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Tucked In: Weighted Blankets to Improve Sleep in Intensive Care Unit Patients

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TUCKED IN: WEIGHTED BLANKETS TO IMPROVE SLEEP IN INTENSIVE CARE UNIT PATIENTS

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ABSTRACT

Sleep deprivation is ubiquitous in hospital settings and deleterious to patients' health. Specifically, sleep deprivation has been reported to play a role in multiorgan dysfunction, leads to poor critical illness outcomes, and can be considered a risk factor for delirium, a highly prevalent disease in intensive care units with even greater implications. To date, there are no evidence-based pharmacological interventions for sleep deprivation, and have even resulted in more adverse effects. However, non-pharmacological solutions have had limited efficacy, displaying a need for novel therapeutic options**. In this randomized control trial, we will investigate and compare mean lengths of total sleep time between weighted blankets and standard of care in adults hospitalized in intensive care units.** This non-pharmacological intervention for sleep deprivation may help enhance sleep and improve overall health outcomes.

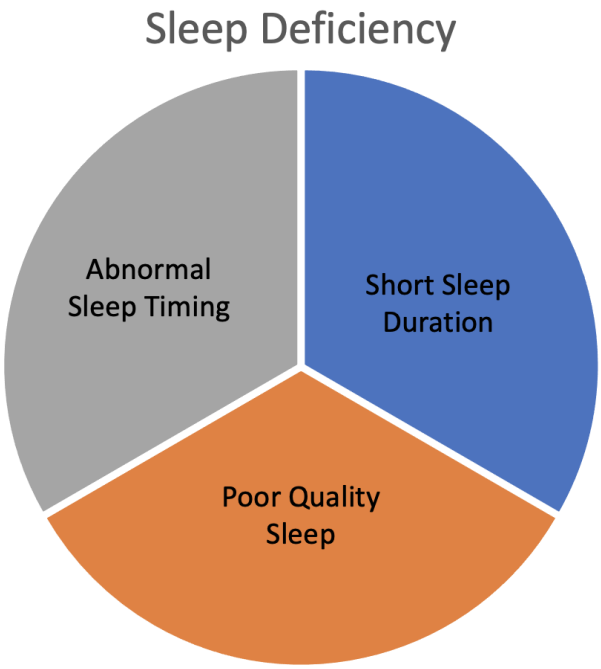
CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 Sleep and Critical Care

Sleep is a crucial physiological process and plays a central role in promoting overall health.[1] Sleep deficiency is an encompassing term including short sleep duration, poor sleep quality, and abnormal sleep timing. Chronic sleep deficiency has been shown to have a negative effect on cardiovascular disease, cancer, diabetes, depression, and immune function.[1,2] Similarly, acute sleep deficiency has been found to increase the risk of both infectious and inflammatory diseases, and contribute to all-cause mortality. [3-5]

Figure 1: Aspects of sleep deficiency



Research shows that poor sleep is especially ubiquitous and deleterious in patients in critical care settings, at a time when their body arguably most needs adequate sleep for

healing, research.[6] In the intensive care unit (ICU), patients have been found to experience a all domains of sleep deficiency (i.e. short sleep duration, poor quality sleep, and abnormal sleep timing). Polysomnography (PSG), the gold standard in the objective measurement of sleep, studies have demonstrated a decrease in total sleep time, frequent awakenings, and changes in sleep stages including dramatic decreases in slow wave and rapid eye movement (REM) sleep stages.[7] Patients also have circadian rhythm disruptions with increased poor-quality daytime sleep and more frequent nighttime awakenings. In the hospital, environmental factors such as increased noise pollution, abnormal lighting schedule, and frequent around-the-clock care can lead to sleep deficiency.[7-9] Other contributing factors to poor sleep include chronic sleep disorders, acute illness-related factors, and medical interventions such as medications. In addition, the stress and anxiety of requiring ICU admission can contribute to insomnia, as emotional state and difficulty initiating/maintaining sleep have proven to be interrelated.[10] As an average length of stay in an ICU can span multiple nights, the culmination of all of these factors can lead to profound acute sleep deprivation. This has been found to have long-standing implications of sleep deficiency in critically ill patients up to twelve months after hospital discharge.[11]

Sleep deprivation can play a role in multiorgan dysfunction that hinders critical illness recovery and thus leads to poor critical illness outcomes. One current area of investigation is the overlap between sleep deprivation and ICU delirium. Delirium is an acutely, reversible disturbed state of mind characterized by restlessness, illusions, and incoherence of thought and speech. Delirium is highly prevalent in the ICU and is associated with increases in mortality, cognitive impairment and hospital length of stay.[12-14] There have also been studies demonstrating increase in days of delirium in the

ICU being directly related to increase in 1-year mortality.[15] Sleep deprivation and delirium are believed to share similar mechanisms in neurohormonal changes and imbalances in neurotransmitters. Experimentally, specific regional brain activity shown on lesion studies and functional imaging studies implicate the prefrontal and the nondominant parietal cortices for both.[14] Clinically, the two issues are similar in poor thought processing, attention and memory deficits, and fluctuating mental status. Studies have found that quality improvement interventions to improve sleep have been associated with significant improvement in incidence of delirium.[16] Given the interrelatedness of the two conditions, sleep deprivation can be considered a possible modifiable risk factor for delirium, a condition which, as discussed, has tremendous implications in the critical care setting.

Sleep deprivation is pervasive in the hospital, especially in the ICU. There are no evidence-based pharmacologic interventions available to treat sleep deprivation or delirium in the critically ill and efforts to enhance sleep medically can result in even more adverse effects. For this reason, non-pharmacological strategies may prove to be more efficacious.[17] Some non-pharmacological interventions have been explored including earplugs and eye masks, aromatherapy massage, and cluster nursing care during night time hours.[18-20] These interventions have shown some promise for subjective perceptions of sleep. The lack of concrete options and objective measures of outcome for non-pharmacological interventions for sleep deficiency leaves more to be explored.

1.1.2 Measuring Sleep

In general, measuring sleep in the ICU is difficult to carry out. The gold standard for diagnosing sleep disorders has been overnight, in-laboratory PSG. PSG includes

measures of EEG (electroencephalogram), electrooculogram (EOG), chin and limb electromyogram, oronasal flow, thoracoabdominal movement, electrocardiogram, and pulse oximetry. [21] PSG has been adapted to be more portable and can be left on patients in the ICU without direct observation. However, PSG has a high cost, practical difficulties with implementation, and can be uncomfortable for patients who are critically ill.

An alternative to PSG is actigraphy, a small accelerometer sensor that measures levels of physical activities and distinguishes between periods of wakefulness and sleep through body motions. It is worn on the wrist similar to a watch and has no tethering wires. In normal healthy adult populations, actigraphy has significant correlation and agreement with PSG.[22] Its primary use in clinical practice is in the assessment of sleep schedules and sleep quality in a non–critically ill population; however, a few studies have used actigraphy to measure sedation/agitation in the ICU.[23] These studies indicate that actigraphy correlates with nurse-directed observation of agitation, sleep, and sedation in alert and calm patients.[24] For Total Sleep Time (TST), a frequently used measure of sleep, agreement between actigraphy and PSG has been shown to be above 90%.[25] For these reasons, actigraphy better option for longitudinal monitoring and is a less invasive, less cumbersome, and more cost-effective method to objectively measure sleep.

For a subjective measure of sleep, the Richards Campbell Sleep Questionnaire (RCSQ) is the only validated tool in critically ill patients. The RCSQ has been found to significantly correlate with corresponding PSG measures.[26] The items are constructed on a visual analog scale (VAS), which has study subjects mark a point on a line that indicates intensity of sensation. The benefit of this style of questioning is that it only

requires ill patients with declined physical stamina to make a single tick mark. RCSQ is able to add a subjective measure in a validated way against objective measures like PSG and actigraphy.

1.1.3 Weighted Blankets

Weighted blankets are blankets of various sizes filled with beads, chain, or other materials to increase the weight of a standard sleeping blanket in an even distribution. They have been increasingly used in various settings as a method of providing Deep Touch Pressure (DTP), or Deep Pressure Stimulation (DPS), to alleviate anxiety and increase sleep in various populations. DTP is a type of touch pressure that provides mechanical stimulation and deformation of the skin and underlying tissues, and has been compared to the sensation of a firm hug, holding, swaddling, or massage. It has been shown to improve arousal modulation, leading to a feeling of calmness.[27] Outcomes such as symptom severity in neonates with neonatal abstinence syndrome (NAS) and autonomic responses while undergoing third molar extractions have been evaluated.[27,28] However, the primary focus of weighted blanket studies have been in sleep and anxiety.

Weighted blankets have been studied in the context of sleep in a wide variety of patient populations with a range of results. Two separate weighted blankets studies on sleep deficiency. A quasi-experimental study found that weighted blankets decreased insomnia and sleep disturbance in children with autism spectrum disorder (ASD).[29] A level IV single-subject design study similarly found that weighted blankets decreased insomnia, but in adults with chronic insomnia.[30] Another study, a randomized control trial (RCT) on children with ASD found that weighted blankets did not improve objective

sleep quality, but that they were favored by participants and subjectively contributed to better sleep.[29]

Weighted blankets use has also been studied in anxiety. A RCT with crossover design was performed in outpatient chemotherapy infusion center, and was shown to reduce anxiety among patients receiving chemotherapy when the blanket was used.[31] Another exploratory study discovered that 78% of non-hospitalized participants self-reported being more relaxed when using weighted blankets.[32] In a pilot study of weighted blankets in acute inpatient psychiatric units, individuals who used the weighted blanket reported significantly greater reductions in distress.[33] As previously mentioned, ICU admission has been linked to increased anxiety, and anxiety has been linked to sleep disturbance in a mutually influencing cycle.[30] A key mechanism of minimizing sleep disturbance in the ICU would be the mitigation of anxiety.

