Effectiveness of complementary and alternative medicine interventions for sleep quality in adult intensive care patients: A systematic review

Author

Cooke, Marie, Ritmala-Castren, Marita, Dwan, Toni, Mitchell, Marion

Published

2020

Journal Title

International Journal of Nursing Studies

Version

Accepted Manuscript (AM)

DOI

10.1016/j.ijnurstu.2020.103582

Title Page

Title: Effectiveness of complementary and alternative medicine interventions for sleep quality in adult intensive care patients: A systematic review

Authors:

Marie Cooke: School of Nursing and Midwifery and Menzies Health Institute Queensland, Griffith University, Nathan Qld 4111.

Marita Ritmala-Castren: Helsinki University Hospital, FI-00029 HUS, Finland.

Toni Dwan: Artius Health, Labrador Qld, 4215.

Marion Mitchell: School of Nursing and Midwifery and Menzies Health Institute Queensland, Griffith University, Nathan Qld 4111. Princess Alexandra Hospital, Department of Emergency Medicine, Ipswich Rd, Wooloongabba, Qld 4102, Australia

Corresponding author:

Marie Cooke, School of Nursing and Midwifery and Menzies Health Institute Queensland, Griffith University, 170 Kessels Road, Nathan, Queensland, Australia 4111.
Email:m.cooke@griffith.edu.au

What is already known about the topic?

- Sleep has a complex role in both physical and emotional healing
- Broken and fragmented sleep is apparent in intensive care patients.
- The use of complementary and alternative medicine therapies to assist sleep have been studied.

What this paper adds

- Some complementary and alternative medicine interventions, in particular melatonin and music, show promise for improving sleep in intensive care patients.
- Methodological and measurement limitations were apparent, requiring further research

Abstract

Background: Pharmacological interventions for sleep (analgesic, sedative and hypnotic agents) can both disrupt and induce sleep and have many negative side effects within the intensive care population. The use of complementary and alternative medicine therapies to assist with sleep has been studied but given the variety of modalities and methodological limitations no reliable conclusions have been drawn.

Objective: To synthesise research findings regarding the effectiveness of using complementary and alternative medicine interventions within the domains of mind and body practices (relaxation techniques, acupuncture) and natural biologically based products (herbs, vitamins, minerals, probiotics) on sleep quality and quantity in adult intensive care patients.

Review method used: Systematic review

Data sources: Five databases were searched in August 2018 and updated in February 2019 and 2020. Review methods: Searches were limited to peer reviewed randomised controlled trials, published in English involving adult populations in intensive care units. Interventions were related to the complementary and alternative medicine domains of mind and body practices and natural products. Included studies were assessed using Cochrane's risk of bias tool.

Results: Seventeen studies were included. The interventions used varied: 4 investigated melatonin; 4 music +/- another therapy; 3 acupressure; 2 aromatherapy and 1 each for relaxation and imagery, reflexology, bright light exposure and inspiratory muscle training. Measurement of sleep quantity and quality was also varied: 5 studies used objective measures such as Polysomnography and Bispectral index with the remaining using subjective patient or clinician assessment (for example, Richards-Campbell Sleep Questionnaire, Pittsburgh Sleep Quality Index, observation). Given the different interventions, outcomes and measures used in the studies a meta-analysis was not possible. Generally, the results support the use of

complementary and alternative medicine for assisting with sleep with 11 out of 17 trials reporting significant results for the interventions examined.

Conclusions: Complementary and alternative medicine interventions, in particular, melatonin and music, have shown promise for improving sleep in adults with critically conditions; however, further research that addresses the limitations of small sample sizes and improved techniques for measuring sleep is needed.

Keywords: sleep, intensive care, complementary therapies, systematic review

What is already known about the topic?

- Sleep has a complex role in both physical and emotional healing.
- Broken and fragmented sleep is apparent in intensive care patients.
- The use of complementary and alternative medicine interventions to assist sleep have been studied.

What this paper adds

- Some complementary and alternative medicine interventions, in particular melatonin and music, show promise for improving sleep in intensive care patients.
- Methodological and measurement limitations were apparent, requiring further research.

Background

The complex role of sleep in both physical and emotional healing has long been studied, with evidence suggesting that non-rapid eye movement sleep promotes physical healing while rapid eye movement (REM) sleep promotes emotional healing (Vyazovskiy & Delogu, 2014). Given the important role that sleep contributes to healing and the particularly vulnerable condition of most patients in an intensive care unit (ICU), the impact of poor sleep can have an array of negative consequences (Fontana & Pittiglio, 2010). Of concern, the fragmented and broken sleep reported by ICU patients as a result of environmental conditions, therapeutic procedures, medication and mechanical ventilation, contributes to an interruption in the typical 90-minute sleep cycle (Boyko, Ording, & Jennum, 2012). A review of studies investigating sleep disturbance in ICU patients found this included changed circadian rhythm, poor sleep quality, and frequent interruption and wakening with a lack of deeper non-REM sleep and REM sleep (Boyko et al., 2012; Kamdar et al., 2012).

Consequences of sleep deprivation particularly relevant to ICU patients include, but are not limited to, increased pain sensitivity (Figueroa-Ramos, Arroyo-Novoa, Lee, Padilla, & Puntillo, 2009; Lautenbacher, Kundermann, & Krieg, 2006; Onen, Alloui, Gross, Eschallier, & Dubray, 2001), reduced respiratory capacity (Figueroa-Ramos et al., 2009; Phillips, Cooper, & Burke, 1987), impaired immunity (Figueroa-Ramos et al., 2009; Phillips, Cooper, & Burke, 1987), and changes in neuroendocrine and metabolic functions (Figueroa-Ramos et al., 2009; Van Cauter et al., 2007). Additionally, psychological consequences of sleep deprivation include memory and mood deficits (Carlson, 2012; Figueroa-Ramos et al., 2009). Although no studies have identified a direct association between sleep deprivation and delirium, they share common symptoms that have prompted an increased awareness of the link between the two and postulations of the potential mechanisms and pathways involved

(Pisani & D'Ambrosio, 2019). These physical and psychological consequences have an impact on patients' recovery from critical illness and, as Kamdar et al. (2012) suggest, success of sleep interventions will concern secondary outcomes including ICU length of stay and post-ICU recovery and functioning.

Sleep disturbances have traditionally been treated with pharmacological interventions (Abad & Guilleminault, 2015), particularly in hospital settings. A mixture of medications including analgesic, sedative and hypnotic agents are often used in the ICU to reduce patients' pain or awareness of their environment, reduce responses to external stimulation, and facilitate endotracheal tube tolerance and mechanical ventilator synchrony, and not primarily to promote sleep (Bourne & Mills, 2004). However, many negative side-effects have been reported with the use of these medications in the ICU, including impaired cognitive function, risk of dependency, depressed ventilation and negative changes to sleep patterns (Mistraletti et al., 2008). In some cases, the sedative properties of some drugs contribute to poor sleep quality; for example, opiates and barbiturates can decrease non-REM and REM sleep, interfering with both the physiological and emotional healing properties of sleep (Young-McCaughan & Miaskowski, 2001). Hence, analgesic, sedative, and hypnotic agents can both disrupt and induce sleep and have many negative side-effects within the ICU population. Therefore, it is important to investigate alternative options available to assist in the reduction of sleep disturbances without introducing further negative side-effects for already critically ill patients.

One alternative involves the use of complementary and alternative medicine interventions, which are commonplace outside the hospital environment. For the purposes of this systematic review, the term 'complementary and alternative medicine' is used and is defined as the

"broad domain of healing resources that encompasses all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period" (National Institute of Complementary Medicine, https://www.nicm.edu.au/health_information/information_for_consumers/understanding_cm). This includes the domains of mind and body practices (relaxation techniques, acupuncture) and natural products (herbs, vitamins, minerals, probiotics). For example, the endogenous hormone melatonin is considered complementary medicine as it is a natural hormone, which also exists in small amounts in many dietary products (Meng et al 2017) and is sold over the counter in many countries. Complementary and alternative medicine involves a whole-body approach incorporating treatments to address the domains of physiological, emotional, cognitive, and spiritual wellbeing (National Institute of Complementary Medicine).

