Sleep deprivation is a harmful yet common condition among intensive care unit (ICU) patients. Sleep deprivation is associated with emotional distress and has also been theorized to contribute to immune system compromise, cognitive problems, muscular complications, respiratory abnormalities, and prolonged mechanical ventilation. Critically ill patients have increased incidences of reduced sleep efficiency, sleep fragmentation, reduced restorative sleep, and frequent night awakenings. Factors associated with sleep deprivation in the ICU include noise, light, patient-ventilator dyssynchrony, medication effects, and frequent care activities. In 2018, the Society of Critical Care Medicine issued updated clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU, commonly referred to as the PADIS guidelines. These guidelines offer clear, actionable evidence to guide current clinical practice with regard to sleep deprivation in the ICU setting.

Purpose of Review

This purpose of this literature review was to identify evidence-based approaches for addressing sleep deprivation in the ICU. The evidence and recommendations gathered were used to develop a concise clinical resource that may be used to guide care (see Figure). This clinical resource is consistent with the 2018...
ICU Sleep Deprivation Clinical Resource

Purpose: Prevention and treatment of sleep deprivation in the ICU setting

Objectives:
- Provide a resource to address sleep deprivation in the ICU setting
- Promote sleep in the ICU setting
- Establish the role of the interdisciplinary team in addressing sleep deprivation
- Establish guidelines for pharmacological management of sleep disturbance
- Standardize care approaches in addressing sleep disturbance in the ICU

Indications: Adult admission to ICU setting

Contraindications: Frequent neurological examinations, active clinical deterioration; not intended for the pediatric population

Steps:
1. Medical provider will initiate ICU Sleep Deprivation Clinical Resource within 24 hours of ICU admission or transfer.
2. Assessment:
   - RN assessment:
     - Patient’s perception of quality and quantity of nocturnal sleep
     - Number of nighttime awakenings
     - Consider using validated sleep assessment tool to assess sleep
   - Pharmacist assessment:
     - Assess home sleep aid use
     - Consider appropriateness of sleep aid use for inpatient setting
   - Medical provider assessment:
     - Perform medication reconciliation
     - Consider restarting home sleep aids where clinically appropriate
3. Plan: RN will create patient-centered goals regarding sleep.
4. Interventions:
   - Implement nighttime quiet hours.
   - Have ear plugs and eye masks available upon request.
   - Encourage relaxation techniques at desired hour of sleep.
   - Encourage daytime light exposure and nighttime light reduction.
   - Minimize nocturnal sleep interruptions; cluster nighttime care activities to allow 90- to 110-minute intervals of sleep.
   - Maximize daytime nursing care goals to increase daytime activity.
   - Employ interventions for cognitive stimulation; place clocks in room, update wall calendar.
   - Reorient patient frequently; involve family per patient preference.
   - Reduce sedation in daytime hours where clinically appropriate.
   - Address pain, anxiety, and fear.
   - Avoid caffeine intake in afternoon hours and at night.
   - Supply patient’s vision or hearing sensory aids.
   - Provide early progressive mobility.
   - Notify medical provider for signs/symptoms of sleep disturbance (i.e. cognitive problems, delirium, emotional distress, or anxiety related to sleep).
5. Medications: Avoid administration of benzodiazepines or tricyclic antidepressants when possible.

<table>
<thead>
<tr>
<th>Medication</th>
<th>PRN dose</th>
<th>Restart home dose where appropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melatonin</td>
<td>3 mg</td>
<td></td>
</tr>
</tbody>
</table>

Figure Intensive care unit sleep deprivation clinical resource.

Abbreviations: ICU, intensive care unit; PRN, as needed; RN, registered nurse.

PADIS guidelines,2 which indicate that a multicomponent protocol addressing sleep in the ICU may have a positive impact on patients’ perceived sleep quality and may also reduce the incidence of delirium in the ICU.2,6

Methods

A comprehensive literature review was conducted using the electronic databases CINAHL, MEDLINE, and the Cochrane Library. The key search terms used were
Sleep deprivation is becoming an increasingly prevalent problem in the ICU population and can lead to difficulties with sleep well beyond the stage of critical illness. Approximately 80% of ICU patients experience sleep deprivation during their hospital stay. A wide range of factors may affect sleep quality in the complex ICU patient, including medications, preexisting sleep conditions, critical illness, delirium, and cerebral perfusion. The complexity of the problem can make sleep deprivation especially difficult to understand in this population, yet addressing it is an important part of patient care.