1.2 Statement of the Problem

Sleep deficiency is pervasive in the critically ill, with no evidence-based pharmacological interventions shown to be effective. Pharmacological interventions can lead to increased adverse effects and drug interactions. For this reason, non-pharmacological strategies must continue to be explored. Currently, the Yale New Haven Hospital (YNHH) medical ICU has a sleep protocol in place utilizing some non-pharmacological techniques, in which from midnight to 4:00 AM, there are no overhead pages, no routine labs or diagnostic testing, and an effort to cluster care by the nursing staff. In addition, patients receive a quiet pack with a card to remind all to be courteous with noise levels, ear plugs, headphones, and an eye mask. There is no formal signal or cue to sleep. There are limited options other than those currently provided to all patients.

Despite these interventions, patients still report poor sleep in the hospital, with disturbances lasting even after discharge.[11] For this reason, it is necessary to continue evaluating different approaches.

Weighted blankets have been shown to help with sleep and anxiety in a variety of populations and settings, including autistic children and adolescents, adult psychiatric inpatient centers, during dental procedures, breast cancer patients in inpatient and outpatient settings, and more. However, there is a lack of literature in this population of hospitalized critically ill adults, where sleep is especially critical, yet jeopardized.

1.3 Goals and Objectives

The overall goal of this study is to investigate whether weighted blankets increase overnight sleep in adult critically ill patients. In this randomized control trial, the primary aim is to investigate and compare mean lengths of TST, measured by actigraphy, between weighted blankets and standard of care in adults hospitalized in the medical ICU. A secondary aim is to determine whether patients subjectively feel that the blanket improves their sleep via RCSQ and whether they enjoy the blanket's use.

1.4 Hypothesis

Weighted blankets used in hospitalized patients over 50 years old in the medical ICU will be associated with an increase in mean TST (minutes) when compared to baseline of those with usual care.

1.5 Definitions

Weighted Blanket: A blanket of various sizes, filled with beads, chain, or other materials to increase the weight of a standard sleeping blanket in an even distribution. They have

been most often used within the scope of occupational therapy practice as a therapeutic modality. The theoretical framework of their use comes from the concept of Deep Touch Pressure (DPT).

Deep Touch Pressure (DTP): Firm tactile sensory input that provides proprioceptive input to the whole body. Examples include firm hugs, firm stroking, cuddling, hugging, squeezing, compression, or swaddling that aims to relax the nervous system. It is considered a sensory-based intervention to relieve anxiety.

Deep Pressure Stimulation (DPS): DPS and DPT are often used interchangeably. For the purpose of this discussion, we will use DPT as the preferred term.

Total Sleep Time (TST): The amount of time that a person spends actually asleep during a planned sleep episode.

Actigraphy: The use of an actigraph to make a record of the activity level of the body, especially when measuring the amount and quality of sleep by sensing physical movement. An actigraph is a small device usually worn on the wrist.

Richards Campbell Sleep Questionnaire (RCSQ): The only validated tool in critically ill patients to subjectively assess sleep. It is a composed of five questions that patients answer using a VAS (0-100mm). The questions relate to sleep depth, sleep latency, number of awakenings, returning to sleep, and sleep quality.

1.6 Abbreviations

Table 1. Abbreviations used throughout proposal

ICU	Intensive Care Unit
PSG	Polysomnography
REM	Rapid Eye Movement
EEG	Electroencephalogram
EOG	Electrooculogram
TST	Total Sleep Time
RCSQ	Richards Campbell Sleep Questionnaire
VAS	Visual Analog Scale
DTP	Deep Touch Pressure
DPS	Deep Pressure Stimulation
NAS	Neonatal Abstinence Syndrome
ASD	Autism Spectrum Disorder
YNHH	Yale New Haven Hospital

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CHAPTER 2: REVIEW OF THE LITERATURE

2.1 Introduction

The literature review search was conducted with initial review in June 2020 and final review in March 2021 using PubMed, Ovid (Embase), and Cochrane. MeSH terms for primary searches included combinations of the terms “Intensive Care Units”, “Weighted Blankets”, “Sleep Disruption”, and “Sleep Disturbance”. Additional search terms included “Deep Touch Pressure”, “Deep Pressure Stimulation”, “Chain Blanket”, “actigraphy”, “sleep-wake disorders”, and “critical illness.” Articles were filtered based on English language and analyzed for relevance to this proposed study. Additional pertinent articles were extracted and compiled from the references of relevant articles.

Searches revealed over 1,500 articles related to sleep in the critically ill, which shows just how extensive, common, and deleterious sleep deprivation is in this population. Conversely, searches yielded less than 10 studies related to weighted blankets, demonstrating a gap in the literature, and the need for studies into this potential non-pharmacological approach to enhancing sleep.

2.2 Review of Empirical Studies

2.2.1 Sleep Deficiency in the ICU

ICUs have been a central location where physicians, nurses, and other healthcare staff have cared for the most critically ill since their inception in the 1960s.[1] Given a multitude of factors, including chronic sleep disorders at baseline, acute critical illnesses, medical interventions, and the ICU environment, sleep in this setting is often deficient.[2] Sleep in the ICU meets all standards of sleep deficiency, such as short duration,

interrupted sleep, poor quality, and abnormal timing. Studies as early as 1971 identified sleep deprivation in the ICU, stating that "the situation becomes circular; the sicker the patient, the longer he must remain in the ICU."[3] While these studies occurred over five decades ago, the findings of poor sleep in hospitals, and especially in ICUs, hold true today. Studies continually attempt to evaluate sleep in ICUs objectively and subjectively.

PSG is the gold standard method of measuring sleep in all settings and has been employed in studying the critically ill. In a study by Elliot, et. al., employing 24-hour PSG to evaluate 57 ICU patients, 90% of patients spent their TST in superficial sleep, meaning they are deprived by the most restorative sleep such as REM. In this population, TST was 5 hours, and 41% of the TST occurred during the day, showing the circadian rhythm disruption. This study stated that they were limited in patient enrollment due to the lack of PSG monitoring equipment available and lack of researchers trained in the interpretation of the PSG data. They concluded an alternative objective sleep assessment method would be more beneficial.[4] Another study demonstrated that critically ill patients experienced 41±28 sleep periods within 24 hours, with sleep periods lasting 15±9 min, showing highly fragmented sleep.[5] A feasibility study for accurate measure of sleep was carried out in an observational pilot study in a medical ICU. 24-hour PSG was conducted in 29 patients with indicators of feasibility including attainment of EEG data sufficient to determine sleep stages, sleep efficiency, and arousal indices. They found that EEG data was not affected by electrical interference. They concluded that unattended, portable PSG can produce high quality sleep data. However, in this study, a limitation was patient discomfort and transfers during recording time that truncated studies.[6]

While PSG remains the gold standard, it can be expensive, requires more extensive training for use and interpretation, and can be cumbersome and uncomfortable for patients. Actigraphy, an accelerometer worn on the wrist to track motion, has been validated against PSG in healthy populations as an objective measure of sleep.[7] For TST, agreement between actigraphy and PSG has been shown to be above 90%.[8] Actigraphy is less burdensome and expensive, and for these reasons, better for longitudinal studies. A cross-sectional study by Naik et. al in 2018 studied sleep in a tertiary hospital MICU with actigraphy. The TST (in minutes) was found to be 522±122 and did not differ significantly between good and poor perceived sleep. Limitations of this study included a sample size of convenience, lack of baseline or follow up actigraphy data in ward or post-discharge for evaluation of contribution of ICU admission on sleep disturbance, lack of noise and light level documentations, and measuring sleep quality as a dichotomous variable, although it occurs in continuum. [9]

Subjective sleep assessments have yielded similar results, in that sleep in critically ill patients was subjectively light, was often fragmented by frequent arousals, and that once awoken, it was difficult to resume sleep. RCSQ is the only validated subjective sleep assessment in the critically ill population compared to PSG, the gold standard.[10] In one study, patients were screened for their sleep via RCSQ prior to admission to the surgical ICU and immediately one night after. When comparing the scores obtained in the ICU with their previous sleep scores, 55% of patients stated that their sleep had worsened in the ICU.[11] A limitation in the applicability of this study is the all surgical patient population, but a strength is the fact that they found no difficulties in the use of RCSQ in this population. The same study by Elliot, et. al., previously discussed regarding PSG,

showed that most of the patients evaluated their sleep as poor using the RSCQ, with the mean being 57.5 on the VAS, which correlated with PSG data of the same study.[4] The same study by Naik et. al, previously discussed regarding actigraphy, showed that poor sleep (RCSQ <50, sensitivity 88% and specificity 87%) was found in 15 out of 37 patients.[9] General limitations of subjective measures are mental capacity changes in intensive care patients such as delirium that may alter responses and physical constraints that would limit the ability to complete a VAS.

Through all of the different methods of measuring and evaluating sleep, it is clear that sleep deprivation is pervasive in the ICU. The causes of this poor sleep are numerous and can fall into different categories of effects on the brain (medications, head trauma, age), stress responses (crucial illness, inflammation). A major category with a large opportunity for investigations into interventions would be the ICU environment including light, noise, and sensory deprivation or overstimulation, and discomfort.