Investigation into the efficacy of using complementary and alternative medicine interventions to assist with sleep have been many and varied. However, they often lack methodological rigour or sufficient participants to enable reliable conclusions to be drawn (Sarris & Byrne, 2011). Additionally, several systematic reviews investigated the efficacy of complementary and alternative medicine interventions for sleep disturbance; however, they focussed on only one domain, thus limiting the broad conclusions drawn (Sarris & Byrne, 2011).

Two systematic reviews investigated the use of herbal medicines on improving sleep (Yeung et al., 2012; Leach and Page, 2014) and did not find strong evidence or statistical significance for their efficacy. A further two systematic reviews into aromatherapy concluded there may be a small-to-moderate benefit with the use of inhaled lavender oil (Fismer & Pilkington, 2012), and a meta-analysis demonstrated aromatherapy was effective in improving sleep

quality (95% confidence interval [*CI*], 0.54–1.75; *Z*=3.72) (Hwang & Shin, 2015). Differing doses or different essential oils were used in the included studies of these reviews and no studies were conducted in the ICU setting.

Seventeen RCTs examining meditative movement including tai chi, qi gong, and yoga on sleep improvement were synthesised and found to have beneficial effects for various populations on a range of sleep measures; none were conducted in the ICU setting (Wang et al., 2015). Similarly, another systematic review considering the use of acupressure on sleep quality with non-ICU participants concluded "that even fragile populations such as the elderly and dialysis patients can benefit from acupressure" (Waits et al., 2016, p. 24).

A broader systematic review for the treatment of chronic adult insomnia included a range of complementary and alternative medicine interventions and found evidence to support acupressure (d = 1.42-2.12), tai chi (d = 0.22-2.15) and yoga (d = 0.66-1.20) and some evidence for acupuncture and a melatonin precursor L-tryptophan (Sarris & Byrne, 2011). However, the authors (Sarris & Byrne, 2011) noted that many of the studies lacked methodological quality.

Given the lack of reviews investigating an ICU population, the mixed findings and at times reported benefits of complementary and alternative medicine interventions on sleep, and the need to seek alternatives to pharmacological interventions for sleep for patients in the ICU, this systematic review aims to investigate the effectiveness of using complementary and alternative medicine interventions across domains of both mind and body practices and natural products on sleep quality and quantity in adult ICU patients.

Methods

The review protocol was registered with the International Prospective Register of Systematic Reviews (CRD42016043914).

Search strategy

A systematic search was conducted on 2 August 2018 of the following databases: Medline (EBSCO host), CINAHL, PsychINFO, Cochrane library and Scopus. MeSH headings, Keywords, Titles and Abstracts were searched with the following combination of terms:

1. Intensive care OR Critical care OR Acute care OR ICU OR CCU

AND

2. CAM OR complementary medicine OR complementary therap* OR complementary therap* OR alternative medicine OR alternative therap* OR acupuncture OR acupressure OR homeopathy OR herbal medicine OR music therap* OR aromatherap* OR massage OR meditation OR mindfulness OR vitamin supplement* OR kava OR chamomile OR melatonin OR medicinal plants OR plant extracts OR flower remedies OR Chinese medicine

AND

3. Sleep OR sleep quality OR insomnia OR length of stay OR delirium.

Melatonin as a search term for this review was predicated on this being considered a complementary and alternative medicine in many research studies on sleep or other conditions (for example, Gooneratne 2008; Hendren 2013; Kedia 2016). As Gooneratne (2008, p.125) argues, "Melatonin is one of the most thoroughly studied CAM biologic compounds used for sleep", and Clarke, Black, Stussman et al (2015) in their national estimates on the use of complementary health approaches in the United States included

melatonin in their survey of 88,962 adults (combined sample over three time points) and found its use more than doubled from 2007 to 2012.

Selection criteria

Original, peer-reviewed full-text articles were selected for review according to the following criteria:

1. Study design must be an RCT;
2. Adults (≥ 18 years) residing in hospital-based ICU;
3. Published in English;
4. Primary outcomes, quantity or quality of sleep was measured using a validated instrument or nursing observation;
5. Secondary outcomes of delirium measured by a validated instrument and length of stay (LOS) collected through hospital records;
6. Quantitative data were reported concerning sleep quality or quantity, delirium or LOS; and
7. A recognised form of complementary or alternative medicine was used in the intervention.

The initial search was conducted (TD) based on the title and abstract, according to the inclusion and exclusion criteria. After duplicates were removed, one member of the team (TD) screened the titles and abstracts of articles identified for inclusion in the review.
The full texts of the initial set of potentially eligible articles were independently assessed by two authors (MC & MM). Any lack of agreement was discussed to reach consensus regarding article inclusion. Additional searches were conducted in February 2019 and 2020; although

14 new articles were yielded in the 2020 search, all were excluded based on title and abstract with no new studies included.