Characterization

Sleep deprivation may be a consequence of inadequate amounts of sleep or poor sleep quality. In most cases, critically ill patients and healthy adults have similar total sleep time. However, subjective sleep quality may be reduced in critically ill patients. Moreover, these patients experience increased sleep fragmentation, daytime sleeping, and longer periods of light sleep compared with healthy adults. Mechanical ventilation may worsen sleep fragmentation and circadian rhythm, but these effects have not yet been well established in the literature. Delirium may also affect circadian rhythm cycles, but its overall impact on sleep remains controversial. Several studies have used polysomnography to examine the quantity and quality of sleep in the ICU and found that although patients do achieve some restorative sleep, their sleep is often fragmented.

The greatest disruptions are noted with reductions in deep and rapid eye movement (REM) sleep stages, which are considered the most restorative stages.

Impact of Sleep Deprivation in the ICU

Sleep deprivation in ICU patients has been linked to both short- and long-term consequences. Consequences of sleep deprivation may include immune system compromise, cognitive problems, delirium, emotional distress, muscular complications, and respiratory abnormalities. These alterations may lead to poor weaning times, poor tolerance of noninvasive ventilation methods, poor glucose control in people with and without diabetes, increased anxiety, and increased perceived pain.

Delirium in the ICU is a multifaceted problem that has been linked to sleep deprivation, advanced age, electrolyte disturbance, blood transfusions, dementia, obstructive sleep apnea, preexisting cognitive impairment, the use of benzodiazepines, and increased Acute Physiology and Chronic Health Evaluation scores. Potential harmful effects of delirium include increased morbidity and mortality and reduced functional level in the elderly. When critically ill patients experience delirium, they are at risk for longer hospital stays, with associated higher costs of care, and long-term cognitive impairment.

Sleep deprivation causes disruptions in melatonin levels and circadian rhythm. Studies have demonstrated that these disruptions can lead to the development of delirium. Although controversial, increasing melatonin supply could reduce the incidence of delirium in this population.

Sleep Assessment in the ICU

Sleep is difficult to assess in the ICU environment. Various studies have examined the routine use of physiological sleep monitoring, such as actigraphy or polysomnography (PSG), but have not yielded sufficient evidence to recommend this practice in the critical care population. Although PSG is considered the most reliable
assessment tool, it is not realistic or cost-effective to use PSG to determine sleep quality for every ICU patient.22 In one observational study, the use of actigraphy and behavioral assessment were deemed invalid compared with PSG results.23 Various subjective measurements of sleep have been examined by researchers. Asking the patient about his or her sleep may be helpful in validating the patient’s experience but does not provide objective data on the quality or quantity of sleep.2 Number of awakenings per hour of sleep is a good indicator of the depth of sleep a patient is experiencing and may be used by a bedside clinician to help determine degree of sleep deprivation.13 Another proposed method is the use of subjective nursing assessments of observed sleep.2 When nursing perceptions of ICU patient sleep were compared with patients’ perceptions, although nurses and patients agreed that the patients experienced poor sleep, nurses generally underestimated the amount of sleep deprivation perceived by the patient.2,24

Although it is difficult to assess sleep in the ICU, the PADIS guidelines maintain that sleep should still be routinely monitored and discussed with patients. Informal bedside assessments of sleep are cost-effective and may be validating for patients.2 Additionally, the Richards-Campbell Sleep Questionnaire is a validated and reliable tool that may be appropriate for evaluating critically ill adults who are alert and oriented.2,25

Factors Contributing to Sleep Deprivation in the ICU

Environmental and nonenvironmental factors may play a role in sleep deprivation.2,9 It is beneficial for clinicians to be aware of these factors, as many of them are preventable or should be addressed proactively.2

