

# Sleep Disturbances in Cancer: A Review

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Sleep problems are one of the major complaints in patients with cancer, before treatment, while undergoing chemotherapy or radiation therapy, and after the completion of cancer treatment. As in other medically ill patients, disturbed sleep in cancer patients may be an important contributor to poor quality of life, to their tolerance to treatment, and to the development of mood disorders, particularly depression. Disruptions in circadian rhythms also affect sleep. The degree of sleep disruption found in patients with cancer is not trivial. Objectively recorded sleep and biological rhythms confirm that these are major problems in cancer patients.

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**Key Words** Sleep, Cancer, Circadian rhythms, Treatment, Cognitive-behavioral therapy.

## INTRODUCTION

Disturbed sleep is one of the major complaints of cancer patients,<sup>1,2</sup> and includes complaints of difficulty falling asleep and staying asleep, before, during and for years after treatment.<sup>3</sup> A few studies have explored the prevalence of sleep disordered breathing (SDB),<sup>4,5</sup> and some studies examined periodic limb movements in sleep (PLMS),<sup>6</sup> but most sleep studies conducted in cancer patients have focused on insomnia.

## PREVALENCE OF SLEEP DISTURBANCES IN CANCER

Studies suggest that 30–75% of newly diagnosed or recently treated cancer patients report sleep problems, which is a rate about two times as high as in the general population.<sup>1,2</sup> On the other hand, insomnia symptoms are found in 30–50% of cancer patients.<sup>3,7</sup> Most of these studies however, have primarily been cross-sectional using convenience samples and examining self-reported sleep disturbances with no objective measures.

### Subjective Sleep Measures

As mentioned, cancer patients report higher rates of sleep disturbances than the general population. Anderson et al.,<sup>8</sup> compared 354 cancer patients with 72 psychiatric patients and 290 non-patient volunteers. Results showed that 62% of the cancer patients reported moderate to severe sleep disturbance, while 53% of the depressed patients and only 30% of the volunteers reported the same complaint.

Patients with different types of cancer report different kinds and different rates of sleep problems. In a large survey among more than 1000 patients with different types of cancer in different phases of treatment, 31% reported insomnia symptoms, 28% reported excessive daytime sleepiness, and 41% complained of restless legs.<sup>9</sup> In this survey, lung cancer patients had the highest or second-highest prevalence of sleep problems in general, while breast cancer patients had a high prevalence of insomnia and fatigue. In another survey, Savard et al.<sup>6</sup> studied the prevalence of insomnia in 300 women with breast cancer, finding that 19% met the diag-

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nostic criteria for insomnia and 95% of those being chronic insomnia. In addition, they found that in greater than 50% the onset of insomnia preceded the breast cancer diagnosis. Nevertheless, 58% of the patients reported that cancer aggravated their sleep problems.

There have been two large-scale longitudinal studies in patients with heterogeneous cancer sites. Savard et al.<sup>10,11</sup> studied almost 1000 patients during the peri-operative phase while they awaited surgery for mixed cancer sites and followed them 2, 6, 10, 14, and 18 months later. Pre-surgery, 59% had insomnia symptoms (28% with insomnia disorder) while at 18 months 36% still suffered from insomnia symptoms (21% with insomnia disorder). In another large-scale prospective study, Palesh et al.<sup>12</sup> examined insomnia in over 800 patients scheduled to receive at least four cycles of chemotherapy for all stages of various types of cancer. Sleep complaints were assessed on the last day of cycle 1 and of cycle 2 of chemotherapy. At cycle 1, 80% of the patients exhibited insomnia symptoms (43% with insomnia disorder) but by cycle 2 the rates decreased to 68% (35% with insomnia disorder).

### Objective Sleep Measures

Polysomnography (PSG), i.e., overnight sleep measurements that record brain waves, eye movement, muscle tension, and often respiration, heart rate and leg movements is the gold standard for recording sleep. Although not invasive, PSG recordings are cumbersome, particularly for cancer patients who are already fatigued or in pain. Therefore, only a few studies have used PSG to study sleep in cancer.