2.2.2 Implications of Poor Sleep in the ICU

The lack of sleep quality and quantity in all settings has great implications for patient outcomes. Acute sleep deficiency, including short sleep duration, has been found to have effects in the shorter term. Examples include cognitive changes, mood changes, metabolic effects such as short-term glucose intolerance, immune changes such as impaired adaptive immunity and increases in inflammation, and cardiac issues such as arrythmias.[12-16] Chronic sleep deficiency has been linked to a number of longer-term effects. Chronic sleep loss has been found to lead to impaired vigilance and performance, slowing of cognitive processes, long term depression, and poor attention.[17,18] Pulmonary function is affected by sleep deprivation through diminished respiratory response to

hypoxemia and hypercapnia.[19] A meta-analysis looking at cross-sectional and longitudinal study data on sleep duration found that shorter sleep duration is associated with an increased risk of hypertension, with an odds ratio of 1.21 (95% CI, 1.09-1.34).[20] A prospective study found that difficulties initiating sleep were related to Coronary Artery Disease related death in males, with a relative risk of 3.1 (95% CI, 1.5-6.3, $p<0.01$).[21] ICUs disturb sleep at a time when systems are often already most compromised or impaired. The list of complications of sleep deficiency is extensive and those that are critically ill are especially susceptible to these implications and their poor effects on patient outcomes.

A specific complication of sleep disturbance in the critically ill is the increased risk of delirium, while this association is still considered controversial. In one study, 52 critically ill medical and surgical patients were studied with the intention of correlating sleep deprivation with the development of mental status changes, and found that mental status changes were more likely in patients with greater sleep deprivation[22] A sleep QI project was conducted to understand the role of sleep promotion on ICU delirium in a medical ICU. They observed a significant reduction in the incidence of delirium/coma during the ICU stay and a significant increase in daily ICU delirium/coma-free status. However, secondary analysis of this data found that perceived sleep quality was unrelated to delirium transition (adjusted OR 1.00, 95% CI 0.99-1.00).[23] While more studies need to be performed to determine the extent of the interrelatedness, many of the risk factors between the two overlap. Overlapping risk factors with direct effects on the brain include the medications used in critically ill such as sedation, dementia, sepsis, advanced age. Overlapping risk factors from the stress response include crucial illness, mechanical

ventilation, pain, inflammation. Lastly, overlapping ICU environment risk factors include noise, light and circadian disruption, and patient care activities.[24] For this reason, interventions on sleep deficiency and deprivation may prove to help with delirium as well.

The sleep deficiency and deprivation that the ICU can cause is not limited to the time spent in the hospital. In one study of 60 patients, 50% reported sleep disturbance during their time in the hospital, while 30% reported continued sleep disturbances up to one year post discharge.[25] An observational cohort study of medical ICU patients showed that total medical ICU days of delirium (p=0.013) were significantly associated with higher levels of sleep disturbance at follow-up.[26] The number of days of ICU delirium was found to be significantly associated with time to death within 1 year post-ICU admission, with a hazard ratio of 1.10 (95% CI, 1.02-1.18).[27] An observational cohort study of 93 medical ICU patients with delirium aimed to evaluate associations between the loss of specific sleep features on EEG (K-complexes, sleep spindles), grade of encephalopathy, and ICU outcomes. They found that patients had more severe encephalopathy and higher odds of death when EEG showed a lack of K-complexes (odds ratio 18.8, p=0.046) and lack of sleep spindles (odds ratio 6.3, p=0.036).[28] The short-term and long-term implications display the need for further research into interventions for sleep deprivation.

2.2.3 Other non-pharmacological interventions for sleep

There are no pharmacological interventions proven to improve sleep in the ICU. In fact, some medications can cause more adverse effects, drug interactions, and patient harm than benefit. Daily sedative interruption is the only known pharmacological strategy

that improves PSG parameters in the ICU.[29] Some ICU medications, such as benzodiazepines and opiates, may increase sleep time, but not restorative sleep. Melatonin has been considered for its sleep-promoting properties, but has mainly been studied using non-validated sleep measuring tools.[30] Though promising, results to date have been mixed. Larger, RCTs with melatonin would need to be performed to fully understand its effect on sleep in this population.[31,32] As such, non-pharmacological interventions are recommended as first line treatment and prevention by the graded guidelines for clinical practice in the prevention and management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS).[33]

The most common non-pharmacological sleep intervention is the premise of a quiet time protocol. A study in an ICU at a level 1 trauma center created a quiet time protocol, limiting noise and light during certain hours. Noise and light levels were recorded and patients were observed for sleep 30 minutes before and every half hour until 30 minutes after the protocol. By simply enacting this protocol, there was a mean reduction in noise levels by 10 decibels (or two sound doublings) statistically significant at the 0.025 level. Light levels also decreased by 15-25% with p values less than 0.025. With these lower levels, patients were significantly more likely to be observed sleeping, with an odds ratio of 4.04 (97.5% CI, 2.24-7.30).[34] A study was carried out to evaluate providers' perceptions and practices regarding sleep in the ICU through surveys. A total of 1,223 surveys were completed from 24 countries, with most respondents indicating that ICU patients experienced "poor" or "very poor" sleep (75%) and that poor sleep could affect the ICU recovery process (88%). The minority (32%) of providers had sleep-promoting protocols, despite most clinicians believing that sleep in the ICU is poor.

These findings highlighted discordant provider perceptions and practices around sleep in the ICU.[35] A study at YNHH in the medical ICU tested the impact of a sleep promotion protocol on overnight in-room disturbance. The sleep protocol restricted non-urgent bedside care from 00:00 to 04:00. Patients were assigned to usual care or the sleep protocol. They found that the sleep time protocol arm had 32% fewer room entries (rate ratio 0.68, p=0.001) and 9 fewer minutes of in-room activity (p=0.0002). These findings proves that a sleep promotion protocol can provide better opportunities for sleep in the ICU.[36]

Interventions to block the ICU environment have been tried with some success. A RCT on patients in the cardiac surgical ICU studied effects of earplugs and eye masks, with subjective sleep quality evaluated using the Chinese version of the RCSQ. Data from 45 patients were analyzed, with significant differences in overall sleep quality ($p<0.05$). Patients perceived sleep quality was better in the group with the intervention. A limitation of this study was that it was solely a subjective measure, with no PSG or actigraphy data.[37] Other studies have been able to show improvement in sleep via PSG in simulated ICU settings.[37,38] An intervention review aimed to assess the efficacy of non-pharmacological interventions for sleep promotion in critically ill adults in the ICU, but found that out of over 30 trials, the quality of evidence for an effect on any outcomes examined was generally low or very low. They used three of these trials with sufficient data for two separate meta-analyses. One meta-analysis showed a lower incidence of delirium during ICU stay (risk ratio 0.55, 95% CI 0.38-0.80, P value = 0.002) with use of earplugs or eye masks or both. The second meta-analysis showed a positive effect of earplugs or eye masks or both on TST (mean difference 2.19 hours, 95% CI 0.41-3.96, P

value = 0.02). However, this study rated the quality of the evidence for both of these results as low.[39] Despite the potential benefits of eye masks and ear plugs, 80% of patients have been shown to decline these interventions, which inherently inhibits their ability to improve sleep deficiency.[40] YNHH currently offers medical ICU patients a quiet pack including these items.

Various relaxation techniques such as milk-honey drinks, massage, aromatherapy, and music have been evaluated through small studies and found to be effective. A unique intervention for sleep quality enhancement was considered in a clinical trial study in hospitalized patients with acute coronary syndrome. Patients in the intervention group received a warm, milk-honey mixture twice per day for three days, while the control group received routine care. Sleep quality was measured beforehand, and each day, using the RCSQ. There was no significant difference in sleep scores between the two groups on the first day of admission (p=0.914), but on the third day of admission, there was a significant difference in sleep scores between the intervention and control group (p=0.001). They concluded that the mixture of milk and honey improves subjective sleep of patients with ACS, and could be an affordable and simple intervention to offer.[41] Aromatherapy massage at bed time has been used in an experimental study in postoperative, hospitalized patients in the ICU. RCSQ indicated a statistically significant difference in sleep between the mean scores of the intervention group (aromatherapy massage, 54±13) and the control group (routine care, 29±9). They concluded that aromatherapy massage enhanced the sleep quality.[42] A non-controlled clinical study was performed in ICUs in Italy to identify whether musical sounds in conjunction with a massage before bed affected sleep, evaluated using the RCSQ. Each patient chose their

favorite music or relaxing sounds of nature and they listened through headphones all night. After one night of the two interventions, significant improvements were observed in patient's perception of the quality of sleep. For example, "depth of sleep" improved (t=2.01, p=0.04). A significant limitation of this study would be the design and lack of randomized control.[43]

A meta-analysis of various sleep promoting interventions showed that in 13 studies involving 296 critically ill patients, sleep quantity was improved (pooled standardized mean difference 0.37, 95% CI, 0.05 to 0.69, P=0.02) and quality through reduction in sleep fragmentation (pooled standardized mean difference -0.31, 95% CI, -0.60 to -0.01, P=0.04).[44] In summary, this shows that it is possible to continue to improve sleep through different interventions and options need to continue to be explored.