Nonenvironmental factors that contribute to poor sleep in the ICU include acute illness, pain, medication effects, psychological factors (anxiety/fear/worry/loneliness), preexisting sleep problems, history of taking a home sleep aid, respiratory factors, and ventilators.2,9 The presence of a ventilator may worsen sleep quality through disruption of circadian rhythm and sleep fragmentation.2 This relationship remains controversial, as some researchers have not found a correlation between sleep deprivation and the presence of a ventilator.2 Environmental factors that may contribute to sleep deprivation include noise, frequent patient care activities, an uncomfortable bed, visitors, bad odors, and continuous exposure to light.9 Many factors influencing sleep are modifiable and can be addressed through a standardized approach. Table 1 provides a list of modifiable and nonmodifiable risk factors for sleep disturbance in the ICU.

Management of Sleep Deprivation in the ICU

Several approaches have been proposed to address sleep deprivation in the ICU. If preventive measures have failed, early identification and management of the problem are the next best option.19 Sleep deprivation is multifactorial, and an individualized regimen based on clinical judgment and general practice principles should be implemented as soon as possible.2 A sleep hygiene routine should include goal-directed nursing care.19 Pharmacological approaches may be appropriate in some patients and could include clinically appropriate pain medication and use of sleep aids.2

### Table 1 Major identified risk factors for sleep deprivation in the intensive care unit

<table>
<thead>
<tr>
<th>Modifiable</th>
<th>Nonmodifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain2,3</td>
<td>Poor sleep at home or need for a home pharmacological sleep aid2,25,26</td>
</tr>
<tr>
<td>Medications2,23</td>
<td>Acute illness19</td>
</tr>
<tr>
<td>Psychological factors (eg, anxiety, fear, worry, loneliness)2,3</td>
<td>Respiratory factors2</td>
</tr>
<tr>
<td>Noise19</td>
<td>Presence of ventilators2</td>
</tr>
<tr>
<td>Frequent patient care interventions2,24</td>
<td>Emergent procedures2</td>
</tr>
<tr>
<td>Uncomfortable bed2</td>
<td></td>
</tr>
<tr>
<td>Visitors20</td>
<td></td>
</tr>
<tr>
<td>Bad odors2</td>
<td></td>
</tr>
<tr>
<td>Continuous light exposure2,19</td>
<td></td>
</tr>
</tbody>
</table>

Sleep Deprivation Protocol

The 2018 PADIS guidelines recommend the use of a multicomponent protocol to address sleep deprivation in the ICU.2 Three observational pre-post studies that examined the effects of a sleep-promoting protocol showed mixed results, with some improvement in sleep. However, pooled data analysis of the 3 studies showed a reduction in delirium prevalence.2,5,26

A multicomponent protocol should involve a multidisciplinary care team and include strategies to reduce
modifiable risk factors while also allowing for individualized assessment of patient care needs. For example, the role of families in preventing delirium and promoting sleep remains controversial. To address this issue, providers should assess patient preference for family involvement in sleep promotion. The American Association of Critical-Care Nurses Synergy Model for Patient Care may be helpful when implementing the protocol. This model emphasizes that the patient’s individual needs should be identified and the nurse should seek competency in the areas of the patient’s needs.

Providing care that is consistent with best practice and current medical knowledge is important in reducing harm and optimizing outcomes for patients in all health care settings. Nursing care is particularly helpful in early development of a plan of care that reduces signs and symptoms of delirium as well as the duration of the problem and minimizes sequelae. Goals of nursing care that are associated with better sleep outcomes include improving the patient’s cognitive status, providing a sense of security and safety, and promoting patient comfort. Physician orders for sleep aids and medications to reduce the symptoms of delirium are often left to the discretion of nurses. Nurses can be instrumental in optimizing medication timing and dosing as well as monitoring and reporting side effects and treatment efficacy to medical staff members. Examples of appropriate, cost-effective, and evidence-based nursing interventions are listed in Table 2.