Silberfarb et al.<sup>13</sup> used PSG to study and compare lung cancer, breast cancer and insomnia patients with normal volunteers. They found that patients with insomnia had the shortest total sleep time. The lung cancer patients spent more time in bed but did not sleep more than the breast cancer or normal controls, and therefore had lower sleep efficiency (the percent of time in bed actually spent asleep). Lung patients also had longer sleep onset latency (time to fall asleep) and spent more time awake during the night than those with breast cancer or the normal sleepers. Our laboratory collected PSG data immediately post-chemotherapy in 33 breast cancer patients and found that patients experienced disturbed sleep, spending more time in lighter levels of sleep (stages N1 and N2) and less time in deep (stage N3) or REM sleep. These women also spent more time awake with lower sleep efficiency than the general population, even after the completion of their chemotherapy.<sup>14</sup>

A few studies have used PSG to examine the prevalence of specific sleep disorders. In the Silberfarb et al.<sup>13</sup> study described above, none of the cancer patients were found to have SDB, but there was a higher preponderance of PLMS in the cancer patients than in controls or insomnia patients. Fiorentino et al.<sup>14</sup> found that 36% of breast cancer patients had PLMS. Since PLMS is treatable, these data suggest that it is important to rule

out PLMS as a cause of sleep disturbance in patients with cancer.

The prevalence of obstructive sleep apnea (OSA) has been studied in patients with head and neck cancer with resulting rates being quite varied (from 12 to 91.7%); however these were all small scale studies (from 17 to 33 patients).<sup>4,5</sup> In breast cancer patients, our laboratory found that 48% of the women had at least mild OSA,<sup>15</sup> a substantially higher prevalence than that reported in age-comparable non-cancer women.

Since PSGs can be burdensome for cancer patients, actigraphy is now commonly used to gather objective sleep measures. An actigraph, a small device about the size of a large wrist watch, is worn on the wrist of the non-dominant hand, records movement via motion-sensitive accelerometers. Special algorithms have been developed to estimate sleep and wake time from the movement, and correlation studies with electroencephalography suggest high reliability.

Miaskowski and Lee<sup>16</sup> used wrist actigraphy recorded over a 48-hour period in 24 patients at various time points during radiation therapy for bone metastases. Subjective sleep complaints increased as the radiation therapy progressed. In these patients, sleep efficiency decreased but frequent urination, rather than pain intensity, was reported to be the main cause of awakening in the night.

In studies from our laboratory, actigraphic sleep measures and patient reports of sleep quality were measured in 82 women before and during chemotherapy for breast cancer. Results showed that breast cancer patients were already complaining of sleep problems prior to the start of chemotherapy,<sup>17</sup> and actigraphic recordings confirmed that the women were asleep on average for only 77% of the night.

Our laboratory also compared 68 patients with breast cancer to age-matched women with no cancer and studied them with actigraphy and questionnaires before the start of chemotherapy, after four cycles of chemotherapy and one year later.<sup>18</sup> Pre-chemotherapy, those with cancer, compared to those with no breast cancer, napped more, had worse sleep quality, more fatigue, more depressive symptoms, more disrupted circadian activity rhythms and worse quality of life. At the end of cycle 4 of chemotherapy, the patients showed worse sleep, increased fatigue, more depressive symptoms, and more disrupted circadian activity rhythms compared to their own pre-chemotherapy levels and compared to the non-cancer women. By one year, the patients' fatigue, depressive symptoms, and quality of lie returned to pre-chemotherapy levels but were still worse than those with no cancer. Nap time and circadian activity rhythms did not differ from those of the non-cancer women.

## RISK FACTORS OF SLEEP DISTURBANCES

There are multiple factors that put cancer patients at greater

risk of sleep problems. Savard et al.<sup>6</sup> studied prevalence, clinical characteristics and risk factors for insomnia in 300 breast cancer patients and found that higher risk of insomnia was associated with sick leave, unemployment, widowhood, lumpectomy, chemotherapy, and a less severe stage of cancer at diagnosis. In advanced cancer patients, higher risk was associated with lower performance status, anxiety, depression and confusion. In a large survey of 982 different types of cancer patients, Davidson et al.<sup>9</sup> found that insomnia-related risk factors included fatigue, age, restless legs, sedative/hypnotic use, low or variable mood, dreams, concerns and recent cancer surgery.

