### Title

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### Publication Date

2022

### DOI

10.3389/fnins.2022.815872

Peer reviewed

# Preventing sleep disruption with bright light therapy during chemotherapy for breast cancer:

# A Phase II randomized controlled trial

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**Keywords: breast cancer, light therapy, sleep, actigraphy, PSQI, activity**

**Abstract**

PURPOSE: The goal of this study was to examine whether daily increased morning light exposure would maintain or improve sleep and the circadian pattern of relatively more activity in the day and less during the night in women undergoing chemotherapy for breast cancer.

PATIENTS AND METHODS: Sleep/wake was measured objectively with wrist actigraphy and subjectively with the Pittsburgh Sleep Quality Index (PSQI) prior to and during chemotherapy cycles 1 and 4. Participants were 39 women with newly diagnosed breast cancer, randomized to either 30-minutes of daily morning bright white light (BWL) or dim red light (DRL). The study was registered with the National Institutes of Health ClinicalTrials.gov (Clinical Trials number NCT00478257).

RESULTS: Results from actigraphy suggested that compared to the DRL group, women in the BWL group had longer night-time sleep, fewer sleep disturbances during the night, and had fewer and shorter daytime naps at the end of cycle 4 of chemotherapy as well as exhibiting less activity at night and more activity during the day by the end of cycle 4. Results from PSQI indicated that components of sleep quality improved but daytime dysfunction deteriorated during cycle 4 treatment in the BWL group; meanwhile the DRL group used more sleep medications in the treatment weeks which might have led to the improved sleep quality during the recovery weeks of both cycles.

CONCLUSION: These results suggest that bright white light therapy administered every morning on awakening may protect women undergoing chemotherapy for breast cancer from nighttime sleep and daytime wake disruption. Randomized clinical trials in larger samples are needed to confirm these findings.

## Introduction

Disturbed sleep is one of the most common and distressing complaints among patients with breast cancer, occurring in 30-50% of patients undergoing chemotherapy (Savard & Morin, 2001). Nighttime sleep disruptions, such as difficulty falling asleep, staying asleep, and frequent awakenings, are aggravated in women with breast cancer undergoing chemotherapy (Ancoli-Israel et al., 2006; Berger et al., 2007; Palesh et al., 2010). Patents with cancer also complain of increased daytime napping (Engstrom et al., 1999) described as longer and more frequent daytime naps as treatment progresses (Berger & Farr, 1999; Levin et al., 2005; Wielgus et al., 2009; Young-McCaughan et al., 2003), which has been associated with decreased daytime activity that, in turn, has been found to predict higher cancer-related fatigue (CRF) (Berger & Farr, 1999; Wielgus et al., 2009).

Many studies measuring sleep in cancer have used actigraphs, a wrist worn device which measured activity which can be used to estimate sleep and wake. Despite the ability of actigraphy to simultaneously measure both sleep and activity (Berger et al., 2008), relatively few studies have evaluated both outcomes in patients with breast cancer undergoing chemotherapy (Berger et al. 2007; Young-McCaughan et al. 2003).

Previous research in our laboratory found that women with breast cancer have decreased daytime light exposure both before and during chemotherapy, with the most pronounced decrease in light exposure during the treatment infusion weeks of chemotherapy (Liu et al., 2005). Synchronized endogenous circadian activity rhythms are related to exposure to diurnal bright light; low diurnal illumination levels have been associated with nocturnal sleep dysfunction (Ancoli-Israel et al. 2002; Terman et al. 1995). Sleep and mood disruptions have been successfully treated with morning exposure to increased artificial bright light in other populations, including individuals with winter depression (Rosenthal et all., 1985; Terman and Terman 2005), nonseasonal depression (Al-Karabi and Jubair, 2016), anxiety (Youngstedt and Kripke 2007), and PTSD (Youngstedt et al. 2021). Our laboratory has shown that morning bright light therapy prevents cancer related fatigue from getting worse, prevents circadian activity rhythms from deteriorating and improves quality of life in women undergoing chemotherapy for breast cancer (Neikrug et al. 2012; Ancoli-Israel et al. 2011; Jeste et al., 2013). Morning light therapy has been combined with cognitive behavioral therapy to improve sleep in women undergoing

chemotherapy (Bean et al. 2020); however, there are no studies evaluating just bright light therapy on sleep or activity in this group. Thus, we evaluated whether administration of bright light upon awakening in the morning would alleviate the poor nighttime sleep and lower daytime alertness experienced during chemotherapy in women with breast cancer.