2.2.4 Weighted blankets and Sleep

Using the search terms previously discussed, we were able to find eight total journal articles on the topic of weighted blankets, which clearly displays the lack of literature on the topic. A systematic review by Eron done on weighted blankets and their role in both sleep and anxiety was performed in 2020, in which they evaluated eight studies. They were able to conclude that research suggests weighted blankets may be an appropriate therapeutic tool, especially in anxiety, but more research on sleep would need to be performed.[45]

One population where weighted blankets and their impact on sleep have been studied is in children with autism. This study was a RCT with the study objective of gauging the effectiveness of a weighted blanket intervention in treating severe sleep problems in this population. This was measured with actigraphy to analyze TST, powered

to 80% with 5% significance. This study used a paired t-test to compare the weighted blanket and control blanket, where the mean difference was -4.2 (34.5, 95% confidence interval (CI) -13.6 to 5.2). They concluded that there was no significant difference in TST between blankets. However, this study was able to display the safety of the use of these blankets, and parents were more likely to rate their child's sleep as better, despite the objective evidence. The strengths of this study were that it was the first randomized study specifically designed and powered to assess the impact on TST in children with ASD, it included a "placebo" control, and used objective measures. The limitations included the lack of ability to mask weighted vs control blankets and that the study required a sample size of 63 patients, but only 54 subjects' data was analyzed.[46]

A repeated measures study looked at the positive effects of weighted blankets on insomnia in adult populations, using sleep bout time, sleep latency, total wake time, and sleep fragmentation as measured through actigraphy. They concluded that the mean sleep bout time (in minutes), equivalent to TST, significantly increased ($p=0.035$) when using the weighted blanket, with a positive outcome on sleep both objectively and subjectively. A limitation of this study and source of potential bias that was not outwardly acknowledged was that their funding came from a weighted blanket company.[47]

A randomized controlled study of weighted chain blankets on insomnia, and sleep-related daytime symptoms for patients with major depressive disorder, bipolar disorder, generalized anxiety disorder, and attention deficit hyperactivity disorder. The outcome was evaluated using the Insomnia Severity Index (ISI), with sleep and daytime activity levels also measured by wrist actigraphy. At four weeks, they found that there was a significant advantage in ISI ratings of the weighted blanket intervention ($p<0.001$).

They concluded that weighted chain blankets are an effective and safe intervention for insomnia in this population.[48] The only limitation suggested by this study was the risk of disclosure of the blanket-type to the rater, who was supposed to be blind to the treatment allocation, which they report only happened once throughout the study.

Lastly, a study on 2 children with ASD studied weighted blankets with an outcome measure of a daily online survey. Results showed that both participants achieved a slight increase (1-3 hour) in total sleep per night and a slight decrease in time to fall asleep per night. A clear limitation of this study is the sample size and power of the study.[49]

The systematic review by Eron summarized that the limitations in all of these studies on sleep and weighted blankets include a narrow sampling methodology, small sample sizes, the inability to blind experimental and control groups due to obvious weight differences in blankets, or low-level designs.

2.2.5 Weighted Blankets with other related outcomes

In addition to studies on sleep, weighted blankets are being evaluated in the use of anxiety treatment in various settings and populations. Anxiety, as previously discussed, is highly prevalent in the critically ill, and is often tied to sleep quantity and quality. A RCT evaluated the effectiveness of weighted blankets on anxiety in adult patients receiving their first and second chemo infusions. The outcome was measured with a VAS over two days. Based on the scores, weighted blankets resulted in a larger reduction in anxiety after 30 minutes compared to no blanket. Weighted blanket use was associated with a reduction in the VAS scores by a mean of 8.89 points (95% CI, 15.69, 1.18) at 30

minutes. A major limitation of this study was that a "convenience sample was used, with the reasoning that a small sample size would be used to first determine effect and feasibility of future studies.[50] To assess the safety and effectiveness of the use of a 30-pound weighted blanket in adult inpatient acute psychiatric settings, an exploratory pilot study was employed using safety metrics of pulse, blood pressure, and pulse oximetry. They found that there was a statistically significant improvement identified in self-rating anxiety data ($p=0.002$).[51]

A pilot study of a sensory room in an acute inpatient psychiatry unit aimed to measure distress in patients and staff perceived disturbed behaviors (loud, pacing, irritable, paranoid, etc.) before and after use of the room. The rooms included weighted blankets, music, rocking chairs, and aromatherapy. The study showed that those individuals who used the weighted blanket specifically, significantly reduced distress and clinician-rated anxiety than those who did not.[52]

Weighted blankets have also been used as interventions for various different outcomes of measure related to sympathetic nervous system responses. A randomized controlled crossover design was used in adolescents who were undergoing third molar extraction. The results indicated that third molar extraction caused significant autonomic parameter changes in both groups, with weighted blanket and without. However, the deep pressure input in the experimental group was associated with less heart rate variability, which they suggest reveals a more balanced sympathovagal activation.[53] A crossover RCT was conducted at a level III neonatal ICU to assess the safety, feasibility, and effectiveness of weighted blankets in the care of neonates with NAS. A total of 16 patients were enrolled for a total of 67 weighted blanket sessions, and there was found to

be a significant decrease in the infant's heartrate (decrease of 7 beats per minute, p=0.011, effect size r=0.448). In addition to this, Finnegan scores, a scoring method of severity of symptoms in babies with NAS, decreased when a weighted blanket was used.[54] The study, notably, only found these effects to be while the blanket was in use, and did not persist when re-checked 30 minutes after taking the blanket off.

In summary, weighted blankets have been used in various other settings and with other outcomes of measure, but similarly regarded as a tool for calming patients, which can reasonably lead to decreased anxiety, or in our study, enhanced sleep through increase in TST.

2.3 Review of Relevant Methodology

The following section will be a review of the literature in the context of relevant methodology to the study being proposed, while more detailed methods, explanations, and justifications can be found in Chapter 3.

2.3.1 Study Design

The proposed study will be a RCT with two arms: weighted blankets and usual care. It will take place in the medical ICU at YNHH in New Haven, CT.

RCTs are the gold standard for determining the effectiveness of an intervention as it allows to control for "unknown variables." The decision to do an RCT will also be beneficial given the previous lack of RCTs in the study of non-pharmacological interventions for sleep and in weighted blanket use. As discussed previously, non-pharmacological intervention studies have not frequently utilized RCTs. An RCT was carried out to test the impact of sleep promotion protocols on in-room disturbances.[36] One

RCT measured sleep subjectively with the RCSQ in cardiac surgical ICUs with an intervention of earplugs and an eye mask.[37] Other studies utilized RCTs to study milk and honey mixtures or aromatherapy.[41,42] These studies were limited by being solely subjective measures and contained smaller sample sizes.

There have been four major RCTs for the study of weighted blankets, but only two of which were studies pertaining to sleep. One weighted blanket that focused on sleep was an RCT on insomnia in psychiatric disorders in an adult outpatient population. This study found that at 4 weeks, insomnia decreased using a severity index. However, they found that there was no significant effect on TST. Participants subjectively reported an improvement in ability to maintain sleep, despite lack of increase in TST. A strength of this study was the controlled design and large sample size.[48] Another RCT that investigated weighted blankets and sleep focused on children with autism and found that TST had no significant difference between intervention and control. However again, subjectively, the participants preferred the blankets.[46] The two other RCTs studied anxiety in patients undergoing chemotherapy and Finnegan scores for babies with NAS, and both studies showed promising results of decreased anxiety and symptom severity.[50,54] The lack of RCTs with objective data, on non-pharmacological interventions with large enough sample sizes, and on weighted blankets and sleep especially in inpatient settings demonstrates a need for such a study.

The study site will be YNHH's medical ICU, which admits over 4,000 patients per year. This study site is appropriate as it allows this study to recruit enough participants to have a significant sample size. The number of patients and the heterogenicity of the study population given the urban metropolitan area will allow for

generalizability of results. Most commonly, with the patient population we aim to use discussed further in chapter 3.2, the reason for admission will include septic shock and GI bleed. While this does not provide for a wide variety of diagnoses, most hospitals across the US have medical ICUs with similar patient population make-ups, allowing for generalizability. This study will also have a primary outcome of objective data and a secondary outcome of subjective data. A strength of this design would be adding objective data, but also collecting subjective data to be able to compare to previous studies, which largely use this measure.

2.3.2 Selection Criteria

Previous studies in YNHH's medical ICU through Dr. Knauert's Lab have included patients that were admitted from home less than 24 hours prior to enrollment. Patients were excluded if they were expected by medical staff to leave the ICU, or expected to die in the next 24 hours (i.e., receiving comfort care only).[36] The proposed study will similarly incorporate these criteria.

Graded guidelines for clinical practice in the prevention and management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) in adult patients in the ICU were published by thirty-two international experts who met monthly to assess data in each category. This panel assessed risk factors before ICU admission for sleep deficiency, and found that older age and specific premorbid conditions (i.e., hypertension, diabetes, cancer, and thyroid disease) have been consistently reported as being associated with perceived lower quality of sleep in the ICU.[33] Another study concluded that patients with poor sleep had a higher median age (43 vs 31 years,

P=0.008).[11] Given this information, the proposed study will focus on patients of older age.

Weighted blankets have been determined to be safe at 10% of body weight by two studies.[51,55] However, these blankets have not been studied in the critically ill population. Based on weighted blanket guidelines and blankets commercially available, previous studies have also excluded patients who weigh less than 45kg.[50] For this reason, using best clinical judgement, we will exclude those with any wounds (open, surgical, pressure, etc.), those in respiratory failure, and those weighing less than 45kg upon admission.