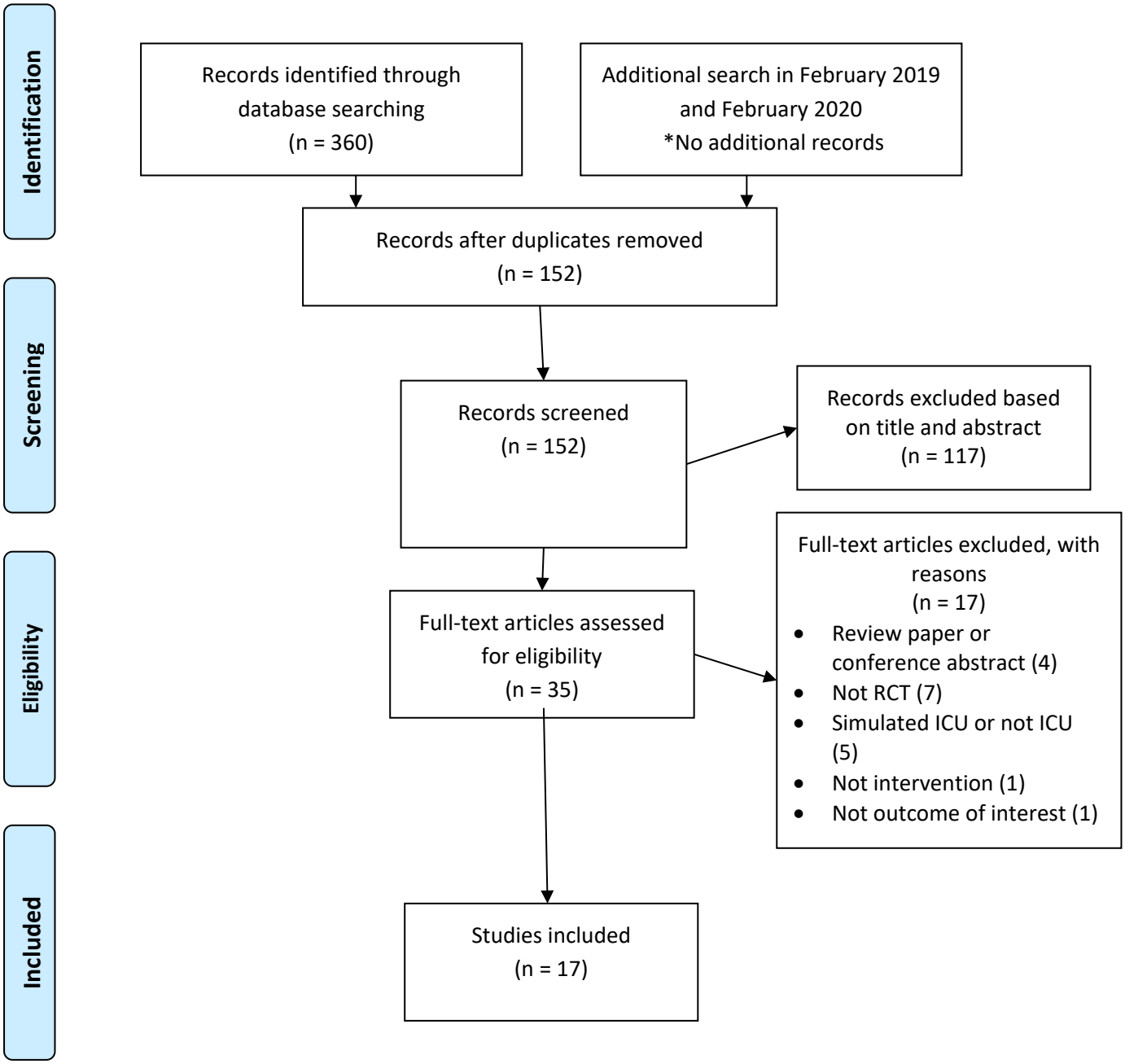

Figure 1. PRISMA flow diagram of search outcomes

Data extraction and quality appraisal

Study methodology and relevant findings were extracted and summarised for all included articles. Methodological quality of the studies was evaluated based on the Cochrane Collaboration's tool for assessing risk of bias (Higgins et al., 2011). Studies were assessed whether they met (YES) the following seven criteria: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data analysis; (6) selective reporting; and (7) other bias. Two authors (MC & MM) independently appraised each study for methodological quality. Discrepancies were resolved through discussion to determine a final rating.

Results

Search outcomes

Figure 1 presents the search results. The initial search yielded a total of 360 articles, which was reduced to 152 articles following duplicate removal. A further 117 were excluded based on title or abstract, leaving 35 articles to be screened for eligibility as full texts. There was 94.12% agreement on study eligibility between the two reviewers. A total of 17 studies involving 520 participants in intervention groups and 409 participants in control groups was included in the review. Table 1 outlines the sample characteristics, intervention, methods, and key findings of the 17 included studies.

Table 1. Characteristics of included studies

Source (Year) Country	Design	Setting	Sample size/ Participant Characteristics	Intervention	Primary outcome Sleep	Secondary outcomes (Delirium, length of ICU stay, length of hospital stay)	Key findings
Akin Korhan et al. (2014) Turkey	RCT Single site	Adult university ICU	Intervention: 30 Control: 30 *M* age = 50.76; *SD* = 15.72 *Male*: *n* = 32 (53.3%) *Female*: *n* = 28 (46.7%) *Severity of illness*: GCS>9 Invasive and non-invasive ventilation support	Reflexology 2 x 30 min reflexology sessions daily for 5 days	Sleep subscale of AACNSAS - sleep scores for intervention group decreased between 1st, 2nd, 4th, and 5th days (NS) Perceived sleep quality improved for intervention group between 1st, 2nd and 3rd days (Significance not reported)		*Reflexology can serve as an effective method of decreasing the required level of sedation in patients receiving mechanically ventilated support.*
Bagheri-Nesam et al. (2015)	RCT Single site	Adult cardiac ICU	Intervention A: 30 Intervention B: 30 Control: 30	Acupressure & Valerian oil	SMHSQ – significant improvement in sleep quality and sleep quantity		*Patients that received acupressure with valerian oil experienced improved sleep quality*

Iran			*M* age = 60.89; *SD* = 11.27 *Male*: *n* = 45 (50%) *Female*: *n* = 45 (50%) *Severity of illness: M* EF = 50.1 Ventilation support not stated	Intervention A: massage with two drops of valerian oil for 2 minutes for 3 nights; Intervention B: Massage 2 minutes for 3 nights without valerian oil	between the control group and both intervention groups ($p < .05$). No significant difference between intervention groups.		
Bourne et al. (2008) UK	RCT Single site	Adult general ICU	Intervention: 12 Control: 12 *M* age = 64.3; *SD* = 12.25 *Male*: *n* = 11 (45.8%) *Female*: *n* = 13 (54.2%) *Severity of illness*: *M* APACHE II = 17.05 Non-invasive ventilation support	Melatonin 10mg was administered at 9 pm for 4 consecutive nights.	BIS, SEI, AUC, RCSQ, OB, SQ Significant difference between groups on BIS-AUC (p = .04). All other differences NS.		*Statistically significant reduction of 7% in BIS AUC with melatonin administration, suggesting sleep improvement.*
Chen et al. (2012)	RCT Single site	Adult general ICU	Intervention: 41 Control: 44	Valerian acupressure	Actigraphy, SSS, OB.		*Valerian acupressure could improve the sleeping time*

Taiwan			*M* age = 70.6; *SD* = 16.65 *Male: n* = 65 (76.4%) *Female: n* = 20 (23.53%) *Severity of illness: M* APACHE II = 12.05 (APS) Ventilation support not stated	Between 7 pm and 10 pm of the 2nd day	Significant difference between groups on Actigraphy measures (sleep hours, minutes awake, waking frequency) and SSS ($p < .001$). OB outcomes NS.		*and quality of ICU patients.*
Foreman et al. (2015) USA	RCT Single site	Adult Neurologic ICU	Intervention: 6 Control: 6 *M* age = 57.5; *SD* = 16.5 *Male: n* = 9 (75%) *Female: n* = 3 (25%) *Severity of illness: M* APACHE II = 11.5 Invasive and non-invasive ventilation support	Melatonin 3mg was administered for 3 days	Polysomnography (TST) Not enough data for adequate analysis	Delirium – developed in one patient from each groups (NS) LOHS between group comparison (NS) LOS-ICU comparison not reported	*Although sleep-promoting interventions were feasible, sleep quantification based on currently accepted criteria limited the ability to score sleep.*

Hajibagheri et al. (2014) Iran	RCT 2 Coronary Care Units of one hospital	Adult Coronary Care Unit (CCU)	Intervention: 30 Control: 30 *M* age = 62.65; *SD* = 10.94 *Male: n* = 25 (41.67%) *Female: n* = 35 (58.33%) *Severity of illness:* EF > 40% Ventilation support not stated	Rosa Dama-scene aromatherapy 3 drops near pillow left for 8 hours	PSQI Significant difference between groups on 5 domains – sleep quality (p = .012), sleep latency (p < .001), sleep duration (p = .042), sleep efficacy (p = .002), sleep disturbances (p = .031).		*Rosa Damascene aromatherapy can significantly improve the sleep quality of patients hospitalized in CCUs.*
Hu et al. (2015) China	RCT Single site	Adult Cardiac surgical ICU	Intervention: 20 Control: 25 *M* age = 56.7; *SD* = 11.1 *Male: n* = 27 (60%) *Female: n* = 18 (40%) *Severity of illness: M* APACHE II = 20.6	Relaxing music with ear plugs and eye masks 30 minutes of relaxing music at the beginning of 1x12 hour nocturnal period, with earplugs and eye masks.	RCSQ Significant difference on 6 subscales – sleep depth (p <.001), sleep latency (p <.001), sleep efficiency (p <.001), quality (p <.001), perceived night-time noise (p = .047)		*This combination of non-pharmacological interventions is useful for promoting sleep in ICU adult patients*