## Materials and Methods

We conducted a small phase II randomized clinical pilot study comparing bright white light (BWL) therapy to dim red light (DRL) therapy in women diagnosed with breast cancer undergoing four cycles of adjuvant or neo-adjuvant chemotherapy.

### Patients

Data were collected from the same women reported in previous publications on the effect of light on fatigue, circadian activity rhythms and quality of life (Ancoli-Israel et al., 2011, Neikrug et al., 2012; Jeste et al., 2013). As reported in those studies, 58 women were referred by physicians for the study (see Fig 1). Of those referred, 17 were ineligible after screening and 41 were consented and randomized. Of the 41 randomized, 2 participants (one from each group) dropped out immediately and were not included in the analysis; 8 women from the BWL and 3 women from the DRL dropped during the treatment phase and were included in the analysis. Therefore, data are presented from 39 women (mean age=53.95 yrs., *SD*=9.06, range=32-70 years).

### Inclusion and Exclusion Criteria

Participants were referred by medical oncologists in the San Diego community or from the UCSD Moores Cancer Center. Inclusion criteria were having a new diagnosis of stage I-III breast cancer and scheduled to receive at least four cycles of adjuvant or neoadjuvant chemotherapy. Exclusion criteria were being pregnant, having metastatic or IIIB (including inflammatory) breast cancer, significant pre-existing anemia, or confounding underlying medical illnesses or any other physiological or psychological impairments that would have limited participation. Breast cancer disease staging was based on the American Joint Committee on Cancer Staging Manual 5th Edition (Greene 2002). Menopausal status was determined using self-report of the occurrence of menses (Rissling et al. 2011).

After referral from the oncologist, informed consent, HIPAA, and release of information were obtained by the study coordinator. Pertinent medical information (e.g., stage of disease and estrogen/progesterone receptor status [ER/PR]) was abstracted from each participant's medical record prior to participation in the study.

Approval for this study was received from the University of California San Diego Office of IRB Administration and by the UC San Diego Moores Cancer Center's Protocol Review and Monitoring Committee. All women provided written informed consent before participation. The study was registered with the National Institutes of Health ClinicalTrials.gov (Clinical Trials number NCT00478257).

**Study Design**

Figure 2 shows the study design which included a baseline assessment, treatment randomization prior to the start of chemotherapy followed by daily morning light treatment for four cycles of chemotherapy. After baseline, actigraphy and questionnaires were repeated only during the treatment and recovery weeks of cycles 1 and 4 of chemotherapy. Wrist actigraphs were worn at 5 time-points: prior to the start of chemotherapy (baseline), chemotherapy treatment week of cycle 1 (C1TW), recovery week of cycle 1 (C1RW), chemotherapy treatment week of cycle 4 (C4TW), and recovery week of cycle 4 (C4RW). Actigraphy periods coincided with each participant's scheduled weekday chemotherapy infusions. Results of questionnaire data assessing fatigue, mood, quality of life, functional outcome, menopausal status and climacteric symptoms have been previously published (Ancoli-Israel et al., 2011; Jeste et al., 2013; Liu et al., 2009, 2012; Neikrug et al., 2012; Rissling et al., 2011).

**Randomization**. The randomization sequence was generated by the study statistician using the R statistical software package (http://cran.r-project.org/). A blocked design with a 2:3 allocation to dim red light (DEL; n=16) versus bright white treatment (BWL; n=23) using a block size of 4. Our hypothesis was that BWL would be more beneficial; and therefore, more participants were randomized to BWL to provide a larger sample with this treatment. Both treatments were noninvasive. The study coordinators were blinded to the randomization allocation of participants.

**Instructions to participants**. Each participant was provided with a Litebook®, a demonstration of proper operation, a paper tape measure and digital timer. Participants were instructed how to position the Litebook® and to operate it for 30 contiguous minutes immediately upon awakening every day throughout their four cycles of chemotherapy. The goal of the study was described to participants by the study coordinators as an evaluation of two frequencies of light therapy (red or white) for improving sleep and fatigue during chemotherapy.

