalence of Shift Work Disorder: A Systematic Review and Meta-Analysis. *Front Psychol*. 2021;12:638252.
3. Wright KP, Abbott SM. Treatment of Extrinsic Circadian Rhythm Sleep Wake Disorder: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *JOURNAL OF CLINICAL SLEEP MEDICINE*. 2025.
4. Wright KP, Abbott SM. Treatment of Extrinsic Circadian Rhythm Sleep Wake Disorder: SUPPLEMENTAL MATERIALS. *JOURNAL OF CLINICAL SLEEP MEDICINE*. 2025.
5. Gunja N, Brown JA. Energy drinks: health risks and toxicity. *Med J Aust*. 2012;196(1):46-9.
6. Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology (Berl)*. 2004;176(1):1-29.
7. Temple JL, Bernard C, Lipshultz SE, Czachor JD, Westphal JA, Mestre MA. The Safety of Ingested Caffeine: A Comprehensive Review. *Front Psychiatry*. 2017;8:80.
8. MEDICATION GUIDE, BELSOMRA® (bell-SOM-rah), suvorexant, Tablets C-IV In: Editor, ed.^eds. MEDICATION GUIDE, BELSOMRA® (bell-SOM-rah), suvorexant, Tablets C-IV. City, 2023.
9. Herring WJ, Connor KM, Ivgy-May N, et al. Suvorexant in Patients With Insomnia: Results From Two 3-Month Randomized Controlled Clinical Trials. *Biol Psychiatry*. 2016;79(2):136-48.
10. Jacobs LG. For older people, medications are common; an updated AGS Beers Criteria(R) aims to ensure they are appropriate, too. *Geriatr Nurs*. 2019;40(2):230-31.
11. Montgomery P, Lilly J. Insomnia in the elderly. *BMJ Clin Evid*. 2007;2007.
12. Drake C, Gumenyuk V, Roth T, Howard R. Effects of armodafinil on simulated driving and alertness in shift work disorder. *Sleep*. 2014;37(12):1987-94.
13. McHill AW, Smith BJ, Wright KP, Jr. Effects of caffeine on skin and core temperatures, alertness, and recovery sleep during circadian misalignment. *J Biol Rhythms*. 2014;29(2):131-43.
14. Carrier J, Fernandez-Bolanos M, Robillard R, et al. Effects of caffeine are more marked on daytime recovery sleep than on nocturnal sleep. *Neuropsychopharmacology*. 2007;32(4):964-72.
15. Muehlbach MJ, Walsh JK. The effects of caffeine on simulated night-shift work and subsequent daytime sleep. *Sleep*. 1995;18(1):22-9.
16. Nunes RA, Mazzotti DR, Hirotsu C, Andersen ML, Tufik S, Bittencourt L. The association between caffeine consumption and objective sleep variables is dependent on ADORA2A c.1083T>C genotypes. *Sleep Med*. 2017;30:210-15.
17. Roehrs T, Roth T. Caffeine: sleep and daytime sleepiness. *Sleep Med Rev*. 2008;12(2):153-62.
18. Hilditch CJ, Dorrian J, Centofanti SA, Van Dongen HP, Banks S. Sleep inertia associated with a 10-min nap before the commute home following a night shift: A laboratory simulation study. *Accid Anal Prev*. 2017;99(Pt B):411-15.
19. Centofanti S, Banks S, Coussens S, et al. A pilot study investigating the impact of a caffeine-nap on alertness during a simulated night shift. *Chronobiology International*. 2020;37(9-10):1469-73.
20. Chellappa SL, Qian J, Vujovic N, et al. Daytime eating prevents internal circadian misalignment and glucose intolerance in night work. *Sci Adv*. 2021;7(49):eabg9910.
21. Jarnefelt H, Sallinen M, Luukkonen R, Kajaste S, Savolainen A, Hublin C. Cognitive behavioral therapy for chronic insomnia in occupational health services: analyses of outcomes up to 24 months post-treatment. *Behav Res Ther*. 2014;56:16-21.

22. Jarnefelt H, Harma M, Sallinen M, et al. Cognitive behavioural therapy interventions for insomnia among shift workers: RCT in an occupational health setting. *Int Arch Occup Environ Health*. 2020;93(5):535-50.
23. Lee KA, Gay CL, Alsten CR. Home-based behavioral sleep training for shift workers: a pilot study. *Behav Sleep Med*. 2014;12(6):455-68.
24. Peter L, Reindl R, Zauter S, Hillemacher T, Richter K. Effectiveness of an Online CBT-I Intervention and a Face-to-Face Treatment for Shift Work Sleep Disorder: A Comparison of Sleep Diary Data. *Int J Environ Res Public Health*. 2019;16(17).
25. Erland LA, Saxena PK. Melatonin Natural Health Products and Supplements: Presence of Serotonin and Significant Variability of Melatonin Content. *J Clin Sleep Med*. 2017;13(2):275-81.
26. Folkard S. Do permanent night workers show circadian adjustment? A review based on the endogenous melatonin rhythm. *Chronobiol Int*. 2008;25(2):215-24.
27. Crowley SJ, Lee C, Tseng CY, Fogg LF, Eastman CI. Complete or partial circadian re-entrainment improves performance, alertness, and mood during night-shift work. *Sleep*. 2004;27(6):1077-87.
28. Boivin DB, Boudreau P, Tremblay GM. Phototherapy and orange-tinted goggles for night-shift adaptation of police officers on patrol. *Chronobiol Int*. 2012;29(5):629-40.
29. Gurubhagavatula I, Barger LK, Barnes CM, et al. Guiding principles for determining work shift duration and addressing the effects of work shift duration on performance, safety, and health: guidance from the American Academy of Sleep Medicine and the Sleep Research Society. *J Clin Sleep Med*. 2021;17(11):2283-306.