			Invasive Mechanical ventilation support				
Ibrahim et al. (2006) Australia	RCT Single site	Adult university ICU	Intervention: 14 Control: 18 *M* age = 60; *Male: n* = 19 (59.38%) *Female: n* = 13 (40.62%) *Severity of illness: M* APACHE II = 18.5 Invasive Mechanical ventilation support	Melatonin Liquid chromatography -purified dose of 3 mg Administered 8pm for 48 hours or until discharge	OB No significant differences found between groups on observed nocturnal or diurnal sleep		*These high levels of melatonin failed to increase observed nocturnal sleep or induce other observable benefits in tracheostomised ICU patients.*
Karadag et al. (2017) Turkey	RCT Single site	Adult Coronary ICU	Intervention: 30 Control: 30 *M* age = 50.33; *SD* = 12.44 *Male: n* = 40 (66.7%) *Female: n* = 20 (33.3%)	Lavender essential oil aromatherapy Inhalation of 2% lavender oil via 2 drops on gauze attached on clothes12 inches from nose (for 20 mins) before	PSQI A statistically significant improvement in quality of sleep was found for the intervention group.		*Lavender essential oil increased quality of sleep and reduced level of anxiety in ICU patients with coronary artery disease.*

			Ventilation support not stated	sleep for 15 nights			
Mistraletti et al. (2015) Italy	RCT Single site	Adult mixed medical/surgical ICU	Intervention: 41 Control: 41 *M* age = 66.5; *SD* = 15 *Male: n* = 49 (59.76%) *Female: n* = 53 (40.24%) *Severity of illness: M* APACHE II = 44.9 Invasive and non-invasive ventilation support	Melatonin 6 mg per day from 3rd day in ICU until discharge	RASS, OB No significant differences between groups on any sleep variables	LOS-ICU No significant differences between groups on LOS-ICU	*Long-term melatonin supplementation may result in a decreased need for sedation, with improved neurological indicators and cost reduction*
Ono et al. (2011) Japan	RCT Single site	Adult surgical ICU	Intervention: 10 Control: 12 *M* age = 63.6; *SD* = 8.75 *Male: n* = 22 (100%) *Severity of illness: M* APACHE II = 8.2	Bright light exposure 2 hours bright light exposure from 7:30am for 4 days	Accelerometry and Heart rate metre to measure physical activity and autonomic nervous system index. Intervention: 24.1 hours	Delirium – Neelon & Champagne Confusion Scale (NEECHAM) No significant differences between groups	*The occurrence rate of postoperative delirium tended to be lower in the exposure group, but there was no significant difference. None of the participants in the exposure group had NEECHAM Scale scores below the cut-off value from the night of Day 4 onwards.*

			No mechanical ventilation support		Control: 21.9 hours Authors state significant differences for activity, arrhythmia and sympathetic nervous index.		
Richards (1998) USA	RCT Single site	Adult medical cardiovascular acute care	Intervention A: 24 Intervention B: 28 Control: 17 *M* age = 65.8; range, 55 – 79 *Male: n* = 69 (100%) No mechanical ventilation support	Back massage, recorded muscle relaxation, imagery and music Intervention A: 6-minute back massage before sleep on 1 night Intervention B: Teaching session on relaxation, 7.5 minute audio tape at bed time (muscle relaxation, mental imagery,	Polysomnography – SEI Although post hoc test indicated a difference between Intervention A and control the Levene test was violated and tests re-run showing non-significance (p = .06)		*Back massage is useful for promoting sleep in critically ill older men.*

				and relaxing background music)			
Richardson (2003) USA	RCT Multi-site 3 critical care units across 2 hospitals	Adult mixed ICU	Intervention: 16 Control: 20 *M* age = 58.4; *SD* = 14.3 *Male: n* = 17 (47.2%) *Female: n* = 19 (52.8%) Ventilation support not stated	Relaxation and imagery Combination of relaxation and guided imagery delivered on 2 evenings	VSH No significant differences between groups on sleep		*All subjects sleep improved over time. A combination of relaxation and imagery is effective in improving the sleep of the critically ill adult, with men responding immediately to relaxation and imagery with improved sleep, and women taking more time to respond to the intervention.*
Ryu et al. (2012) South Korea	RCT Single site	Adult cardiac care unit	Intervention: 29 Control: 29 *M* age = 61.2; *Male: n* = 38 (65.5%) *Female: n* = 20 (345%) No mechanical ventilation support	Music with earplugs and eye shield Sleep inducing music delivered through earplugs for 52-minutes at 10pm on 1 night	VSH Quantity of sleeping questionnaire Significant difference between groups on quantity of sleep (p =.002)		*Sleep-inducing music significantly improved sleep in patients with percutaneous transluminal coronary angiography at a cardiac care unit*

					And quality of sleep ($p < .001$)		
Savci et al. (2011) Turkey	RCT Single site	Adult cardiac unit	Intervention: 22 Control: 21 *M* age = 60.15; *SD* = 10.09 *Male: n* = 38 (88.37%) *Female: n* = 5 (11.63%) *Severity of illness:* EuroSCORE – Low risk Invasive Mechanical ventilation support	Inspiratory muscle training (IMT) IMT training 2 x 30-minutes per day, for 10 days (5 days pre-operatively,5 days post-operatively)	Sleep subscale – NHP Improved quality of sleep for intervention group ($p < .05$)	LOS-ICU; LOHS Significantly shorter LOS-ICU for intervention group ($p < .05$) LOHS between group comparison (NS)	*IMT results in faster recovery of inspiratory muscle strength, functional capacity, intensive care unit stay, quality of life and psychosocial status after CABG*
Su et al. (2013) Taiwan	RCT Single site	Adult medical ICU	Intervention: 14 Control: 14 *M* age = 61.68; *SD* = 9.82 *Male: n* = 17 (60.7%) *Female: n* = 11 (39.3%)	Sedating music 45-minutes of sedating music on the third night in ICU	Polysomnography VSH Intervention group had significantly shorter stage 2 sleep ($p = .014$), longer stage 3 sleep ($p = .008$)		*Participants in the music group had shorter stage N2 sleep and longer stage N3 sleep in the first 2 hours of the nocturnal sleep and improved self-reported sleep quality, compared with those in the control group*.

			Severity of illness: M APACHE II = 18.57 Invasive and non-invasive ventilation support		and improved sleep quality (p = .012)		
Yaghoubi et al. (2017) Iran	RCT Single site	Adult surgical ICU	Intervention: 30 Control: 30 *M* age = 54.2 *SD* = 7.2 *Male: n* = 40 (66.6%) *Female: n* = 20 (33.3%) Invasive Mechanical ventilation support	Acupressure 15 minutes of acupressure conducted at sleep time for 2 consecutive nights	SMHSQ Intervention group had significantly better quality of sleep (p = .001). Significant decline in sleep quality for the control group between pre and post measures (p < .001). No change for intervention group.		*Acupressure led to significantly better sleep quality for post-CABG patients when compared to a control group.*

Note. AACNSAS – American Association of Critical Care Nurses Sedation Assessment Scale; APS – Acute Physiology Score; AUC – Area under the curve; BIS – Bispectral index; EF – Ejection fraction; GCS – Glasgow Coma Scale; ICU – Intensive Care Unit; IMT – Inspiratory muscle training; LOHS – Length of hospital stay; LOS – Length of stay; NHP – Nottingham Health Profile; NS – Not significant; OB – Observation; PSQI – Pittsburgh Sleep Quality Index; RASS – Richmond Agitation-Sedation Scale; RCSQ – Richards Campbell Sleep Questionnaire; SEI – sleep efficiency index; SMHSQ – St.Mary's Hospital Sleep Questionnaire; SQ – Sleep quantity; SSS – Stanford Sleepiness Scale; TST – Total sleep time; VSH – Verran and Snyder-Halpern sleep scale.

Quality of methodology

As shown in Table 2, the methodological quality of studies was mixed, with only one study meeting all seven quality criteria. (Mistraletti et al., 2015). The main concerns were inappropriate allocation concealment, blinding of outcome assessors, and selective reporting, and only five studies clearly reported that participants or personnel were blinded to study procedures (Bagheri-Nesami, Gorji, Rezaie, Pouresmail, & Cherati, 2015; Bourne, Mills & Minelli, 2008; Ibrahim et al., 2006; G. Mistraletti et al., 2015; Ryu, Park & Park, 2012).