**Light.** Light was administered via a Litebook 1.2 (Litebook®, Ltd. Alberta, Canada). The Litebook® is a small (6"x5"x1") and lightweight (8 oz.) light box designed to be placed on a table about 18" from the patient's head and within a 45° visual field. The Litebook® utilizes 60 premium white light emitting diodes (LED) which mimic the visible spectrum of sunlight for minimum glare and maximum eye comfort. The Litebook® emits no ultraviolet (UV) light for safety. Two women randomized into the BWL group reported the light aversive and dropped out during treatment; however, these data are included in the analysis. An identical-appearing device utilizing red LEDs emitting dim red light at <50 lux was used for the comparison DRL group. No participants reported the dim red light aversive.

The Litebooks® were modified to include an integrated meter which allowed for monitoring treatment adherence by recording operation time and duration. Partial adherence data were available for 30 participants (BWL n=17; DRL n=13); analysis indicated similar frequency of use (BWL = 55.0%; DRL = 70.2% of days assigned) and duration of use (BWL = 31.5 min; DRL = 33.9 min per day used) with no significant difference between the groups.

**Measures**

**Pittsburgh Sleep Quality Index (PSQI).** (Buysse et al., 1989) Sleep quality was measured with the PSQI, a 19-item questionnaire which rates patients' reports of sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The total PSQI scores range from 0-21 with high scores reflecting poor sleep quality. A total score above 5 is generally considered poor sleep.

**Actigraphy**. Wrist actigraphy devices were used for obtaining objective measures of nighttime and daytime sleep as well as for activity levels. Wrist actigraphy measures motion over time by recording the amount of electrical deflection during a fixed interval (e.g., minute by minute) (Ancoli-Israel, et al., 2003; Ancoli-Israel et al., 2015). In the current study, two similar actigraphy devices were used. The Actillume® was used with the first 11 participants (Ambulatory Monitoring, Inc., Ardsley, New York). Actillume® data were analyzed using the Action-3 software program (Ambulatory Monitoring Inc., Ardsley, NY, USA). Actillume® data for 9 participants ( BWL=5; DRL=4) are included in these analyses. The Actiwatch-Light® (Mini-Mitter|Respironics/Philips, Eindhoven, The Netherlands) was used in the remainder of the participants (n=28). Actiwatch-Light® data were analyzed using the Actiware® 5 sleep and activity monitoring software program (Mini-Mitter|Respironics). Activity sensitivity threshold was set to medium. Both devices record continuous acceleration data on the non-dominant wrist using a battery-operated microprocessor that senses motion with a piezoelectric beam and detects movement in all three axes. Device equivalency was evaluated by comparing data collected by paired devices worn simultaneously for 72-hours by eight healthy adult volunteers. The software-scored sleep/wake data based on the two types of activity count were highly correlated (both $r's>0.85$, both $p's<0.0001$), therefore, these variables were deemed equivalent for the purpose of this study. Data from 39 participants (BWL=23, DRL=16) are included in analyses.

Actigraphic sleep variables were derived from a mean of three contiguous sleep and wake (night/day) periods using 1-minute epochs. Self-report via sleep log was used to edit actigraphy data and determine daytime and nighttime sleep and wake periods. Nighttime variables included: nighttime average activity counts per minute, sleep percentage (%sleep), nighttime total sleep time (TST) and nighttime total waketime (TWT). Daytime variables included: daytime average activity counts per minute, mean nap duration (mNAP) number of daytime naps (nNAP) and total nap time (TNT). A daytime sleep episode, or nap, was defined as any period of 10 or more minutes of consecutive actigraphic inactivity (i.e., sleep) during the period between final out of bedtime in the morning and into bedtime the following night.

**Statistical Analyses**

Descriptive statistics were calculated for the entire sample as well as separately for the two treatment groups. Group differences were assessed with *t*-tests at baseline for possible confounders (i.e., demographic variables, clinical characteristics, and chemotherapy regimen). Variables that significantly differed between the treatment groups at a 0.05 significance level were controlled for in the inferential analysis.