Radiation and chemotherapy are both reported to produce sleep disturbances, yet, as mentioned, studies are now showing that sleep disturbances already exist before the start of treatment. Cimprich<sup>19</sup> administered self-report items relating to sleep quality, fatigue and distress to breast cancer patients who had not yet undergone treatment and found that insomnia was correlated with high levels of distress and was the most frequent symptom with 88% of the sample reporting difficulty sleeping. Subjective reports of distress and anxiety were correlated with insomnia, and even before treatment had begun, self-ratings of fatigue and sleep difficulty were high. In patients whose self-ratings of anxiety (as well as anger) were low, levels of insomnia and fatigue were still high. Data from our laboratory showed that disturbed sleep pre-treatment was correlated with fatigue, depressive symptoms and functional outcome in breast cancer patients,<sup>17</sup> and sleep quality during chemotherapy was associated with the prevalence and severity of pre-treatment symptoms.<sup>20</sup> This contrasts with the general notion that disturbed sleep prior to treatment is attributable to the increased anxiety and stress accompanying the recent diagnosis of a life-threatening illness.

Studies on symptom clusters have revealed that sleep and fatigue are often part of a same cluster of three or more symptoms.<sup>20-25</sup> Moreover, most cross-sectional and prospective studies have found a strong correlation between sleep disturbances and fatigue,<sup>25-28</sup> with a similar trajectory over time.<sup>18</sup>

The relationship between sleep disturbances and depressive symptoms are also not well described in cancer patients. It is known that insomnia is often comorbid with depression, that sleep disturbance is a risk factor of depressive symptoms and that the amount of insomnia in cancer patients has been shown to be as high as the amount of insomnia found in depressed patients, yet studies revealed that depression and sleep disturbances already exist before the start of cancer treatment.<sup>17,19</sup> This suggests that sleep problems may be independent of these psychological/physiological factors.

Poor sleep in cancer patients also increases the risk of poor quality of life. Our laboratory studied the effect of quality of life and actigraphic measurements of sleep in 166 women with breast cancer.<sup>29</sup> As with previous studies from our laboratory, data were collected pre-chemotherapy and at the end of cycle 4

of chemotherapy. Poor quality of life was reported at both time points. Short total sleep time and long naps were also recorded at both time points. Decreased quality of life was associated with the poor sleep.

## BIOLOGICAL RHYTHMS

Studies among animals and humans suggest that cancer itself may be a result of disturbed biological rhythms. The disruptions in biological rhythmicity are relevant to cancer, to the mitotic properties of cancerous cells themselves, to the treatments of cancer and the time-of-day of their administration, and possibly to the quality of life in cancer patients. There is growing interest in examining the biological rhythms of cancer patients. Actigraphy, described above, is a convenient and effective instrument to measure circadian activity rhythms.

Mormont et al.,<sup>30</sup> using actigraphy, studied the circadian rhythm of the rest/activity cycle and of serum cortisol, leukocyte counts and neutrophil counts in patients with metastatic colorectal cancer for three consecutive days prior to beginning chronomodulated chemotherapy. Patients with marked activity rhythms (i.e., greater activity when out of bed than when in bed), had a 5-fold higher survival at two-year follow-up than those with less synchronized rhythms. Patients with marked activity rhythms also had better quality of life and reported significantly less fatigue. Circadian rhythms in activity and in white blood cells were jointly prognostic of response. The authors concluded that the rest/activity cycle can be used to determine prognosis for cancer patients' survival and tumor response.

Chemotherapy appears to be particularly disruptive of rest/activity circadian rhythms,<sup>11,31</sup> although radiation therapy was also found to have a detrimental effect.<sup>16</sup> Our laboratory also used actigraphy to measure circadian activity rhythms as well as sleep/wake patterns in breast cancer patients. We found that the first administration of chemotherapy was associated with transient circadian disruption, but that repeated administration of chemotherapy resulted in progressively worse and more enduring rhythm impairments.<sup>11</sup> In addition, while circadian activity rhythms were often robust at baseline, the desynchronization during chemotherapy was correlated with fatigue, low daytime light exposure and decreased quality of life.<sup>17,32</sup>

Another study conducted among 49 patients with advanced cancer, assessed with actigraphy from 3 days before to 10 days after the administration of a chemotherapy cycle, found a significant proportion (45%) of patients showing a sustained deterioration of their rest-activity pattern following chemotherapy administration, with both increased nighttime activity level and decreased diurnal activity level.<sup>33</sup> While there are some data suggestive of improvement of the rest-activity patterns back to pre-cancer treatment levels once the active phase of cancer treatment is over, at least among patients with early-stage disease, the