2.3.3 Potential Confounding Variables

Confounding variables threaten the validity of a study's findings. One source of potential confounding would be frequently used medications in the ICU, including sedatives. Medications, including sedating medications, can cause changes in the amount and quality of sleep. These medications can affect the Central Nervous System directly, through the blood brain barrier, or indirectly, by interfering with a medical or psychiatric condition. They can have equally disturbing effect when withdrawn abruptly.[56] Benzodiazepine, a sedative, may improve sleep efficiency because of decreased sleep latency, decreased number of arousals, and increased TST. However, the chronic use of benzodiazepines is associated with superficial sleep and withdrawal is associated with rebound insomnia. Propofol, which is used primarily for deep sedation, such as when someone is on mechanical ventilation, suppresses REM sleep and can be associated with delirium.[57,58] Medications are necessary in ICUs and are unavoidable. For the proposed study, we will limit the confounding variable of known medications that interfere with

sleep by excluding those in respiratory distress, who are often on ventilators and therefore under sedation.

Another potential confounding variable would be reported sleep quality or use of regular sleep aid medication at home. In three studies, these factors have been consistently reported as being associated with perceived lower quality of sleep in the ICU.[40,59,60] We will record home medication list as baseline variables during enrollment and will control for this variable.

2.3.4 Randomization and Blinding

Randomization of participants will be via simple randomization with assignment via random number generator to either intervention or control with a 1:1 allocation. This is based on previous studies carried out by the Knauert Lab in YNHH's medical ICU. In one pilot study, they studied implementation of a sleep promotion protocol in the medical ICU on overnight in-room disturbance, where the primary measures were sound and light. Randomization was carried out using a computerized random number generator and a 1:1 allocation to the intervention and control groups and allowed for a reduced possibility of bias from confounding variables in enrolled patients.[36] Previous weighted blanket studies have similarly used this 1:1 allocation, using a concealed lottery method.[48]

The blinding of the proposed study will blind participants to the hypothesis and the content of other treatment groups through specific consent phrasing, discussed in Chapter 3.6. Other weighted blankets have struggled to find methods of blinding participants given the weighted nature of the blanket.[46,50,52,53] Two studies have created control blankets that matched in size and fabric, but are not weighted.[48] For the purpose

of our study, we will consent patients to a more broad idea of "non-pharmacological sleep interventions" and not specifically mention the blanket as our intervention of interest. The control group will still be provided with standard non-pharmacological interventions of eye mask and earplugs. Our proposed study, for this reason, should have more protection against information bias. In accordance with weighted blanket studies, investigators and research assistants interpreting outcome will be blinded to subject allocation at baseline and during assessment points.[46,53]

2.3.5 Intervention

The intervention will be a weighted blanket. There are countless brands of weighted blankets, made of different materials and different weights, some being considered medical grade, while others not. Some studies have used metal chain-weighted blankets or blankets filled with heavy beads that can be purchased and some studies have manufactured their own blankets. [47,50,53]

No previous research was found that supported a validated weight or pressure recommendation for weighted blanket therapy. However, manufacturers of different weighted blankets, such as Mosaic Weighted Blankets, Price, and Sensory Direct, publish guidelines for their products. Most consistently, manufacturers recommend a weighted blanket should be 10% of an individual's body weight. Some research studies have been performed and have found this weight to be safe, and even recommend weights more than 10%.[51,55]

An ideal weighted blanket for our study would contain small, stitched "bladders", or contained sections, of beads. These small sections would allow the weight to stay fixed

and not shift with blanket manipulation, which is important for consistent and effective DTP. For the purpose of our study, we also wanted to use a blanket that would be able to be sanitized and reused between patients. We will use blankets that are closest to 10% of an individual's body weight, as this is the recommended weight from manufacturers, it has been found to be safe, and we do not want blankets to be too heavy or be considered restraint.

A study by Vinson on patients undergoing chemotherapy used a blanket most in line with our ideal blanket, obtained from CapeAble Weighted Products. This blanket is 34 inches by 62 inches with an outer antimicrobial fabric. The inner bladders were stitched in small sections and filled with clean recycled glass beads. In this study, they were easily wiped clean after each patient's use with Sani-Cloth germicidal disposable wipes, which are currently stocked on YNHH's medical ICU.[50]

2.3.6 Primary and Secondary Outcome Measures

The primary outcome for the proposed study will be TST (in minutes), which has been used in countless sleep studies and is a common basic measure of sleep.[4,5,9] TST has also been used in numerous weighted blanket studies and sleep.[46-48] The primary outcome will be measured by actigraphy. As previously discussed, actigraphy has been validated against the gold standard, PSG in healthy populations.[7] For TST, the agreement between actigraphy and PSG has been shown to be above 90%.[8] The actigraph will be used on the non-dominant wrist, as it has been in other weighted blanket studies.[46,48]

However, it is worth acknowledging the drawbacks in using TST or actigraphy based on the literature. In the sole two RCTs on weighted blankets and sleep, the outcome of TST was not significantly affected by the weighted blanket use.[46,48] Despite

this, given that there are only two total studies with limited sample size with this intervention, and no RCTs with this intervention, outcome, and critically ill population, we still feel TST will be a useful primary outcome for this proposed study. In addition, actigraphy's validity in critically ill populations is still unclear. An observational study with simultaneous PSG, actigraphy, and behavioral assessments from nursing concluded that actigraphy overestimated TST and that the agreement between the two was <65%. Their explanation was the few changes in body position made it difficult for the actigraphy to measure sleep. However, this was a single study with a sample size of 12.[61] A systematic review in 2018 concluded that actigraphy is being used more frequently as a surrogate measure of sleep, but is limited by processing algorithms. They determined that prior ICU-based studies using actigraphy were heterogenous and lacked data. Larger, more rigorous, and standardized studies are needed to better understand its role.[62] As we are specifically excluding patients in respiratory failure, who are often intubated, sedated, and restrained, which would severely limit wrist motion and measurements via actigraphy, we hope to overcome some of the limitations.

In addition, a study by Sadeh in 2011 suggested that given these limitations of actigraphy, it is best that a complementary assessment measure should be used whenever possible.[63] For this reason, our proposed study's secondary outcome will be the RCSQ global scale, or total five subsections of the RCSQ, and each subsection individually. As previously discussed in Chapter 2.2.1, RCSQ has been validated against PSG in medical ICU patients evaluating aspects of nighttime sleep including 1) depth, 2) latency (time to fall asleep), 3) number of awakenings, 4) efficiency (percent time awake), and 5) quality.[10] The proposed study will be novel as RCSQ, a valid and commonly used sleep

assessment, has not yet been used to evaluate weighted blankets as an intervention, especially concurrently with objective measures.

2.3.7 Sample Size and Statistical Significance

TST has been found to have significant variation across studies in the critically ill. For example, one study by Elliot et.al. in critically ill patients found TST to be approximately 5 hours, or 300 minutes. In another study by Naik et. al., TST in minutes the crucially ill was found to be 522±122 minutes. When using weighted blankets as an intervention, a study by Gringas found TST to be 452±59 minutes. For this reason, we determined that we will use preciously collected data from Dr. Knauert's Lab for which the manuscript is in process. Advantages of using this data includes using the same sample population, same environmental conditions as it will be the same medical ICU where the study will take place, and the same actigraph devices and program for data interpretation will be used. The historical data from YNHH's medical ICU showed an overnight TST of 94 minutes, with a high degree of variance of 61 minutes.

There have been no studies on weighted blankets in this critically ill population. Weighted blanket studies have used powers of 80% and alpha of 0.05.[46,47] There have also been no direct studies on effect size. One weighted blanket study used data from a pilot study on 5 participants to calculate an effect size. Using Cohen's d, an effect size of 0.75 was determined to be appropriate.[47] Other non-pharmacological interventions, as discussed in Chapter 2.2.3, have largely used RCSQ as their primary outcome, rather than TST, and therefore do not provide any insight on effect size.[34,37,41-43,64-66] Most studies with TST have been aiming to validate actigraphy against other measures, such as PSG, and therefore did not include an effect size. For this reason, it is difficult to determine an

appropriate effect size. Using best clinical judgement, we decided that 20% increase in sleep (18 minutes when using data from Dr. Knauert's historical data) would be an appropriate effect size.

Given this data and designs of previous studies, for a power of 80% and alpha of 0.05, and an effect size of 20% increase in sleep (18 minutes), the calculated sample size is 324 participants, or 162 per group. For more information, please refer to Chapter 3.9.

2.4 Literature Review Conclusion

Upon reviewing the literature, it became clear that sleep deficiency is pervasive in the critical care setting and has implications on patient outcomes in the short and long term. Pharmacological interventions may cause side effects, or otherwise decrease sleep quality. Non-pharmacological interventions have been explored, but with limited studies that are mostly subjective in nature, and with inconclusive results. Weighted blankets have subjectively shown promise in both sleep and anxiety. Sleep disturbance can often be linked to anxiety or emotional distress of being hospitalized. Weighted blankets have not been studied extensively in an objective way, such as actigraphy. The few studies that have made an attempt lacked generalizability, had small sample sizes, and were not in the critically ill population. They have also lacked simultaneous objective and subjective measures, which our proposed study will offer. We propose an RCT comparing usual care (control) versus weighted blankets (intervention).

2.5 References

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CHAPTER 3: METHODS

3.1 Study Methodology

This study design will be a blinded RCT of usual care (control) versus weighted blankets (intervention).

3.2 Study Population and Study Site

This study will take place at Yale-New Haven Hospital, a 1,500 bed, tertiary, academic hospital. We will recruit from the Medical Intensive Care Unit (MICU), which contains 38 beds and admits over 4,000 patients per year. The median MICU stay at Yale is three nights. All patients will be evaluated for eligibility daily as they are admitted to the ICU. The population will be critically ill adults.