Linear mixed-effects models were used for analyzing changes of subjective sleep quality, objective activity count and sleep/wake variables before and during chemotherapy, with group, time and group-by-time interaction included as fixed covariate effects. Baseline was the reference time point and the DRL group was the reference group. Each of the outcome variables were modeled separately. If a significant group, time or group-x-time interaction was found, further post-hoc tests were conducted using appropriate contrasts: between group differences at each time point, and/or within group changes from Baseline to the other time points. Linear mixed-effects models and restricted maximum likelihood methods (Diggle, Liang, & Zeger, 1996) were employed for analyzing and comparing sleep and activity variables for each treatment group. This paradigm relies on the "missing at random" assumption (Diggle, 2002) and allows for modeling partial data where the number of measures per person could vary and participants with missing time points could still be included in the analysis. Thus, mixed model protects from a "completers only" bias.

## Results

### Demographics

Table 1 shows the sociodemographic characteristics of our sample. There were no significant differences between the treatment groups in age, BMI, race, income, education, marital status, ER/PR status, or stage of disease.

### Objective sleep measures

#### *Nighttime Sleep*

At baseline, the BWL group had significantly less TST than the DRL group ($p$=0.01), thus the baseline TST was adjusted in all linear mixed-effects models. No other group differences were found at baseline (both $p$'s>0.2 for %sleep and TWT). The BWL group had increased TST at C1TW, C4TW and C4RW compared to

baseline (all *p*'s<0.03), while the DRL group had decreased %sleep and increased TWT at C4RW (both *p*'s<0.05). A significant group-by-time interaction at both C4TW (p=0.042) and C4RW (*p*=0.012) for TST (Fig. 3A), and at C4RW for both %sleep (Fig. 3A) and TWT (Fig. 3C) (both *p*<0.05), suggests that over the course of chemotherapy the BWL group had spent significantly more time asleep and less time awake compared to the DRL group while controlling for baseline differences.

(Place Fig 3A, B, C here)

***Daytime sleep***

No group differences in daytime sleep at baseline were detected (all *p*'s>0.3). During C1TW, the DRL group had increased nNAP (Fig. 4A), increased TNT (Fig. 4B), and increased mNAP (Fig. 4C; all *p*'s<0.03) as compared to baseline. Both nNAP and TNT also increased in the DRL group at C4TW (both *p*'s=0.0003). mNAP increased from baseline to C1TW (*p*=0.0003) in the DRL group (Fig. 4C). There were no significant differences in the BWL group.

Group-by-time interactions for nNAP (Fig. 4A), TNT (Fig. 4B) and mNAP (Fig. 4C) at both C4TW and C4RW (all *p's*<0.05) suggest that the DRL group had a larger increase in overall frequency and duration of naps at cycle 4 than the BWL group. Group-by-time interactions for mNAP at both C1TW and C4TW (both *p*'s<0.03) suggest that average nap duration in the DRL group increased more than that in the BWL group during the treatment weeks of both cycles.

(Place Fig 4A, B, C here)

**Activity**

***Activity During the Nighttime Sleep Period***

As shown in Fig. 5A, activity counts during the nighttime sleep period did not differ between groups at baseline (*p*=0.16). The DRL group had more nighttime sleep period activity at C4RW (*p*=0.033) compared to baseline, but the BWL group showed no significant changes during either cycle 1 or 4 (all *p*'s>0.3). At C4RW a significant group-by-time interaction suggested that the average amount of activity counts during the nighttime sleep period in the DRL group increased from baseline over the course of chemotherapy while conversely, in the BWL group, sleep period activity counts decreased (*p*=0.047).

(Place Fig 5A and B here)

***Activity During the Daytime Wake Period***

As shown in Fig. 5B, activity counts during the daytime wake period did not differ between groups at baseline ($p$=0.35). The DRL group showed less daytime wake activity counts at C1TW and C4TW as compared to baseline (Fig. 5B; both $p$'s<0.001). No significant changes in the BWL group during either cycle 1 or 4 were observed (all $p$'s>0.08). However, a significant group-by-time interaction was observed at C4TW suggesting that the DRL group showed more decrease in daytime wake activity counts from baseline than the BWL group ($p$=0.013).