Table 2. Quality of methodology of included studies

	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Akin Korhan 2014	-	-	-	+	+	+	? No protocol registered
Bagheri-Nesam 2015	+	?	+	+	+	?	? No protocol registered
Bourne 2008	+	+	+	?	+	+	? No protocol registered
Chen 2012	+	?	-	?	+	+	+
Foreman 2015	+	+	?	+	+	+	? No protocol registered
Hajibagheri 2014	+	+	-	-	+	+	? No protocol registered
Hu 2015	?	+	-	?	+	+	+

Ibrahim 2006	+	+	+	+	+	+	? No protocol registered
Karadag 2017	-	-	-	?	?	?	? No protocol registered
Mistraletti 2015	+	+	+	+	+	+	+
Ono 2011	+	+	-	-	?	?	? No protocol registered
Richards 1998	?	?	-	+	+	+	? No protocol registered
Richardson 2003	+	?	-	-	+	+	? No protocol registered
Ryu 2012	-	?	+	+	+	+	? No protocol registered
Savci 2011	+	+	?	?	+	+	? No protocol registered
Su 2013	+	+	-	+	+	+	? No protocol registered
Yaghoubi 2017	?	?	-	?	?	?	? No protocol registered

Population

The populations in the included studies ranged across adult critical care areas, with the majority reported to be in medical/cardiac and surgical units.

Interventions

The type of complementary and alternative medicine interventions used in the included studies was mixed (see Table 3). The most prevalent intervention was the hormone, melatonin, utilised in four studies (Bourne, Mills, & Minelli, 2008; Foreman, Westwood, Claassen, & Bazil, 2015; Ibrahim et al., 2006; Mistraletti et al., 2015), and relaxing music, also used in four studies (Hu, Jiang, Hegadoren, & Zhang, 2015; Richards, 1998; Ryu, Park,

& Park, 2012; Su et al., 2013). In two studies, music was combined with the use of earplugs and eye masks (Hu et al., 2015; Ryu et al., 2012); one study compared back massage with combined muscle relaxation, mental imagery, and relaxing background music to a group receiving back massage only (Richards, 1998); and in one study, music designed to promote relaxation was used alone (Su et al., 2013). Acupressure combined with the use of valerian oil was used in two studies (Bagheri-Nesami et al., 2015; Chen, Chao, Lu, Shiung, & Chao, 2012), and acupressure was used alone in one study. Aromatherapy was used in two studies, with one study evaluating the use of the plant Rosa Damascene (Hajibagheri, Babaii, & Adib-Hajbaghery, 2014) and another the use of lavender oil (Karadag, Samancioglu, Ozden, & Bakir, 2017). Other interventions such as relaxation and imagery (Richardson, 2003), reflexology (Akin Korhan, Khorshid, & Uyar, 2014), healing touch (MacIntyre et al., 2008), bright light exposure (Ono, Taguchi, Kido, Fujino, & Doki, 2011), and inspiratory muscle training (Savci et al., 2011) were each used in only one of the included studies.

Assessment of sleep and secondary outcomes

As displayed in Table 3, approaches to assessing outcomes varied across the included studies. Approaches to assessment of sleep quality or quantity included self-report questionnaires, observational methods and diagnostic technology. Additionally, several different instruments and methods were used with each approach. Of the studies directly measuring sleep quality or quantity, seven studies used a self-report approach (Bagheri-Nesami et al., 2015; Hajibagheri et al., 2014; Hu et al., 2015; Karadag et al., 2017; Richardson, 2003; Ryu et al., 2012; Savci et al., 2011); three studies used diagnostic technology (Foreman et al., 2015; Ono et al., 2011; Richards, 1998); and two studies used an observational approach (Ibrahim et al., 2006; Mistraletti et al., 2015). One study used a combination of self-report and observational approaches to measure sleep quality or quantity (Akin Korhan et al., 2014) and another used

a combination of self-report and diagnostic technology (Su et al., 2013). Two studies used a combination of self-report, observational and diagnostic technology approaches to assess sleep quality or quantity (Bourne et al., 2008; Chen et al., 2012).

Further, some studies assessed the intervention effectiveness through secondary measures of delirium or ICU/hospital length of stay (LOS) in combination with sleep-related measures. Two studies included both ICU and hospital LOS as outcome measures (Foreman et al., 2015; Savci et al., 2011) with one study including ICU length of stay alone (Mistraletti et al., 2015). Two of the studies included measures of delirium as an additional outcome in combination with direct measures of sleep quality or quantity (Foreman et al., 2015; Ono et al., 2011).

Table 3. Interventions and outcome measures of included studies

Intervention	**Study**	**Sleep Quality/Quantity**			**Length of Stay (LOS) Intensive Care Unit (ICU) or Hospital**	**Delirium**
		Self-report	**Observational approach**	**Diagnostic technology**		
Melatonin	Bourne et al.	Richards Campbell Sleep Questionnaire	Nurses observation	Bispectral index Actigraphy		
	Foreman et al.			Polysomnography	ICU & Hospital	Clinical diagnosis
	Ibrahim et al.		Nurses observation			
	Mistraletti et al.		Nurses observation		ICU-LOS	
Music only	Su et al.	Verran and Snyder-Halpern Sleep Scale		Polysomnography		
Music with additional techniques • Back massage, recorded muscle relaxation, imagery • Earplugs & eye masks	Richards			Polysomnography		

	Ryu et al.	Verran and Snyder-Halpern Sleep Scale				
	Hu et el.	Richards Campbell Sleep Questionnaire				
Acupressure • stimulation with valerian	Yaghoubi et al.	St.Mary's Hospital Sleep Questionnaire				
	Bagheri-Nesam et al.	St.Mary's Hospital Sleep Questionnaire				
	Chen et al.	Stanford Sleepiness Scale	Nurses' observation	Actigraphy		
Aromatherapy • Rosa Damascene • Lavender	Hajibagheri et al.	Pittsburgh Sleep Quality Index				
	Karadag et al.	Pittsburgh Sleep Quality Index				
Reflexology	Akin Korhan et al.	American Association of Critical-Care Nurses Sedation Assessment Scale	American Association of Critical-Care Nurses Sedation Assessment Scale			
Bright light exposure	Ono et al.			Accelerometre Heart-rate metre		Neelon & Champagne Confusion Scale
Relaxation & imagery	Richardson	Verran and Snyder-Halpern Sleep Scale				
Inspiratory muscle training	Savci et al.	Nottingham Health Profile			ICU & Hospital	

Evidence for the use of complementary and alternative medicines to assist with sleep in the adult ICU

Given the heterogeneous nature of the interventions, outcomes and measurement approaches in the included studies, direct comparisons were not possible. A narrative summary of intervention outcomes follows.

Melatonin. There was mixed evidence for the efficacy of using melatonin to improve sleep in the ICU. Four studies evaluated the use of melatonin with two reporting significant results (Bourne et al., 2008; Mistraletti et al., 2015) and two reporting no significance with the dose of 3 mg (Foreman et al., 2015; Ibrahim et al., 2006). Bourne et al. (2008) (n = 24) found that melatonin 10 mg was associated with increased nocturnal sleep quality as indicated by a decrease in the bispectral index (Area Under Curve [AUC] difference = -54.23, 95% *CI* -104.47 to -3.98; p = .04), and although it did not reach significance, melatonin was associated with a one-hour increase in nocturnal sleep. Results from the study by Mistraletti et al. (2015) (n =82) indicated that daytime sleep, as observed by nurses, significantly decreased in the melatonin 6 mg group (p <.001) and night-time sleep significantly increased (p = .03).