disturbance remains worse than in matched controls.<sup>18</sup>

## SUMMARY

In summary, the risk factors of sleep disruptions in cancer patients are multifactorial. Savard and Morin<sup>7</sup> summarized insomnia-related factors in cancer into three categories: 1) predisposing factors that increase the individual's general vulnerability to develop insomnia, such as hyperarousability, being female, aging, and a personal and a familial history of insomnia; 2) precipitating factors that trigger the onset of sleep disturbances, such as the cancer itself, cancer-related emotional impact and functional loss, and cancer-related treatments and symptoms such as pain, and delirium; and 3) perpetuating factors that contribute to the maintenance of sleep disturbance over time, such as maladaptive sleep behaviors and faulty beliefs and attitudes about sleep. It is likely that sleep disruptions in cancer patients, particularly insomnia, are more likely comorbid with cancer and with other cancer-related symptoms, rather than secondary to cancer treatments and other cancer-related symptoms, such as fatigue, pain and depression.

## TREATMENT OF SLEEP DISTURBANCES IN CANCER

### Pharmacotherapy

Although pharmacotherapy is the most prescribed therapy for cancer patients with sleep disturbances,<sup>7,9</sup> there is a paucity of studies examining pharmacologic interventions in cancer patients. One review concluded that evidence is not sufficient to recommend specific pharmacologic interventions for sleep disturbances in cancer patients.<sup>2</sup> Clinicians need to evaluate the relative effectiveness and side-effect profiles of pharmacologic agents and researchers need to be challenged to evaluate the impact of pharmacologic treatment on sleep disturbances among cancer patients.<sup>2</sup>

### Non-Pharmacotherapy

The NIH State of the Science Conference on Insomnia concluded that cognitive-behavioral therapy (CBT) is the most effective and most durable treatment for insomnia.<sup>34</sup> There are now multiple studies supporting the efficacy for behavioral treatment of insomnia in cancer survivors.<sup>3,35-43</sup> These studies have been quite consistent in demonstrating that CBT (combining stimulus control, sleep restriction, cognitive restructuring, sleep hygiene and sometimes relaxation) results in increased sleep efficiency and reduced total wake time, decreased psychological distress, and improved quality of life.

Bright light therapy is another non-pharmacological treatment option that appears promising. Daily 30 minute exposure

to bright light during chemotherapy resulted in circadian activity rhythms and fatigue staying at stable levels and quality of life improving.<sup>44-46</sup> Similar results, including improvement in sleep, have been found in cancer survivors.<sup>47</sup> Bright light might be an excellent, non-invasive, non-pharmacological treatment for cancer patients.

## CONCLUSION AND FUTURE DIRECTIONS

Sleep disturbances in cancer patients are common and are often multifactorial, and likely are comorbid with cancer. In addition, the cancer itself, cancer related symptoms and cancer treatment may all exacerbate sleep problems. Further animal and clinical trials are needed to help understand the cellular and molecular mechanisms of those symptoms, particularly the roles of cytokines, and to help develop biological interventions. Pharmacologic treatments are still the most common interventions for sleep disturbances in cancer patients, yet CBT may be more advantageous due to the durability of cognitive behavior modification. The long-term goal of research on sleep disturbances in cancer patients should be to find treatment approaches that will improve quality of life during treatment and/or during the course of treatment.

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### Conflicts of Interest

Sonia Ancoli-Israel has consulted for Merck, Pernix and Lacrima.

### REFERENCES

1. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *Eur J Cancer Care (Engl)* 2001; 10:245-55.
2. Berger AM, Parker KP, Young-McCaughan S, Mallory GA, Barsevick AM, Beck SL, et al. Sleep wake disturbances in people with cancer and their caregivers: state of the science. *Oncol Nurs Forum* 2005;32:E98-126.
3. Fiorentino L, Ancoli-Israel S. Insomnia and its treatment in women with breast cancer. *Sleep Med Rev* 2006;10:419-29.
4. Payne RJ, Hier MB, Kost KM, Black MJ, Zeitouni AG, Frenkiel S, et al. High prevalence of obstructive sleep apnea among patients with head and neck cancer. *J Otolaryngol* 2005;34:304-11.
5. Nesse W, Hoekema A, Stegenga B, van der Hoeven JH, de Bont LG, Roodenburg JL. Prevalence of obstructive sleep apnoea following head and neck cancer treatment: a cross-sectional study. *Oral Oncol* 2006; 42:108-14.
6. Savard J, Simard S, Blanchet J, Ivers H, Morin CM. Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. *Sleep* 2001;24:583-90.
7. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. *J Clin Oncol* 2001;19:895-908.
8. Anderson KO, Getto CJ, Mendoza TR, Palmer SN, Wang XS, Reyes-Gibby CC, et al. Fatigue and sleep disturbance in patients with cancer, patients with clinical depression, and community-dwelling adults. *J*