**Subjective sleep quality**

PSQI global and component scores are listed in Table 2. There were no significant differences in the PSQI global or component scores between the BWL group and the DRL group at baseline (all $p$'s>0.05), and also no significant group-by-time interactions for the global or component scores during either cycle (all $p$'s>0.05). Within the BWL group, compared to baseline, there were significantly lower scores in three subscales (i.e., improvement in subjective sleep quality, sleep duration, sleep disturbances) during C4RW, however, the daytime dysfunction component score increased (i.e., worse daytime function) during both weeks of cycle 4 (both $p$'s<0.05). Within the DRL, compared to baseline, the subjective sleep quality component score decreased during the recovery weeks of both cycles (i.e., sleep quality improved) but the use of sleeping medication increased during the treatment weeks of both cycles (all $p$'s<0.05).

## Discussion

The results of this study suggest that morning bright white light administered daily during chemotherapy to women with breast cancer may prevent deterioration of nighttime sleep and sleep quality and reduce daytime sleepiness.

During the weeks of chemotherapy administration, the weeks of greatest distress, the women in both light treatment groups took more and longer naps. During the recovery week of cycle 1, both groups returned

to the pre-chemotherapy levels. However, by the fourth cycle, the cumulative effects of chemotherapy resulted in less sleep at night and more and longer naps during the day in the women in the DRL group while women in the BWL group showed an increase in nighttime sleep and a return to pre-chemotherapy levels of napping.

Similar results were observed in sleep quality. While no significant group by time interaction was observed by the end of cycle 4 chemotherapy, compared to baseline, the BWL group reported improvement in nighttime sleep quality (subjective sleep quality, sleep duration and sleep disturbance components). Reports of daytime dysfunction however increased. This deterioration of daytime functioning during the fourth cycle of treatment might be attributed not only to disturbed sleep, but also to the cumulative side-effects of cancer treatment. The finding that the DRL group reported improved sleep quality during the treatment weeks of both cycles may be explained by the concurrent increase in sleep medication use (Huedo-Medina et al. 2013). Taken together, the objective sleep and subjective sleep quality results suggest that overall the bright white light resulted in less deterioration of sleep.

In addition to the effects on sleep, significant changes in the amount of activity both during the sleep period and the wake period were observed. Berger et al. (2009) showed that there is little distinction between night and day activity, as measured by actigraphy during chemotherapy, which suggested both disrupted sleep at night and disrupted wake during the day (2009). Having high actigraphic activity counts during the wake period and low counts during the sleep period has been associated with higher survival (Mormont et al., 2000; Innominato et al., 2009), better quality of life (Innominato et al., 2009), and lower levels of depression (Du-Quiton et al., 2010 and fatigue (Innominato et al., 2009) in patients with cancer. In the current study, women exposed to dim red light had decreased wake-time activity during chemotherapy treatment weeks of cycle 1 and cycle 4, as might be expected during chemotherapy, while those exposed to bright white light had no significant changes in daytime activity compared to baseline. During the sleep period, those in the BWL group showed less activity than those in the DRL group. These data suggest that bright white light also protected the women from the deterioration in wake-time physical activity usually experienced during chemotherapy.

The impetus for this study was the prior observation that women undergoing chemotherapy receive progressively less bright light exposure as treatment progresses, particularly in the days following

chemotherapy infusion, and that this decrease is associated with fatigue and sleep disturbances (Liu et al. 2005). Previously reported data from this sample demonstrated that bright light therapy prevented cancer-related fatigue (Ancoli-Israel et al. 2011) and prevented deterioration of both the circadian activity rhythm (Neikrug et al. 2012) and subjective quality of life during chemotherapy (Jeste et al. 2013). The current results demonstrate not only a lack of deterioration of sleep and activity in the bright white light group but also improvement in daytime sleep and nighttime activity compared to pre-chemotherapy levels. Whether the observed benefit of bright light therapy was due to the alerting effect of light, to the improvement in circadian activity rhythms or some other unobserved mechanism, cannot be determined from this study.

While there have been a few other studies examining the effect of bright light treatment on sleepin cancer survivors, (Wu et al. 2018; Valdimarsdottir et al. 2018; Johnson et al. 2016; 2018; Fox et al. 2020; Starreveld et al. 2018), to our knowledge, is the first randomized controlled trial examining the effect of bright light therapy on sleep (measured both objectively and subjectively) and activity during chemotherapy in women with breast cancer. Berger et al. (2009) found a positive effect on sleep in a similar population using a modified behavioral therapy that included both nighttime and daytime sleep restriction; however, the improvement in the treatment group was limited to an improvement in subjective sleep quality and fewer objectively measured awakenings at night (daytime sleep was not reported). While these results are suggestive that targeting both nighttime and daytime sleep disruption using a behavioral treatment may be beneficial during chemotherapy, the lack of objective improvement in sleep also suggests that additional intervention may be needed.