Nonpharmacological Approaches

Several approaches to managing sleep deprivation are available that do not involve medications. Sleep hygiene routines may result in improved patient sleep patterns. Specific sleep hygiene interventions include increasing the patient’s activity and energy expenditure during the day, optimizing mobility through early progressive mobility programs, purposefully varying the amount of ambient light during daytime versus nighttime, clustering nocturnal care activities, and reducing noise. Playing relaxing music in the hour before sleep may be helpful. However, there is insufficient evidence to support the use of music as a routine intervention for sleep deprivation. One case report indicated that back massage may improve the quality of sleep in the ICU setting, but again, this intervention not well validated.

### Table 2 Nursing interventions for delirium prevention and sleep promotion

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reorient patients frequently</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Provide appropriate cognitive stimulation</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Place visible and accurate clocks in patient rooms</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Minimize evening light</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Minimize evening noise (e.g., place noncritical alarms in a central area at a reasonable sound level, provide ear plugs, implement nighttime quiet hours, and avoid unnecessary maintenance such as floor buffing in the evening hours)</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Provide eye covers or ear plugs when not clinically contraindicated</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Promote daytime wakefulness using mobility, daytime visitations, and other appropriate patient activities</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Reduce sedation in daytime hours when clinically appropriate</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Initiate early progressive mobility when clinically appropriate</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Promote use of corrective eye lenses when indicated</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Promote use of hearing aids when indicated</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Avoid use of benzodiazepines when possible</td>
<td>2,27-31</td>
</tr>
<tr>
<td>Do not administer medications to prevent delirium</td>
<td>2,27-31</td>
</tr>
</tbody>
</table>

### Noise Reduction

In 1999, the World Health Organization (WHO) and the US Environmental Protection Agency recognized the adverse effects of noise in their “Guidelines for Community Noise” documents. At night, indoor continuous background noise should not exceed 35 dB and individual bursts of noise should not exceed 40 dB. A common ventilator emits noise that measures approximately 43.5 dB at its baseline function and with alarms can vary from 47.2 dB to 61.2 dB. The adverse effects of noise have been listed as noise-induced hearing impairment; interference with speech communication; disturbance of rest and sleep; psychophysiological, mental-health and performance effects; effects on residential behavior and annoyance; and interference with intended activities.

Many of these factors affect the lives of ICU patients. The WHO noise guidelines discuss noise measurement and noise standards and call for policies to reduce noise that are cost-effective and efficient. In recent years, many hospitals have moved toward implementing “quiet time” hours to address the problem of noise. Tainter et al examined the effects of implementing quiet time...
hours and found that noise levels measured an average of 50 dB at night and 53 dB during the day. Despite strict adherence to nighttime quiet hours, noise levels remained consistently high and above the standards recommended by the WHO and the Environmental Protection Agency.

In a study of 22 ICU patients, Freedman et al. found a correlation between sleep deprivation and environmental noise using polysomnography measurements. Patients’ perceptions of sleep deprivation were often more severe than their actual measured sleep deficit. This finding may indicate that although noise reduction may improve sleep quality and is a cost-effective intervention, factors other than environmental noise are involved in the fragmented sleep patterns seen in the ICU patient population. Clearly, however, efforts should be made to reduce the noise generated by machinery and equipment in the ICU in order to mitigate sleep deprivation.

Reducing the Frequency of Care Interventions. Critically ill patients often require frequent care interventions to maintain an appropriate level of care, which often leads to disruption of sleep patterns for both ventilated and nonventilated patients. Tamburri et al. performed a randomized retrospective review of medical records of 50 patients for 147 nights to evaluate nocturnal care interactions and their effects on sleep. They found a high frequency of nocturnal care interactions, leaving patients with few opportunities for restorative sleep. The study indicated that fewer critical interventions were required around 3 AM, leading the authors to suggest minimizing care interactions around this time to promote sleep. Another study involving 200 patients examined sleep disruptions related to nocturnal nursing interventions from 10 PM to 6 AM. The authors found that approximately 13% of these interventions could have been safely omitted. Moreover, several separate interventions could have been easily clustered into the same patient encounter. Examples are bedding changes, bathing, routine medication delivery, routine radiology examinations, and laboratory blood draws. Routine or serial assessments in stable patients may also be safely deferred when continuous monitoring is in place. Determining the safety of omitting care interactions should be left to the discretion of the multidisciplinary team caring for the patient. The authors recommended promoting nighttime sleep through the use of a protocol or standardized care approach to reduce the frequency of nighttime nursing care interventions. Table 3 provides a more comprehensive list of nursing care activities that occur at night. Individualized nursing plans should be developed to reduce nighttime awakenings while optimizing outcomes in critical care patients.