Enrollment must occur within 24 hours of hospital admission (as of 08:00 on the day of enrollment). Adults 50 years and older and patients that weigh over 45kg admitted to the medical ICU are eligible for inclusion. Participants must also be able to read and write in English in order to fill out a written survey. The exclusion criteria include respiratory failure and active wounds (open, surgical, pressure, etc.). Patients that are expected by their care team to leave within the next 24 hours will also be excluded. Therapy will be started on the first night following enrollment.

3.3 Recruitment

We will evaluate all admitted ICU patients daily. If the patient is unable to consent for themselves, consent will be obtained from the patient's legally authorized representative. Patients or legal representatives that agree to the study will be informed that the study is investigating "different non-pharmacological sleep interventions".

Research staff will inform the patient or legal representative of risks and benefits. Recruitment and enrollment will be on a rolling basis over eighteen months.

3.4 Subject Protection and Confidentiality

YNHH's medical ICU will be IRB approved under the Yale Human Investigation Committee (HIC). All members of the research team will participate in Health Insurance Portability and Accessibility Act (HIPAA) training prior to the start of the study. All information regarding the patient will be obtained through the hospital approved electronic health record, Epic, or directly from the patient. Each participant or representative will be informed of risks and benefits of the study and be informed of the confidentiality they will be provided with opportunities to ask questions. They will be provided with the IRB-approved Authorization and Consent form (see Appendix A) and will be asked sign the form indicating understanding and consent.

Confidentiality will be maintained throughout the study. Once a participant enters the study, they will be assigned a unique identifier number. Videotaping will occur for one night during the study, on study night two, and the camera will be positioned at the top of the bed such that only the body and blanket will be visible. The participant's face and other identifying features will not be visible. Following the scoring of the video for hours of blanket use, the video will be destroyed.

Once extracted, data will be stored in REDCap, a program on a Yale University secure server with standard encryption. Any hard copies of data such as notes or surveys taken while abstracting will be shredded per hospital and/or university mechanism (approved shredding bins). Data management procedures will ensure accurate and efficient data storage and analysis; confidentiality; and real-time, on-demand study

monitoring reports. All data will be maintained in accordance with HIPAA guidelines for participant confidentiality and privacy. All data will reside on secure, HIPAA-compliant data base and file-sharing resources managed by Yale ITS. Access to data resources will strictly be limited to members of the research team. Data or information will never be placed on any portable devices such as flash drives and will only be placed on local networks, not accessible outside of the secure Yale environment.

3.5 Assignment of the Intervention

After obtaining informed consent, patients will be randomized using a simple randomization tool through a program, REDCap. Baseline characteristics will be recorded and assigned to the participant's unique study identification number. The intervention group will be weighted blanket with standard of care and the control group will be standard of care alone. Investigators will not have access to participant data before allocation.

3.6 Study Variables and Measures

Overall study timeline: patient will be enrolled and then randomized per above. Then on the first night of the study, they will be exposed to usual care or intervention for an acclimation night. Adherence will be monitored and outcome measures including actigraphy and subjective sleep scores will be collected based on study night two.

Weighted Blanket Intervention: The intervention will be a weighted blanket that will be worn for a minimum of one hour per night's sleep. The brand of the medical-grade weighted blankets will be CapeAble Products for consistency with other studies. Another benefit of using this blanket is its ability to be sanitized between uses, as discussed in Chapter 2. There will be three weights- 13.2lb, 17.6lb, or 22lb, (6, 8, or 10kg)- and

patients will wear use the blanket that is closest to 10% of their body weight (rounding up). Participants will be encouraged, when possible, to wear the blanket while sleeping, and they will be instructed that the study is based on the amount of time the blanket is in use. These patients will also be provided with the standard of care, discussed below. Patients will have the option to use the blanket for the rest of their hospital stay. The blankets will be returned to be sanitized and used again. We will operationalize the outcome variable with means of TST, measured with actigraphy. The weighted blanket intervention will be initiated within 24 hours of patient admission.

Standard of Care: The control will be standard of care, where patients will be provided with a quiet pack that the hospital currently provides all patients. Patients will not be informed that this is standard of care, but rather that this is their "intervention". This includes an eye mask, ear plugs, and headphones to listen to the television to minimize noise for other patients. Other quiet time protocols will continue to be followed. Overnight pages are eliminated from 0000 to 0400. Nursing is expected to cluster their care to the best of their ability. Patients have blankets, heated blankets, and sheets available for their comfort.

Fidelity: Patient will consent to being videotaped on night 2 of use of blanket. Participants' faces will not be included in the video as the camera will only point toward the lower half of the body and area that the blanket will cover. A research assistant will view these videos once to assess for adherence, recorded based on the study's unique patient identifier number, and these videos will be later destroyed for confidentiality and privacy purposes. Adherence will be considered one hour of continuous blanket use.

Primary and Secondary Outcomes: Both the primary and secondary outcome will be based on data collection from night two of the study. The primary outcome will be TST in minutes measured via actigraphy on night two of the study. TST will be considered a continuous variable. The actiwatch data will be uploaded to Phillips Actiware 6 (or current version) and TST will be determined via the program's standard algorithms. The secondary outcome will be a qualitative study on the patients' subjective sleep quality on night two of the study. This will be measured with the RCSQ, the only validated subjective sleep questionnaire for ICU patients (see Appendix B). The questionnaire will be administered on morning three of the study, immediately after night two. Lastly, patients will be asked if they subjectively enjoy using the blanket in an exit interview on day seven (see Appendix C).

Baseline Variables: The age, gender, presence of regular use of sleep aid medication, admission diagnosis, and nursing staff for night two of the patients' stay (night of intervention and data collection) will be recorded as baseline variables.

Monitoring of Adverse Events: Weighted blankets have been proven safe in various populations. However, we will be prepared in advance to manage adverse events. Patients will be informed that they may remove their intervention at any time desired or required. Nursing will be informed to continue to document any skin or respiratory changes and notify PI if conditions show any signs of worsening per unit protocol. PI will evaluate safety as needed and as necessary.

3.7 Blinding of the Intervention and Outcome

Blinding of the intervention: The patients will be informed that they will be a part of a non-pharmacological interventional sleep study. This is accurate as the intervention

(blanket) and standard of care (eye mask, earplugs) contain non-pharmacological sleep interventions. By phrasing the IRB study description and the interventions to the patients in this way, the participants can be blinded to the other interventions. Participants will also be blinded to the hypothesis. A daytime research assistant will consent the patient, set up the camera, and put the actigraph on participants' wrists. Study participants will be randomly assigned to either the weighted blanket group or the standard of care group using the program REDCap. A second, night research assistant will implement the intervention or control. The following day, the daytime research assistant will return and administer the RCSQ. In this way, the research assistants can remain blinded to the intervention.

Blinding of the outcome: The research assistant in charge of interpreting the actigraphy data and running statistics will be blinded to allocation. The research assistants interpreting the subjective RCSQ will remain blinded to the allocation.

3.8 Data Collection

Actigraphy wrist device will be placed on all participants at the same time on their non-dominant wrist. For the primary outcome, data collection and analysis will be based off of night two of use of the blanket/standard of care, as it will assume that all patients are accustomed to weight of blanket and the wearing of actigraphy. Patients will only be videotaped on this night to monitor for adherence. "Night" will be considered 8pm to 6 am, as this is just after and before the noise/commotion of nursing shift change. We acknowledge that this is a broad window, but it will allow us to capture a wide range of nighttime sleep habits. Because our objective primary outcome is TST, it will not be

affected by a large window of sleep. Actigraphy data will be aggregated in Phillips Actiware 6 (or current version) and the program algorithms will determine TST.

The secondary outcome of subjective sleep measures will be measured with the RCSQ. A research assistant who was blinded to the intervention will administer the RCSQ before noon on the day immediately following night 2 of the study. The RCSQ is a VAS questionnaire rated from 0-100 with five subsections (discussed in Chapter 1.6). Data will be collected for each section.

Lastly, an exit interview will be performed for each patient in the intervention group. A research assistant will make contact with the patient, in person or via telephone, on day seven to gain a more qualitative understanding of the experience during the study. Please see Appendix C for exit interview script.

3.9 Sample Size Calculation

The statistical assumption to estimate sample size is based off of historical data in Yale's MICU, collected by a study by Dr. Knauert for which the manuscript is in process. The overnight TST from this data set was found to be 94 minutes, with a high degree of variance of 61 minutes. Given this data, for a power of 80% and alpha of 0.05, and an effect size of 20% increase in sleep (18 minutes), the calculated sample size is 324 participants, or 162 per group. To calculate, the ClinCalc online tool was used (see Appendix D). With this calculation, we hope to have a sample size of 330 to allow for correction.

3.10 Analysis

The primary outcome data will be analyzed using intention to treat. Secondary analysis will be performed with per protocol. The intervention and control groups will have TST averaged within groups. Given that TST, the primary outcome, is a continuous variable of means**,** a t-test will be used to study and compare the groups. The secondary outcome data will also be analyzed with intention to treat and secondary analysis of per protocol. The secondary outcome will be the RCSQ global scale (i.e. combined five subsections of the RCSQ). The global scale averages between intervention and control will be compared using a t-test. Secondary analysis of the secondary outcome will be comparing the individual subsections of the RCSQ. Lastly, qualitative analysis will be performed to identify, consolidate, and review themes from the exit interview.