Music. Three of the four music intervention studies reported significant results (Hu et al., 2015; Ryu et al., 2012; Su et al., 2013). Su et al. (2013) (n = 28) using sedating music alone, reported that the intervention group had significantly shorter stage N2 sleep (p = .014) and longer stage N3 sleep (p = .008), measured by polysomnography, and improved sleep quality (p = .012), measured by the Verran and Synder-Halpern Sleep Scale. Both studies that included eye masks and earplugs with relaxing music reported significant results. Using the Richards-Campbell Sleep Questionnaire (RCSQ, participant reported) to measure various

aspects of sleep quality, Hu et al. (2015) (n =45) reported finding significant differences on five subscales: sleep depth (p <.001), sleep latency (p <.001), sleep efficiency (p <.001), quality (p <.001), and perceived night-time noise (p = .047). Ryu et al. (2012) (n = 58), reported a significant difference between groups on sleep quantity (p =.002) and quality (p < .001). The Richards (1998) study, using three groups (back massage, n =28; relaxing music, imagery and muscle relaxation, n = 28; control group, n = 17), found that back massage had greater effect on improving sleep than the music/imagery/muscle relaxation group. Both groups had improved sleep over the control group. However, adjustments due to a violation of Levine's test for equality of variance, rendered the results insignificant (p = .06).

Acupressure. All three included studies testing the efficacy of acupressure with valerian to improve patient sleep in the ICU reported significant results (Bagheri-Nesami et al., 2015; Chen et al., 2012; Yaghoubi et al., 2017). Bagheri-Nesami et al. (2015), using three groups (acupressure with valerian oil, n = 30; acupressure without valerian oil, n = 30; control, n = 30), reported significant improvements in sleep quality and quantity between the control group and both intervention groups (p < .05). No significant difference was found between the two intervention groups. Chen et al. (2012) (n = 85) assessed sleep quality and quantity and reported a significant difference between groups on actigraphy measures (sleep hours, minutes awake, waking frequency) and Stanford Sleepiness Scale (p < .001). Yaghoubi et al (2017), evaluated the use of acupressure as a standalone intervention on sleep quality for people following coronary artery bypass surgery. They reported a significant improvement in the sleep quality of participants in the intervention group (n = 30) compared to the control group (n = 30; p =.001). Additionally, they found that the intervention group maintained the same level of sleep quality between the pre and post measures, whereas the sleep quality of the control group declined significantly between pre and post measures.

Aromatherapy. The two studies evaluating the efficacy of aromatherapy to improve sleep in the ICU reported significant results (Hajibagheri et al., 2014; Karadag et al., 2017). Using Rosa Damascene and measuring outcomes with the Pittsburgh Sleep Quality Index , Hajibagher et al. (2014) (n = 60) reported significant differences between groups on five domains: sleep quality (p = .012), sleep latency (p < .001), sleep duration (p = .042), sleep efficacy (p = .002), and sleep disturbances (p = .031). Karadag et al. (2017) tested the efficacy of using lavender oil (n = 60) and reported that a statistically significant improvement in quality of sleep for the intervention group (p = .006).

Reflexology. Akin Korhan et al. (2014) assessed the efficacy of reflexology to assist patient sleep in the ICU and reported that sleep sub-scale scores for the intervention group decreased between the first, second, fourth, and fifth days: decrease in scores indicated a decrease in sedation needs. Also, the perceived quality of sleep subscale showed an improvement for the intervention group between the first, second, and third days. The analysis was conducted using ANOVA and post hoc results of the individual sleep subscales were not reported.

Bright light exposure. Using an accelerometer instrument that measures the acceleration vector of movements and the number of movements exceeding the baseline as a proxy for measuring sleep and the Neelon and Champagne Confusion Scale to assess delirium, Ono et al. (2011) reported a significant difference in the circadian spectrum cycle after four days of bright light exposure between the intervention group (n = 10) and control group (n = 12) with 24.1 hours in the circadian cycle of the intervention group and 21.9 hours in the control group. The authors reported a tendency towards less delirium in the intervention group; however, the difference did not reach significance.

Relaxation and imagery. Using a combination of relaxation and imagery over two nights Richardson (2003) reported improved sleep in both the intervention group (n = 16) and control group (n = 20) with no significant differences between groups. However, the author reported improvements in the intervention group with men responding immediately to relaxation and imagery with improved sleep, and women taking more time to respond to the intervention.

Inspiratory muscle training. Savci et al. (2011) (n = 43) assessed the efficacy of inspiratory muscle training for improving recovery after coronary artery bypass grafting and reported a significant improvement in sleep quality for the intervention group ($p < .05$). Additionally, they reported that the intervention group had a significantly shorter ICU LOS than the control group.

Discussion

This systematic review examined the effectiveness of using complementary and alternative medicine interventions on sleep quality and quantity in adult ICU patients. Generally, the results support the use of complementary and alternative medicine for assisting with sleep with 11 out of 17 RCTs reporting significant results for the different interventions examined. Melatonin to assist with sleep is one of the most commonly investigated complementary health modalities as it is thought that melatonin plays a role in the sleep-wake cycle and may have sedative effects (Gooneratne, 2008). From this review, the use of melatonin to assist sleep for ICU patients appears promising, but the different doses (3 mg – 10 mg), durations, and formulations studied preclude making any definitive recommendation. Five studies included assessment of secondary outcomes alongside the primary outcome of sleep: three included assessment of length of stay (either ICU or hospital) and two included assessment of

delirium. Although length of ICU stay was significantly reduced in one study (Savci et al., 2011) and less delirium was found in another (Ono et al., 2011), the evidence is too limited but does provide a broad understanding of the evidence around complementary and alternative medicine interventions and sleep.

Given the variability between types of complementary and alternative medicine interventions, outcomes and measures used, it is difficult to draw any conclusions related to the effectiveness of specific interventions. In addition, as the sample sizes of all studies were small, and most were single site studies across a range of critical care environments generalisability of results is limited. Intervention fidelity is also of concern for single-site studies where contamination from the same group of carers is a possibility. Cluster randomised controlled trials involving many critical care sites would be preferable for testing complementary and alternative medicine interventions, but such trials are expensive and complex.

Measurements used in the studies to assess intervention effectiveness varied markedly making it difficult to make comparisons between studies or pool results in a quantitative synthesis. Accurate measurement of sleep in critical care populations is problematic; polysomnography is the gold standard for measuring the quality, quantity and architecture of sleep cycles (Marino et al., 2013), but it is costly, intrusive, and not practical. Another objective measure, bispectral index, uses electroencephalogram monitoring to analyse waveforms to detect levels of consciousness (not specifically sleep), and although this does not require a technician in attendance, as does the PSG, it has practical limitations for use with critically ill patients as it is affected by electrical interferences (Bourne, Minelli, Mills, & Kandler, 2007). Most measurements of sleep on critical care patients use subjective

measurements; one study reported moderate correlation between Richards-Campbell Sleep Questionnaire and polysomnography (Richards, O'Sullivan, & Phillips, 2000) however, the Richards-Campbell Sleep Questionnaire is only able to be used on proportion of critical care patients. Frisk and Nordstrom (2003) reported that only around half of an ICU population were able to respond to the Richards-Campbell Sleep Questionnaire given confusion, inability or unconscious state. Nurses' evaluation of critical care patients' sleep has been shown to be inaccurate (Bourne et al., 2007).

The focus of care by healthcare professionals in critical care settings is by nature interventionalist, given the need for frequent treatments to maintain homeostasis and well-being that interrupt sleep and wake cycles. The acknowledgement of the importance of sleep in this cohort is relatively new and has become more accepted in recent years due to the measurement of delirium which is related to sleep. Delirium has been shown to have long term detrimental effects on the recovery of critical care patients up to 12 months post discharge (Girard et al., 2010; Mitchell, Shum, Mihala, Murfield, & Aitken, 2018) and as delirium is reported in 11% – 80% of critical care populations (Ouimet, Kavanagh, Gottfried, & Skrobik, 2007), the need to examine and promote sleep as a strategy has emerged. Complementary and alternative medicine interventions, in particular, melatonin and music have shown potential for improving sleep; however, further research that addresses the limitation of small sample sizes and improved techniques for measuring sleep is needed.