Table 3  Nocturnal nursing care activities

<table>
<thead>
<tr>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bathing</td>
</tr>
<tr>
<td>Breathing treatments</td>
</tr>
<tr>
<td>Medication delivery</td>
</tr>
<tr>
<td>Intravenous catheter placement</td>
</tr>
<tr>
<td>Intravenous catheter flushing</td>
</tr>
<tr>
<td>Laboratory draws</td>
</tr>
<tr>
<td>Wound care</td>
</tr>
<tr>
<td>Nursing assessments</td>
</tr>
<tr>
<td>Vital sign measurements</td>
</tr>
<tr>
<td>Neurological checks</td>
</tr>
<tr>
<td>Intravenous pump monitoring</td>
</tr>
<tr>
<td>Patient-initiated contact</td>
</tr>
<tr>
<td>Bedding changes</td>
</tr>
<tr>
<td>Routine radiology testing</td>
</tr>
</tbody>
</table>

Eliminating Continuous Light Exposure. Dimming lights at night and purposefully exposing patients to light during the day has been shown to be effective in improving patients’ observed sleep. In her environmental theory, Florence Nightingale recognized the importance of exposing patients to light. She recommended taking patients outside when clinically appropriate and opening the blinds during the day when patients were confined to their rooms. Her primary emphasis was on the importance of exposure to the sun’s rays. These interventions are cost-effective and seem to create a pleasant experience for patients. Although few studies have focused solely on light exposure as a contributor to sleep deprivation, several studies have identified light exposure as a nocturnal irritant for patients. One study showed that inadequate light exposure during the day was associated with worsened sleep patterns.
Medication Adjustment. Medications can influence sleep in both positive and negative ways. Patients admitted to an ICU often have multiple disease processes that require polypharmacy. As reported by Dines-Kalinowski, many ICU patients are prescribed medications such as glucocorticoids, β-blockers, benzodiazepines, morphine, barbiturates, sedative-hypnotics, and analgesics, which are known to reduce deep sleep while promoting sleep in the lighter stages. Dobing et al found that patients who received intravenous sedatives perceived improved sleep patterns. Benzodiazepines, hypnotics, and tricyclic antidepressants can have adverse effects on restorative sleep. These medications have also been associated with poor patient outcomes in the inpatient setting, including cognitive dysfunction, delirium, and falls.

Patients are also at risk for withdrawal symptoms if they were regularly consuming any prescribed or recreational addictive substances at home, such as alcohol, opiates, benzodiazepines, sleeping pills, or tranquilizers. Physical symptoms of withdrawal from these substances may be masked by sedatives and critical illness in the ICU. This situation can result in difficulties during titration of sedatives, including disturbed sleep. Previous use of marijuana, cocaine, and ecstasy may result in emotional withdrawal symptoms that are also problematic for patients during hospitalization. Nicotine users are also at risk for sleep dysregulation during hospitalization, especially if they experience withdrawal. One study showed that patients who were withdrawing from nicotine had an increased arousal index and increased wake times compared with their smoking state. The multidisciplinary care team must be aware of how each medication is affecting the patient and use a team approach to appropriately address the patient’s pharmacological needs through medication reconciliation and interdisciplinary review.

Pharmacological Approach
Pharmacological interventions to promote sleep are often requested by patients and families in the ICU. Clinicians may feel pressured to provide a pharmacological intervention and should be aware of the implications of doing so. Many sleep-promoting medications have adverse side effects and can worsen delirium in critical care patients.