- Pain Symptom Manage* 2003;25:307-18.
9. Davidson JR, MacLean AW, Brundage MD, Schulze K. Sleep disturbance in cancer patients. *Soc Sci Med* 2002;54:1309-21.
  10. Savard J, Ivers H, Villa J, Caplette-Gingras A, Morin CM. Natural course of insomnia comorbid with cancer: an 18-month longitudinal study. *J Clin Oncol* 2011;29:3580-6.
  11. Savard J, Liu L, Natarajan L, Rissling MB, Neikrug AB, He F, et al. Breast cancer patients have progressively impaired sleep-wake activity rhythms during chemotherapy. *Sleep* 2009;32:1155-60.
  12. Palesh OG, Roscoe JA, Mustian KM, Roth T, Savard J, Ancoli-Israel S, et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol* 2010;28:292-8.
  13. Silberfarb PM, Hauri PJ, Oxman TE, Schnurr P. Assessment of sleep in patients with lung cancer and breast cancer. *J Clin Oncol* 1993;11:997-1004.
  14. Fiorentino L, Mason W, Parker B, Johnson S, Amador X, Ancoli-Israel S. Sleep disruption in breast cancer patients post-chemotherapy. *Sleep* 2005;28:A294.
  15. Cornejo M, Liu L, Trofimenko V, Johnson SS, Ancoli-Israel S. Obstructive sleep apnea in breast cancer patients. *Sleep* 2008;31:A302.
  16. Miaskowski C, Lee KA. Pain, fatigue, and sleep disturbances in oncology outpatients receiving radiation therapy for bone metastasis: a pilot study. *J Pain Symptom Manage* 1999;17:320-32.
  17. Ancoli-Israel S, Liu L, Marler MR, Parker BA, Jones V, Sadler GR, et al. Fatigue, sleep, and circadian rhythms prior to chemotherapy for breast cancer. *Support Care Cancer* 2006;14:201-9.
  18. Ancoli-Israel S, Liu L, Rissling M, Natarajan L, Neikrug AB, Palmer BW, et al. Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. *Support Care Cancer* 2014;22:2535-45.
  19. Cimprich B. Pretreatment symptom distress in women newly diagnosed with breast cancer. *Cancer Nurs* 1999;22:185-94.
  20. Liu L, Fiorentino L, Natarajan L, Parker BA, Mills PJ, Sadler GR, et al. Pre-treatment symptom cluster in breast cancer patients is associated with worse sleep, fatigue and depression during chemotherapy. *Psychooncology* 2009;18:187-94.
  21. Fleming L, Randell K, Harvey CJ, Espie CA. Does cognitive behaviour therapy for insomnia reduce clinical levels of fatigue, anxiety and depression in cancer patients? *Psychooncology* 2014;23:679-84.
  22. Kim E, Jahan T, Aouizerat BE, Dodd MJ, Cooper BA, Paul SM, et al. Changes in symptom clusters in patients undergoing radiation therapy. *Support Care Cancer* 2009;17:1383-91.
  23. Lengacher CA, Reich RR, Paterson CL, Jim HS, Ramesar S, Alinat CB, et al. The effects of mindfulness-based stress reduction on objective and subjective sleep parameters in women with breast cancer: a randomized controlled trial. *Psychooncology* 2015;24:424-32.
  24. Fiorentino L, Rissling M, Liu L, Ancoli-Israel S. The symptom cluster of sleep, fatigue and depressive symptoms in breast cancer patients: severity of the problem and treatment options. *Drug Discov Today Dis Models* 2011;8:167-73.
  25. Donovan KA, Jacobsen PB. Fatigue, depression, and insomnia: evidence for a symptom cluster in cancer. *Semin Oncol Nurs* 2007;23:127-35.
  26. Jim HS, Small B, Faul LA, Franzen J, Apte S, Jacobsen PB. Fatigue, depression, sleep, and activity during chemotherapy: daily and intraday variation and relationships among symptom changes. *Ann Behav Med* 2011;42:321-33.
  27. Jim HS, Jacobsen PB, Phillips KM, Wenham RM, Roberts W, Small BJ. Lagged relationships among sleep disturbance, fatigue, and depressed mood during chemotherapy. *Health Psychol* 2013;32:768-74.
  28. Liu L, Rissling M, Natarajan L, Fiorentino L, Mills PJ, Dimsdale JE, et al. The longitudinal relationship between fatigue and sleep in breast cancer patients undergoing chemotherapy. *Sleep* 2012;35:237-45.