Limitations

Although a systematic approach and health librarian were used to create comprehensive database search strategies, it is recognised that some studies may have been missed. Only English language studies were included which may have resulted in relevant studies being

excluded. The lack of consistency of complementary and alternative medicine interventions either in dose or composition, together with differing outcome measures and evaluation tools, prevented further quantitative comparative or effectiveness analyses being conducted.

Conclusion

Examining the effectiveness of complementary and alternative medicine interventions to improve sleep in ICU patients is a relatively new area of research and to our knowledge this is the first systematic review of the evidence. Despite the limitations of the studies included in the review there is a promising body of evidence to suggest that some complementary and alternative medicine interventions may support improvement in sleep quantity and for ICU patients.

Acknowledgement

The authors acknowledge the support provided through funding from a successful Seed Grant from the School of Nursing & Midwifery, Griffith University.

References

Abad, V. C., & Guilleminault, C. (2015). Pharmacological treatment of sleep disorders and its relationship with neuroplasticity. In P. Meerlo, R. Benca & T. Abel (eds.) *Sleep, Neuronal Plasticity and Brain Function* (pp. 503-553), Heidelberg: Springe.

Akin Korhan, E., Khorshid, L., & Uyar, M. (2014). Reflexology: its effects on physiological anxiety signs and sedation needs. *Holistic Nursing Practice, 28*(1), 6-23. doi:10.1097/HNP.0000000000000007

Bagheri-Nesami, M., Gorji, M. A. H., Rezaie, S., Pouresmail, Z., & Cherati, J. Y. (2015). Effect of acupressure with valerian oil 2.5% on the quality and quantity of sleep in patients with acute coronary syndrome in a cardiac intensive care unit. *Journal of Traditional and Complementary Medicine, 5*(4), 241-247. doi:10.1016/j.jtcme.2014.11.005

Bourne, R., & Mills, G. (2004). Sleep disruption in critically ill patients–pharmacological considerations. *Anaesthesia, 59*(4), 374-384.

Bourne, R., Mills, G., & Minelli, C. (2008). Melatonin therapy to improve nocturnal sleep in critically ill patients: encouraging results from a small randomised controlled trial. *Crit Care, 12*(2), R52. doi:10.1186/cc6871

Bourne, R. S., Minelli, C., Mills, G. H., & Kandler, R. (2007). Clinical review: Sleep measurement in critical care patients: research and clinical implications. *Crit Care, 11*(4), 226. doi:10.1186/cc5966

Boyko, Y., Ording, H., & Jennum, P. (2012). Sleep disturbances in critically ill patients in ICU: how much do we know? *Acta Anaesthesiol Scand, 56*(8), 950-958. doi:10.1111/j.1399-6576.2012.02672.x

Carlson, N. R. (2012). *Physiology of Behavior*.Boston: engthPearson Education.

Chen, J.-H., Chao, Y.-H., Lu, S.-F., Shiung, T.-F., & Chao, Y.-F. (2012). The effectiveness of valerian acupressure on the sleep of ICU patients: A randomized clinical trial. *Int J Nurs Stud, 49*(8), 913-920.

Clarke, T., Black L., Stussman, B., Barnes M., & Hahin R. (2015). Trends in the use of complementary health approaches among adults: United States, 2002-2012. *National Health Statistics Report*, 79, 1 – 16.

Figueroa-Ramos, M. I., Arroyo-Novoa, C. M., Lee, K. A., Padilla, G., & Puntillo, K. A. (2009). Sleep and delirium in ICU patients: a review of mechanisms and manifestations. *Intensive Care Med, 35*(5), 781-795.

Fismer, K. L., & Pilkington, K. (2012). Lavender and sleep: A systematic review of the evidence. *Eur J Integr Med, 4*(4), e436-e447. doi:https://doi.org/10.1016/j.eujim.2012.08.001

Fontana, C. J., & Pittiglio, L. I. (2010). Sleep deprivation among critical care patients. *Crit Care Nurs Q, 33*(1), 75-81. doi:10.1097/CNQ.0b013e3181c8e030

Foreman, B., Westwood, A. J., Claassen, J., & Bazil, C. W. (2015). Sleep in the neurological intensive care unit: feasibility of quantifying sleep after melatonin supplementation with environmental light and noise reduction. *Journal Of Clinical Neurophysiology, 32*(1), 66-74. doi:10.1097/WNP.0000000000000110

Frisk, U., & Nordstrom, G. (2003). Patients' sleep in an intensive care unit--patients' and nurses' perception. *Intensive Crit Care Nurs, 19*(6), 342-349.

Girard, T. D., Jackson, J. C., Pandharipande, P. P., Pun, B. T., Thompson, J. L., Shintani, A. K., Gordon, S., Canonico A., Dittus, R., Bernard G. & Ely, E. W. (2010). Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med, 38*(7), 1513-1520. doi:10.1097/CCM.0b013e3181e47be1

Gooneratne, N. S. (2008). Complimentary and Alternative Medicine for Sleep Disturbances in Older Adults. *Clin Geriatr Med, 24*(1), 121-viii. doi:10.1016/j.cger.2007.08.002

Hajibagheri, A., Babaii, A., & Adib-Hajbaghery, M. (2014). Effect of Rosa damascene aromatherapy on sleep quality in cardiac patients: a randomized controlled trial. *Complement Ther Clin Pract, 20*(3), 159-163. doi:10.1016/j.ctcp.2014.05.001

Hendren R. (2013). Autism: Biomedical complementary treatment approaches. *Child Adolesc Psychiatric Clin N Am,* 22, 443-456.

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savovic, J., Schulz, K., Weeks, L., Sterne, J. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ, 343*, d5928.

Honkus, V. L. (2003). Sleep deprivation in critical care units. *Crit Care Nurs Q, 26*(3), 179-189; quiz 190-171.

Hu, R. F., Jiang, X. Y., Hegadoren, K. M., & Zhang, Y. H. (2015). Effects of earplugs and eye masks combined with relaxing music on sleep, melatonin and cortisol levels in ICU patients: a randomized controlled trial. *Crit Care, 19*, 115. doi:10.1186/s13054-015-0855-3

Hwang, E., & Shin, S. (2015). The effects of aromatherapy on sleep improvement: a systematic literature review and meta-analysis. *J Altern Complement Med, 21*(2), 61-68.

Iber, C., Ancoli-Israel, S., Chesson, A. L., & Quan, S. F. (2007). *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications.* Westchester, IL.: American Academy of Sleep Medicine.

Ibrahim, M. G., Bellomo, R., Hart, G. K., Norman, T. R., Goldsmith, D., Bates, S., & Egi, M. (2006). A double-blind placebo-controlled randomised pilot study of nocturnal melatonin in tracheostomised patients. *Critical Care And Resuscitation, 8*(3), 187-191.

Karadag, E., Samancioglu, S., Ozden, D., & Bakir, E. (2017). Effects of aromatherapy on sleep quality and anxiety of patients. *Nursing In Critical Care, 22*(2), 105-112. doi:10.1111/nicc.12198

Kamdar, B., Needham, D., & Collop, N. (2012). Sleep deprivation in critical illness: Its role in physical and psychological recovery. *Journal of Intensive Care Medicine*, 27(2), 97-111.

Kedia, S. (2016). Complementary and Integrative Approaches for Pediatric Headache. *Seminars in Pediatric Neurology*, 23, 44-52.

Lautenbacher, S., Kundermann, B., & Krieg, J. C. (2006). Sleep deprivation and pain perception. *Sleep Med Rev, 10*(5), 357-369.

Leach, M. J., & Page, A. T. (2014). Herbal medicine for insomnia: A systematic review and meta-analysis. *Sleep medicine reviews, 24*, 1-12. doi: 10.1016/j.smrv.2014.12.003

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., . . . Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS medicine, 6*(7), e1000100.