3.11 Timeline and Resources

The proposed study will occur over the span of two years. Past experience in the Knauert Lab suggests that at least 40 patients meeting age criteria per week are admitted to the MICU. However, respiratory failure is often the leading diagnosis and is expected to be present in approximately one-half of admitted patients over 50 years of age, thus reducing our estimate of eligible patients per week to 20. In addition, the Knauert Lab's historic eligible to enroll rate is >25%. Therefore, we estimate conservatively the enrollment of 5 patients per week. To achieve our goal of enrollment of 330 study participants, we would need 66 weeks, or approximately 16 months, of active enrollment. We expect interruptions in enrollment for holidays, staff vacations, and day-light savings time (no enrollment during the week following start and stop), up to 8 weeks per year. Based on these numbers, we estimate that we will require approximately 18 months.

The timeline of the study will occur in three phases. Phase 1 will include IRB approval, database development, research staff training, and nursing in-service training, which will each occur over the course of three months. Phase 2 will include recruitment, enrollment, and data collection, which will each occur on a rolling basis over 18 months. Phase 3 will be analysis and manuscript composition, which will overlap the end of enrollment and occur in the nine months prior to study completion.

Table 2: Tucked In Timeline

"X" represents three months	**Year 1**				**Year 2**			
Phase 1								
IRB approval	X							
Database Development	X							
Research Staff Training	X							
Nursing In-Service	X							
Phase 2								
Recruitment		X	X	X	X	X	X	
Enrollment		X	X	X	X	X	X	
Data Collection		X	X	X	X	X	X	
Phase 3								
Analysis						X	X	X
Manuscript						X	X	X

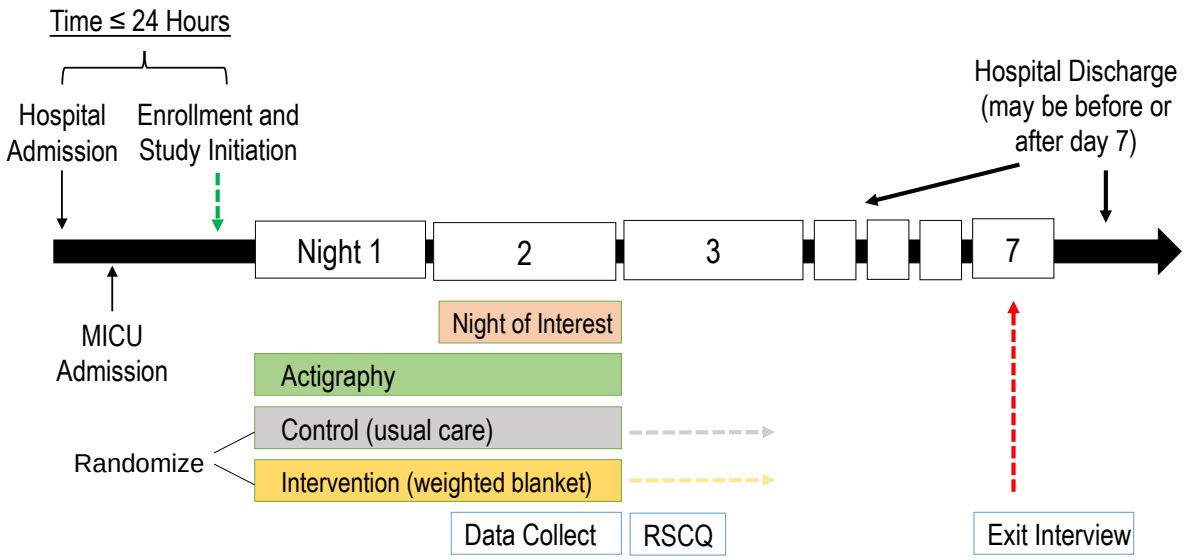
The principal investigator (PI) for the study will be Dr. Melissa Knauert, MD, PhD. The co-principal investigator (co-PI) will be Jaime Conway, PA-SII. Two additional research assistants will be hired on an hourly basis for recruitment, enrollment, and data collection. The MICU at Yale is a total of 38 beds. There should be no more than ten currently enrolled patients at a time due to expected losses of eligibility and consent. The MICU Research Working Group has a library of equipment already purchased, which includes ten Actiwatch Spectrum Plus units and the associated

programs for data interpretation. Video recording devices will also be obtained through the Working Group's equipment library.

The weighted blanket will be purchased from CapeAble Weighted Products in three weights (13.2lb, 17.6lb, or 22lb,) and will be produced such that it will be able to be wiped down and sanitized between patients with Sani-Cloth wipes (described further in Chapter 2.3.5). Four blankets in each weight category will be purchased for a total of twelve blankets. The approximate cost of these blankets will be $500 per blanket ($6,000).

3.12 Summary

Figure 2: Study timeline for each participant



CHAPTER 4: CONCLUSION

4.1 Advantages and Disadvantages

This study will be the first to use a blinded RCT design to compare the use of a weighted blanket to standard care with a goal of improving sleep in the adult critically ill population. Other non-pharmacological studies such as quiet time protocols, clustered care, earplugs, and eye masks have been studied with some success and are now implemented at YNHH.[1-6] Other weighted blanket studies have attempted to improve sleep in different populations, but lacked significant sample sizes, combinations of objective and subjective data, or showed signs of bias.[7-10] Through a randomized controlled design, we hope to gain insight into the benefits of a weighted blanket. We hope to limit bias through attempts at blinding and yield results with generalizability through a larger sample size than previous studies. Lastly, by measuring outcomes subjectively and objectively, we hope to allow for more compelling evidence for the benefits of weighted blanket use.

There are limitations to the proposed study that should be acknowledged. Blinding will be difficult given the weighted nature of the intervention and could cause bias on both the side of the research staff and of the participants. We will attempt to blind staff by 1) having separate research assistants apply intervention/control and collect subjective data and 2) collecting objective actigraphy data. We will attempt to blind participants through phrasing of the consent form as a "non-pharmacological interventions for sleep study." Another limitation of our study would be the lack of heterogenicity of patient population. In the medical ICU, with our inclusion and exclusion criteria, we will be limited to a very specific subset of critical illnesses.

However, this should not limit generalizability, as most hospitals across the country would have medical ICUs with similar conditions. Lastly, the accuracy of actigraphy, an accelerometer based on body movement, can be limited in this population given the restricted movement of patients. We combat this issue through our exclusion criteria. By excluding those in respiratory distress, we are excluding those on mechanical ventilation who are sedated or restrained, thus precluding those that are moving less. In addition, by combining objective and subjective outcomes, we are able to compare and account for less movement. In summary, while there are limitations of the proposed study, measures were taken in development of the methods to mitigate these issues.

4.2 Clinical Significance

Sleep deprivation in the ICU can adversely affect patient outcomes in the short and long term. Pharmacological interventions are not recommended as first line options as they have not been shown to help and can often have adverse effects.[11-14] Non-pharmacological options such as quiet time protocols, eye masks, and earplugs have proven successful. However, patients continue to have poor sleep in this setting. Given the limited number of options available for those suffering from sleep deprivation in the ICU, providers often find themselves distressed by the lack of potential solutions they can offer. In some cases, medical teams may even cause secondary harm with medications that are not approved, but used out of desperation to find an answer to the lack of sleep.

For these reasons, depending on the results of the study, another non-pharmacological option of a weighted blanket could be offered to patients as a solution to poor sleep. Weighted blankets, after initial investment, can be a cost-effective

intervention. In the clinical setting, the blanket may also prove to be a method of supporting patient satisfaction.

While this study is limited to a specific population that is most vulnerable to sleep deficiency, it would have the potential to be applicable and extrapolated to a wider population with further study. Lastly, with limited research on weighted blankets, it would allow PAs and all providers in practice to better inform and guide patients when asked about or confronted with anecdotal evidence around weighted blankets relating to a variety of sleep related issues.

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APPENDIX A: Authorization and Consent Form

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE
YALE NEW HAVEN HOSPITAL

Study Title: TUCKED IN: WEIGHTED BLANKETS TO IMPROVE SLEEP IN INTENSIVE CARE UNIT PATIENTS

Principal Investigator: Dr. Melissa Knauert, MD, PhD

Co-Investigator: Jaime Conway, PA-SII

Funding Source: Yale University School of Medicine Physician Associate Program

Invitation to Participate and Description of Project

You are invited to participate in a research study investigating different non-pharmacological sleep interventions that aim to help sleep in intensive care units. You have been asked to participate because you have been admitted to the Medical Intensive Care Unit (MICU). Approximately 330 people will participate in this study.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of the research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits, and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

If you agree to participate in this study, you will be randomly assigned to one of two groups. Each group has a different non-pharmacological sleep intervention, meaning something that is not a medication that aims to enhance your sleep during your stay in the MICU. Examples include blankets, masks, earplugs. Random assignment is similar to flipping a coin; there is a 50% chance you end up in one group or the other. You will be asked to use your intervention while you sleep in the MICU.

You will be asked to wear an actigraph, similar to a FitBit, which measures your sleep while you wear it, for two total nights. Your lower body will be video recorded, but your face and other identifying features will be obscured. You will be asked a series of questions the morning following your use of the intervention. As a courtesy, you will be able to use your intervention for the remainder of your stay in the hospital, should you

desire. You will be asked to participate in a 5-minute exit interview via telephone one week after the study completes.

You will be told of any significant new findings that are developed during the course of your participation in this study that may affect your willingness to continue to participate. Research results will not be returned to your doctor. If research results are published, your name and other personal information will not be given.

Risks and Inconveniences

We do not anticipate any major risks in participating in this study. Potential risks would include discomfort while using your intervention, skin irritation from contact with different fabrics, or skin breakdown, though these are highly unlikely.

There is a risk of breach of confidentiality about your health status and participation in this study, though this is unlikely to occur. All research staff will be thoroughly trained and certified in the privacy of research studies.