The strengths of the current study include the randomized controlled and longitudinal design; in particular, the inclusion of a baseline prior to chemotherapy in addition to data collection during chemotherapy. Additional strengths include the inclusion of both subjective and objective measures of sleep and the utilization of the mixed model statistical analysis which allowed for partially complete subject records (i.e., missing data at some time-points), thereby avoiding the biases of “completers only” analysis.

However, there are also limitations to the study. The first major limitation is the small sample size. With a larger sample size, trends such as the deterioration found in the DRL group may have been statistically significant. However, this was a preliminary study intended to provide Phase II data for a larger randomized

trial. Secondly, the physical activity results should be interpreted with caution as we did not employ waist actigraphy. Our main interest was on sleep for which wrist actigraphy is a reliable measure (Ancoli-Israel, et al., 2003; Ancoli-Israel et al., 2015). More detailed assessment of physical activity and exercise is needed in future work.

In summary, the breast cancer chemotherapy group receiving dim red light showed expected and progressive deterioration during chemotherapy, particularly in daytime sleepiness and inactivity during the day during cycle 4. The bright white light group however, showed significantly less deterioration and were less sleepy and more active during the day at cycle 4 showing a greater ability to recover from the cumulative negative effects of chemotherapy. Larger studies are needed to replicate these findings; however, the study suggests that morning bright light, an easy, non-invasive, non-harmful behavioral treatment, may at least prevent deterioration of nighttime sleep and promote daytime activity and alertness in women undergoing chemotherapy for breast cancer.

**Conflict of Interest.** Sonia Ancoli-Israel is a consultant for Eisai, Biogen, Merck, Idorsia and Pear Therapeutics. Neelum Jeste was a student at UCSD at the time of the study and currently works for J&J which has had no influence or funding of this study. The other authors have no relevant financial or non-financial interests to disclose.

**Author Contributions.**

Sonia Ancoli-Israel was the PI of the study and contributed to the study conception, design, material preparation and writing and commenting on all versions of the manuscript.

Michelle Rissling led the writing of the manuscript, and contributed to data collection and interpretation.

Lianqi Liu contributed to the study conception, design, material preparation and commenting on all versions of the manuscript.

Shawn Youngstedt contributed to writing and commenting on previous versions of the manuscript.

Vera Trofimenko contributed to the study conception, design, material preparation, and writing and commenting on previous versions of the manuscript

Loki Natarajan contributed to the study conception, design, material preparation, and writing and commenting on previous versions of the manuscript Dr. Natarajan also performed the statistical analyses.

Ariel Neikrug contributed to material preparation, data collection and commenting on all versions of the manuscript.

Neelum Jeste contributed to the study conception, design, material preparation and writing and commenting on all versions of the manuscript.

Barbara Parker contributed to the study conception, design, material preparation and writing and commenting on all versions of the manuscript.

All authors read and approved the final manuscript.

**Funding.** Supported by California Breast Cancer Research Program11IB-0034, Litebook Inc.(which supplied light boxes but was not involved in study design, analysis, interpretation of data, writing this article or the decision to submit for publication), NCI CA112035, UL1RR031980 (CTRI), UC San Diego Moores Cancer Center (NCI P30 CA-23100), the UCSD Stein Institute for Research on Aging, and the Department of Veterans Affairs Center of Excellence for Stress and Mental Health (CESAMH).

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Figure Legends:

Figure 1. Consort Table depicting sample sizes at each point of the study

Figure 2. Flow diagram depicting study procedures including timing of actigraphy and questionnaire assessments.

Figure 3. Bar graphs depicting nighttime (A) total sleep time, (B) sleep percentage and (C) total wake time for both bright white light (BWL) and dim red light (DRL) treatment groups from baseline through the treatment weeks (TW) and recovery weeks (RW) of chemotherapy cycles 1 and 4. With the exception of recovery week of cycle 1 (C1RW), the BWL group demonstrated longer total sleep time (A) compared to baseline. On the other hand, DRL group demonstrated longer total wake time (C) and lower sleep percentage (B) during the recovery week of cycle 4 (C4RW). * $p<0.05$ for group-by-time interaction, indicating that compared to DRL group, BWL group had significant longer total sleep time during cycle 4 (both C4TW and C4RW), significant higher sleep percantage and shorter total wake time during C4RW.