MacIntyre, B., Hamilton, J., Fricke, T., Ma, W., Mehle, S., & Michel, M. (2008). The efficacy of healing touch in coronary artery bypass surgery recovery: a randomized clinical trial. *Alternative Therapies In Health And Medicine, 14*(4), 24-32.

Marino, M., Li, Y., Rueschman, M. N., Winkelman, J. W., Ellenbogen, J. M., Solet, J. M., Dulin, H., Berkman, L. &. Buxton, O. M. (2013). Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. *Sleep, 36*(11), 1747-1755. doi:10.5665/sleep.3142

Meng, X., Li Y., Li, S., Zhou, Y., Gan R., Xu, D., & Li, H. (2017). Dietary Sources and Bioactivities of Melatonin. *Nutrients,* 9, 367. doi:10.3390/nu9040367

Mistraletti, G., Carloni, E., Cigada, M., Zambrelli, E., Taverna, M., Sabbatici, G., Ombrello, M., Elia, G., Destrebecq, A., & Iapichino, G. (2008). Sleep and delirium in the intensive care unit. *Minerva Anestesiol, 74*(6), 329-334.

Mistraletti, G., Umbrello, M., Sabbatini, G., Miori, S., Taverna, M., Cerri, B., Mantovani, E., Formenti, P., Spanu, P., D'Agostino, A., Salini, S., Morabito, A., Fraschini, F., Reiter, R. & Iapichino, G. (2015). Melatonin reduces the need for sedation in ICU patients: A randomized controlled trial. *Minerva Anestesiol, 81*(12), 1298-1310.

Mitchell, M. L., Shum, D. H. K., Mihala, G., Murfield, J. E., & Aitken, L. M. (2018). Long-term cognitive impairment and delirium in intensive care: A prospective cohort study. *Aust Crit Care, 31*(4), 204-211. doi:10.1016/j.aucc.2017.07.002

National Center for Complementary and Integrative Health. Complementary, Alternative, or Integrative Health: What's In a Name? Retrieved September 2019 from https://nccih.nih.gov/health/integrative-health

National Institute of Complementary Medicine. Understanding Complementary and Integrative Medicine. Retrieved September 2019 from https://www.westernsydney.edu.au/nicm/health_information/information_for_consumers/understanding_cm

Onen, S. H., Alloui, A., Gross, A., Eschallier, A., & Dubray, C. (2001). The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. *Journal of Sleep Research, 10*(1), 35-42.

Ono, H., Taguchi, T., Kido, Y., Fujino, Y., & Doki, Y. (2011). The usefulness of bright light therapy for patients after oesophagectomy. *Intensive Crit Care Nurs, 27*(3), 158-166. doi:10.1016/j.iccn.2011.03.003

Ouimet, S., Kavanagh, B. P., Gottfried, S. B., & Skrobik, Y. (2007). Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med, 33*(1), 66-73. doi:10.1007/s00134-006-0399-8

Phillips, B. A., Cooper, K. R., & Burke, T. V. (1987). The effect of sleep loss on breathing in chronic obstructive pulmonary disease. *Chest, 91*(1), 29-32.

Pisani, M., & D'Ambrosio, C. (2019). Sleep and delirium in adults who are critically ill: A contemporary review. *Chest*, doi:https://doi.org/10.1016/j.chest.2019.12.003

Porkka-Heiskanen, T., Zitting, K. M., & Wigren, H. K. (2013). Sleep, its regulation and possible mechanisms of sleep disturbances. *Acta Physiol 208*(4), 311-328. doi:10.1111/apha.12134

Richards, K. C. (1998). Effect of a back massage and relaxation intervention on sleep in critically ill patients. *American Journal Of Critical Care, 7*(4), 288-299.

Richards, K. C., O'Sullivan, P. S., & Phillips, R. L. (2000). Measurement of sleep in critically ill patients. *J Nurs Meas, 8*(2), 131-144.

Richardson, S. (2003). Effects of relaxation and imagery on the sleep of critically ill adults. *Dimensions Of Critical Care Nursing: DCCN, 22*(4), 182-190.

Ryu, M.-J., Park, J. S., & Park, H. (2012). Effect of sleep-inducing music on sleep in persons with percutaneous transluminal coronary angiography in the cardiac care unit. *Journal Of Clinical Nursing, 21*(5/6), 728-735. doi:10.1111/j.1365-2702.2011.03876.x

Sarris, J., & Byrne, G. J. (2011). A systematic review of insomnia and complementary medicine. *Sleep Med Rev, 15*(2), 99-106. doi:https://doi.org/10.1016/j.smrv.2010.04.001

Savci, S., Degirmenci, B., Saglam, M., Arikan, H., Inal-Ince, D., Turan, H. N., & Demircin, M. (2011). Short-term effects of inspiratory muscle training in coronary artery bypass graft surgery: a randomized controlled trial. *Scand Cardiovasc J, 45*(5), 286-293. doi:10.3109/14017431.2011.595820

Su, C.-P., Lai, H.-L., Chang, E.-T., Yiin, L.-M., Perng, S.-J., & Chen, P.-W. (2013). A randomized controlled trial of the effects of listening to non-commercial music on quality of nocturnal sleep and relaxation indices in patients in medical intensive care unit. *J Adv Nurs, 69*(6), 1377-1389. doi:10.1111/j.1365-2648.2012.06130.x

Van Cauter, E., Holmbäck, U., Knutson, K., Leproult, R., Miller, A., Nedeltcheva, A., Pannain, S., Penev, Pl, Tasali, E. & Spiegel, K. (2007). Impact of sleep and sleep loss on neuroendocrine and metabolic function. *Horm Res Paediatr, 67*(Suppl. 1), 2-9.

van der Helm, E., Yao, J., Dutt, S., Rao, V., Saletin, J. M., & Walker, M. P. (2011). REM sleep depotentiates amygdala activity to previous emotional experiences. *Curr Biol, 21*(23), 2029-2032. doi:10.1016/j.cub.2011.10.052

Vyazovskiy, V. V., & Delogu, A. (2014). NREM and REM Sleep: Complementary Roles in Recovery after Wakefulness. *Neuroscientist, 20*(3), 203-219. doi:10.1177/1073858413518152

Waits, A., Tang, Y.-R., Cheng, H.-M., Tai, C.-J., & Chien, L.-Y. (2016). Acupressure effect on sleep quality: A systematic review and meta-analysis. *Sleep Med Rev, 37*, 24-34. doi:10.1016/j.smrv.2016.12.004

Wang, F., Eun-Kyoung Lee, O., Feng, F., Vitiello, M. V., Wang, W., Benson, H., Fricchione, G. & Denninger, J. W. (2015). The effect of meditative movement on sleep quality: A systematic review. *Sleep Med Rev, 30*, 43-52. doi:10.1016/j.smrv.2015.12.001

Yaghoubi, A., MD; Golfeshan, E., Azarfarin, R., Nazari A., Alizadehasl, A., Ehasni, A. (2017). Effects of Acupressure on Sleep Quality After Coronary Artery Bypass Surgery. *Iranian Heart Journal* , 18(3), 28-34

Yeung, W.-F., Chung, K.-F., Man-Ki Poon, M., Yan-Yee Ho, F., Zhang, S.-P., Zhang, Z.-J., Tat-Chi Ziea, E. & Wong, V. T. (2012). Chinese herbal medicine for insomnia: A systematic review of randomized controlled trials. *Sleep Med Rev, 16*(6), 497-507. doi:10.1016/j.smrv.2011.12.005

Young-McCaughan, S., & Miaskowski, C. (2001). Definition of and mechanism for opioid-induced sedation. *Pain Manag Nurs, 2*(3), 84-97. doi:10.1053/jpmn.2001.25012