Benefits

Benefits of participation in this study may include improvements in sleep, anxiety, and comfort while staying in the MICU. This study may also provide insight on improving your sleep outside of the hospital.

Economic Consideration

Your non-pharmacological intervention will be provided free of charge during your stay in the hospital. A promotional code will be provided to purchase your intervention from the manufacturer once you are discharged from the hospital.

Treatment Alternatives/ Alternatives

The alternative to participating in this study is to decline participation. If you do not wish to participate you will be provided the standard treatment.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or state law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Information will be kept confidential by using only identification numbers on study forms, storing signed forms in locked cabinets, and password protecting data stored on a computer. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific permission for this activity is obtained.

We understand that information about your health is personal, and we are committed to protecting the privacy of the information. If you decide to be in this study, the researcher will get information that identifies your personal health information. This may include information that might directly identify you, such as your name, birth date, or address. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you and your coded information, and this link will be kept secure and available only to the principal investigator or selected members of the research team. Any information that can identify you will remain confidential. The link to your personal information will be kept for 5 years, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

The information about your health that will be collected in this study includes:

- Research study records
- Records about your time in the hospital
- Records about phone calls made as part of this research

Information about you and your health which might identify you may be used by or given to:

Representatives from Yale University, the Yale Human Research Protection Program, and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.

By signing this form, you authorize the use and /or disclosure of the information described above for this research study. The purpose of the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and those hospitals involved in this study are required to comply with HIPAA and to ensure the confidentiality of your information. You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. This authorization to use and disclose your health information collected during your participation in this study will never expire.

Voluntary Participation and Withdrawal

Participation in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are

otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing from the Study

If you do become a subject of this study, you are free to stop and withdraw at any time during its course.

To withdraw from the study, you can inform nursing staff at any time and tell them you no longer wish to participate. You can simply remove your intervention and no longer use it. Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw or take away your permission to use and disclose your health information at any time. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary, to ensure the integrity of the study and/or study oversight.

You do not give up any of your legal rights by signing this form.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you do not understand and to consider this research and the consent form carefully—as long as you feel is necessary—before you make a decision.

Authorization and Permission:

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purpose, the particulars of my involvement, and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purpose described in this form. By refusing to give permission, I understand that I will not be able to be in this research study.

Name of Subject: _____

Signature: _____

Date: _____

_____ _____

Signature of Person Obtaining Consent Date

If after you have signed this form you have any questions about your privacy rights, please contact the *Yale Privacy Officer at (203) 432-5919.*

If you have further questions about this project or if you have a research-related problem, you may contact the co-Principal Investigator, Jaime Conway. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the *Yale Human Investigation Committee at (203) 785-4688.*

APPENDIX B: Richards Campbell Sleep Questionnaire

Richards Campbell Sleep Questionnaire (RCSQ)

Code Number_____	Date_____

Each of these questions is answered by placing an "X" on the answer line. Place your "X" ***anywhere*** on the line that you feel ***best*** describes your sleep last night. The following are examples of the type of questions you are to answer.

EXAMPLE A
Right now I feel:

Very Sleepy ***X*** _____ ***Not sleepy at all***

If you were very sleepy, you would place an "X" as is shown at the beginning of the line next to the words ***"Very Sleepy."***

EXAMPLE B
Right now I feel:

Very Sleepy _____ ***X*** _____ ***Not sleepy at all***

If you were somewhat sleepy, you would place an "X" near the center of the line. Mark the answer line near the center to indicate the answer ***"Somewhat Sleepy."***

EXAMPLE C
Right now I feel:

Very Sleepy _____ ***X*** ***Not sleepy at all***

If you were not sleepy at all, you would place an "X" at the end of the line next to the words ***"Not Sleepy At All."***

Please turn to next page

You are now ready to begin to answer the questions. Place your "X" ***anywhere*** on the answer line that you feel ***best*** describes your sleep last night.

1. My sleep last night was:

Deep Sleep _____ ***Light Sleep***

2. Last night, the first time I got to sleep, I:

Fell Asleep _____ ***Just Never Could Fall Asleep***
Almost Immediately

3. Last night I was:

Awake _____ ***Awake All Night Long***
Very Little

4. Last night, when I woke up or was awakened, I:

Got Back To Sleep Immediately _____ ***Couldn't Get Back To Sleep***

5. I would describe my sleep last night as:

A Good Night's Sleep _____ ***A Bad Night's Sleep***

Optional Noise Item:

6. I would describe the noise level last night as:

Very Quiet _____ ***Very Noisy***

APPENDIX C: Scoring Richards Campbell Sleep Questionnaire

Richards Campbell Sleep Questionnaire (RCSQ)

Scoring Directions:

1. Scores may range from 0 (indicating the worst possible sleep) to 100 (indicating the best sleep).

100_____0

2. A score for each question is given based on the length of the line in millimeters from the 0 point to the cross of the patient's "X".

3. The total RCSQ sleep score is derived by adding the individual scores for items 1-5 for each question and dividing by five.

4. Item 6 should be scored individually. It was not part of original RCSQ, but can be used as a measure of noise.

Note: Photocopying or use of various fonts' sizes may change the length of the lines on the visual analogue scale. Please measure to be certain that the lines are exactly 100 millimeters prior to using the scale.

APPENDIX D: Exit Interview

INTERVENTION EXIT INTERVIEW

Code Number_____ Date_____

1) During the past month, how would you rate your sleep quality overall?
    a. Very good
    b. Fairly good
    c. Fairly bad
    d. Very bad

2) Did you use the blanket while sleeping? Y/N

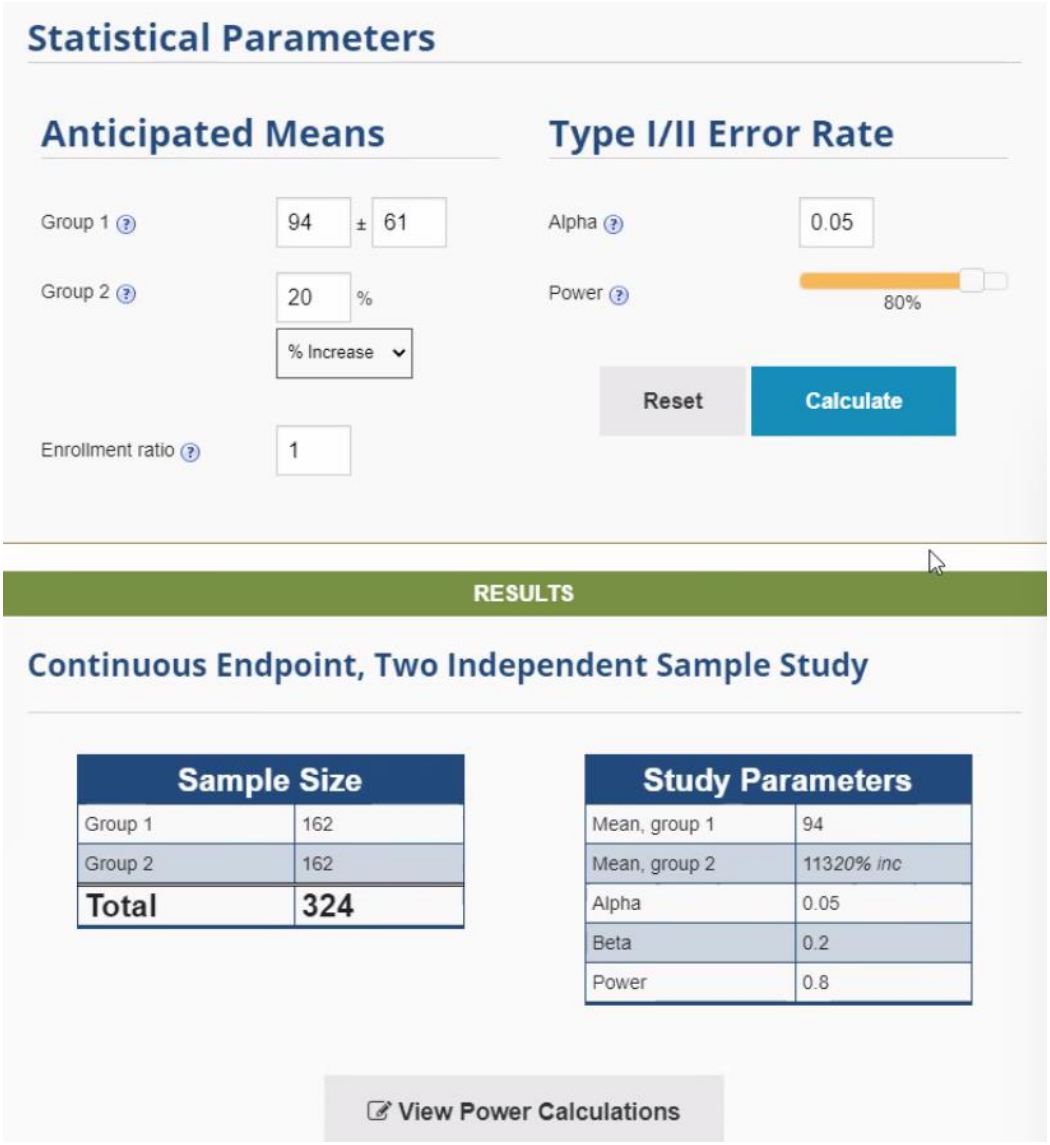
    Comments:

3) Did the blanket help you sleep better? Y/N

    Comments:

4) What did you think of the blanket?

APPENDIX E: Sample Size Calculation



ClinCalc LLC, Sample Size Calculator

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