Figure 4. Bar graphs depicting daytime (A) number of naps, (B) total nap time and (C) mean nap duration for both bright white light (BWL) and dim red light (DRL) treatment groups from baseline through the treatment weeks (TW) and recovery weeks (RW) of chemotherapy cycles 1 and 4. With the exception of recovery weeks (C1RW, C4RW), the DRL group demonstrated more frequent (A) and longer (B) naps as chemotherapy treatment progressed. Mean nap duration (C) also increased at C1TW for the DRL group, * $p<0.05$ for group-by-time interaction, indicating that compared to DRL group, BWL group had significant fewer naps and shorter total nap time during cycle 4 (both C4TW and C4RW).

Figure 5. Bar graphs depicting average counts per minute for both (A) the nighttime sleep period and (B) the daytime wake period activity in the bright white light (BWL) and dim red light (DRL) treatment groups from baseline through the treatment weeks (TW) and recovery weeks (RW) of chemotherapy cycles 1 and 4. As depicted in 5A, the average nighttime activity decreased in the BWL group while the DRL increased from baseline to the end of cycle 4 (C4RW). Conversely, as depicted in 5B, the average daytime activity decreased in the DRL group from baseline to the treatment weeks of cycle 1 (C1TW) and cycle 4 (C4TW). * $p<0.05$ for

group-by-time interaction, indicating that compared to DRL group, BWL group had significant less daytime activity decrease during C4TW.

**Table 1**. Demographic and medical characteristics at baseline (N=39).

| Variable | BWL (n=23) | DRL (n=16) | *p* value[a] |
|---|---|---|---|
| Age: mean years (*SD*) | 54.26 (9.31) | 53.50 (8.96) | 0.799 |
| BMI (*SD*) | 29.03 (7.78) | 29.58 (8.25) | 0.836 |
| Marital Status: (*n* [%]) | | | 0.882 |
| Never Married | 1 (4.4) | 1 (6.3) | |
| Divorced | 7 (30.4) | 3 (18.8) | |
| Widowed | 2 (8.7) | 1 (6.3) | |
| Married | 13 (56.5) | 11 (68.8) | |
| Ethnicity/Race: (*n* [%]) | | | 0.952 |
| African American Black | 4 (17.4) | 2 (12.5) | |
| Asian | 2 (8.7) | 1 (6.3) | |
| Caucasian | 15 (65.2) | 13 (81.3) | |
| Other | 2 (8.7) | 0 (0.0) | |
| Education: (*n* [%]) | | | 0.879 |
| Some High School or Less | 2 (8.7) | 0 (0.0) | |
| Completed High School | 6 (26.01) | 6 (37.5) | |
| Some College | 8 (34.8) | 4 (25.0) | |
| College Degree | 7 (30.4) | 6 (37.5) | |
| Annual Family Income: (*n* [%]) | | | 0.222 |
| ≤ $15,000 | 5 (21.7) | 3 (18.8) | |
| ≤ $30,000 | 6 (26.1) | 0 (0.0) | |
| ≤ $50,000 | 1 (4.4) | 2 (12.5) | |
| ≤ $100,000 | 4 (17.4) | 2 (12.5) | |
| > $100,000 | 5 (21.7) | 6 (37.5) | |
| Did not Answer | 2 (8.7) | 3 (18.8) | |
| Menopausal Status Pre-chemotherapy: (*n* [%]) | | | 0.982 |
| Premenopausal | 5 (21.7) | 4 (25.0) | |
| Perimenopausal | 3 (13.0) | 2 (12.5) | |
| Postmenopausal | 8 (34.8) | 7 (43.8) | |
| Post-hysterectomy | 6 (26.1) | 3 (18.8) | |
| Unknown | 1 (4.4) | 0 (0.0) | |
| Cancer Stage: (*n* [%]) | | | 0.789 |
| Stage I | 4 (17.4) | 5 (31.3) | |
| Stage II | 10 (43.5) | 6 (37.5) | |
| Stage III | 4 (17.4) | 2 (12.5) | |
| Unknown | 5 (21.7) | 3 (18.8) | |
| Surgery: (*n* [%]) | | | 0.750 |
| Lumpectomy | 7 (30.4) | 8 (50.0) | |
| Mastectomy | 9 (39.1) | 6 (37.5) | |
| Double Mastectomy | 4 (17.4) | 1 (6.3) | |
| Pre-op Chemotherapy | 2 (8.7) | 1 (6.3) | |
| Unknown | 1 (4.4) | 0 (0.0) | |
| Chemotherapy Regimen: (*n* [%]) | | | 0.162 |
| Exactly 4 cycles of AC | 3 (13.0) | 3 (18.8) | |
| Exactly 4 cycles of AC + Taxotere | 5 (21.7) | 0 (0.0) | |
| Exactly 4 cycles of AC + Taxol | 6 (26.1) | 2 (12.5) | |
| 6 cycles of TAC | 2 (8.7) | 4 (25.0) | |