In the pharmaceutical realm of approaches to sleep deprivation, melatonin has received considerable attention. Melatonin is typically taken orally 1 hour before sleep. It helps to regulate circadian rhythm and has been shown to have beneficial effects on the immune system, oxidant activity, and neuroprotection. The 2018 PADIS guidelines contain no recommendation regarding the use of melatonin but recognize its common use as a sleep aid in the ICU environment. Melatonin is relatively inexpensive and has been shown to be safe with minimal side effects (headache and mild sedation). However, its effectiveness in promoting sleep in the ICU remains controversial.

Other medications that have been considered for sleep management include benzodiazepines, nonbenzodiazepines (ie, zolpidem, zopiclone, zaleplon), and antihistamines. In the inpatient setting, benzodiazepines and nonbenzodiazepines have been associated with multiple poor sequelae including falls, delirium, and altered cognition; therefore, their routine use should be avoided. Antihistamines used as sleep aids have shown mixed results with use in the inpatient setting. Their side effects may be more severe or more frequent in the inpatient setting and may include impaired cognition, anticholinergic effects, and cardiac toxicity. Thus, these medications are not recommended for routine use in the inpatient setting.

Sleep experiences of patients receiving and not receiving mechanical ventilation in the ICU have been studied during administration of propofol and dexmedetomidine. Dexmedetomidine has been shown in 2 separate studies to improve the quantity of stage 2 sleep and decrease that of stage 1 sleep, which is considered favorable. However, in these studies, the patients continued to experience sleep fragmentation and did not have any improvement in restorative or REM sleep patterns, which are the most important sleep stages in recovery. Dexmedetomidine is expensive and can result in hypotension and bradycardia when given in high doses. The 2018 PADIS guidelines do not recommend routine use of dexmedetomidine for sleep promotion. However, the guidelines do state that in a patient receiving mechanical ventilation who requires sedative infusion, this drug may be an appropriate choice given its...
favorable profile with regard to sleep structure. Propofol has been examined for use in sleep deprivation in 3 randomized controlled trials. Two trials compared it with benzodiazepines, and the other compared it with placebo. Each study found that sleep was not improved and that the drug actually resulted in REM suppression. Respiratory depression and hemodynamic instability were also observed as side effects. The 2018 PADIS guidelines recommend against using propofol for sleep promotion.

Evidence Gaps

Few studies have specifically addressed sleep in the ICU environment. Of the studies that have been conducted, few have differentiated the various categories of ICU patients affected by sleep deprivation and the effects of such sleep loss. These studies have examined mortality, ICU length of stay, and duration of mechanical ventilation. However, their results are not generalizable to a broader population because of the studies’ small sample sizes. Information is also lacking on the long-term effects of sleep deprivation in the ICU. Among the factors that should be addressed is the impact of ICU sleep deprivation on postdischarge sleep patterns, mental health, and quality of life. Descriptive studies on patient experiences of sleep in the ICU may also provide valuable insight.

Although various sleep assessment tools have been suggested, the reliability and validity of these tools have not been adequately addressed in the ICU setting. Significant alterations to the reliability and validity of these data may be present and require further scrutiny. Current recommendations regarding sleep assessment in the ICU are controversial and require further investigation.

The effects of various pharmacological therapies, particularly in the ICU setting, are poorly understood. Considering the wide range of patients with different comorbidities who are treated in the ICU setting, it would be difficult to determine a single drug approach to managing sleep deprivation.

The use of nurse-driven interventions to address sleep problems has been suggested in the literature but remains controversial. Although substantial evidence exists to suggest that single interventions have little to no effect on sleep or delirium, more information is needed to determine which combination of interventions would be most beneficial in improving patient sleep and reducing the incidence of delirium.

Conclusion

Sleep deprivation is a major problem in the ICU setting. Assessment of sleep deprivation is complicated by elements of critical illness and impeded by lack of adequate research on reliability and validity of cost-effective assessment tools. Prevention is the best approach to dealing with sleep deprivation in the ICU. Management approaches should be multifaceted and include sleep hygiene routines, nursing care plans involving sleep promotion, and appropriate medication regimens. CCN

Acknowledgments

The author acknowledges Dr Lori Passey, University of Utah, for her contributions to this article.

Financial Disclosures

None reported.

See also


References