  29. Liu L, Fiorentino L, Rissling M, Natarajan L, Parker BA, Dimsdale JE, et al. Decreased health-related quality of life in women with breast cancer is associated with poor sleep. *Behav Sleep Med* 2013;11:189-206.
  30. Mormont MC, Waterhouse J, Bleuzen P, Giacchetti S, Jami A, Bogdan A, et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response, and longer survival in patients with metastatic colorectal cancer and good performance status. *Clin Cancer Res* 2000;6:3038-45.
  31. Berger AM, Grem JL, Visovsky C, Marunda HA, Yurkovich JM. Fatigue and other variables during adjuvant chemotherapy for colon and rectal cancer. *Oncol Nurs Forum* 2010;37:E359-69.
  32. Liu L, Marler MR, Parker BA, Jones V, Johnson S, Cohen-Zion M, et al. The relationship between fatigue and light exposure during chemotherapy. *Support Care Cancer* 2005;13:1010-7.
  33. Ortiz-Tudela E. Crosstalk between sleep disturbances and cancer survival. *Sleep Med* 2015;16:315-6.
  34. National Institutes of Health. National Institutes of Health State of the Science Conference statement on manifestations and management of chronic insomnia in adults, June 13-15, 2005. *Sleep* 2005;28:1049-57.
  35. Fiorentino L, McQuaid JR, Liu L, Natarajan L, He F, Cornejo M, et al. Individual cognitive behavioral therapy for insomnia in breast cancer survivors: a randomized controlled crossover pilot study. *Nat Sci Sleep* 2010;2:1-8.
  36. Garland SN, Johnson JA, Savard J, Gehrman P, Perlis M, Carlson L, et al. Sleeping well with cancer: a systematic review of cognitive behavioral therapy for insomnia in cancer patients. *Neuropsychiatr Dis Treat* 2014;10:1113-24.
  37. Berger AM, Kuhn BR, Farr LA, Von Essen SG, Chamberlain J, Lynch JC, et al. One-year outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. *J Clin Oncol* 2009;27:6033-40.
  38. Davidson JR, Waisberg JL, Brundage MD, MacLean AW. Nonpharmacologic group treatment of insomnia: a preliminary study with cancer survivors. *Psychooncology* 2001;10:389-97.
  39. Epstein DR, Dirksen SR. Randomized trial of a cognitive-behavioral intervention for insomnia in breast cancer survivors. *Oncol Nurs Forum* 2007;34:E51-9.
  40. Espie CA, Fleming L, Cassidy J, Samuel L, Taylor LM, White CA, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. *J Clin Oncol* 2008;26:4651-8.
  41. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: sleep and psychological effects. *J Clin Oncol* 2005;23:6083-96.
  42. Simeit R, Deck R, Conta-Marx B. Sleep management training for cancer patients with insomnia. *Support Care Cancer* 2004;12:176-83.
  43. Quesnel C, Savard J, Simard S, Ivers H, Morin CM. Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. *J Consult Clin Psychol* 2003;71:189-200.
  44. Neikrug AB, Rissling M, Trofimenko V, Liu L, Natarajan L, Lawton S, et al. Bright light therapy protects women from circadian rhythm desynchronization during chemotherapy for breast cancer. *Behav Sleep Med* 2012;10:202-16.
  45. Ancoli-Israel S, Rissling M, Neikrug A, Trofimenko V, Natarajan L, Parker BA, et al. Light treatment prevents fatigue in women undergoing chemotherapy for breast cancer. *Support Care Cancer* 2012;20:1211-9.
  46. Jeste N, Liu L, Rissling M, Trofimenko V, Natarajan L, Parker BA, et al. Prevention of quality-of-life deterioration with light therapy is associated with changes in fatigue in women with breast cancer undergoing chemotherapy. *Qual Life Res* 2013;22:1239-44.
  47. Redd WH, Valdimarsdottir H, Wu LM, Winkel G, Byrne EE, Beltre MA, et al. Systematic light exposure in the treatment of cancer-related fatigue: a preliminary study. *Psychooncology* 2014;23:1431-4.