| | | | |
|---|---|---|---|
| Other regimen | 4 (17.4) | 6 (37.5) | |
| Unknown | 3 (13.0) | 1 (6.3) | |
| Prior Use of Hormone Replacement Therapy: (*n* [%]) | | | 0.155 |
| Yes | 2 (8.7) | 4 (25.0) | |
| No | 13 (56.5) | 10 (62.5) | |
| Unknown | 8 (34.8) | 2 (12.5) | |

Abbreviations: BWL = bright white light, DRL = dark red light, BMI = Body Mass Index
[a]Two sample *T* test for continuous variables and Fisher's Exact test for categorical variables

**Table 2 Mean (*SE*) PSQI total and component scores by group condition and mixed model analysis**

| PSQI | Bright White Light | | | | | Dim Red Light | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Baseline N = 16 | C1TW N = 14 | C1RW N= 13 | C4TW N = 12 | C4RW N = 14 | Baseline N = 22 | C1TW N = 17 | C1RW N = 18 | C4TW N = 16 |
| Global | 8.9 (0.9) | 9.1 (0.8) | 8.6 (1.0) | 8.5 (0.9) | 6.9 (0.9) | 7.9 (0.9) | 8.1 (1.1) | 7.1 (1.3) | 7.9 (0.9) |
| Subjective sleep quality | 1.3 (0.2) | 1.4 (0.2) | 1.0 (0.2) | 0.9 (0.2) | 0.4 ** (0.1) | 1.6 (0.2) | 1.4 (0.3) | 1.0 * (0.3) | 1.1 (0.2) |
| Sleep latency | 1.4 (0.2) | 1.4 (0.2) | 1.4 (0.2) | 0.9 (0.3) | 0.8 (0.3) | 1.5 (0.3) | 1.1 (0.3) | 1.2 (0.3) | 1.0 (0.3) |
| Sleep duration | 1.3 (0.2) | 0.9 (0.2) | 0.9 (0.2 | 0.9 (0.2) | 0.9 * (0.2) | 0.8 (0.1) | 0.8 (0.2) | 0.5 (0.2) | 0.4 (0.2) |
| Habitual sleep efficiency | 1.8 (0.3) | 1.9 (0.3) | 1.3 (0.3) | 1.6 (0.3) | 1.1 (0.3) | 1.3 (0.3) | 0.9 (0.3) | 0.9 (0.3) | 1.2 (0.4) |
| Sleep disturbances | 1.5 (0.1) | 1.4 (0.2) | 1.2 (0.1) | 1.3 (0.2) | 1.1 * (0.2) | 1.6 (0.1) | 1.5 (0.2) | 1.4 (0.1) | 1.7 (0.2) |
| Use of sleeping medication | 1.1 (0.3) | 1.4 (0.4) | 1.7 (0.3) | 1.8 (0.4) | 1.6 (0.4) | 0.7 (0.3) | 1.5 * (0.4) | 1.3 (0.4) | 1.4 * (0.4) |
| Daytime dysfunction | 0.6 (0.2) | 0.8 (0.2) | 0.9 (0.2) | 1.1 * (0.1) | 1.0 * (0.2) | 0.6 (0.2) | 0.9 (0.2) | 0.7 (0.2) | 1.0 (0.2) |

Note: compared to Baseline in each group: * $p<0.05$, **p<0.01; there were no significant group by time interaction for both groups at any time point (all p's>0.1).