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Patient characteristics associated with sleep disturbance in breast cancer survivors

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Abstract

Background: Disturbed sleep is common among breast cancer survivors. Identifying patients at risk for disturbed sleep and its sequelae will aid in improving screening and intervention strategies to improve sleep and cancer-related quality of life (QOL).

Methods: Women with stage I-III breast cancer undergoing neoadjuvant or adjuvant chemotherapy (N = 415) reported subjectively-assessed sleep quality (PSQI) and actigraphy-assessed wake after sleep onset (AAS-WASO), total sleep time (AAS-TST), and sleep efficiency (AAS-SE), sociodemographic and clinical characteristics, and completed questionnaires assessing physical and mental health QOL at the study entry, and 3, 6, 12, and 15 months later.

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Results: Being from a racially/ethnically underserved population was associated with poorer sleep in all indices (p's < .04). Lower income was associated with poorer subjective sleep and greater AAS-WASO (p's < .02). BMI was associated with lower AAS-SE (p < .001). Baseline subjective sleep complaints were positively associated with depression, fatigue, and health-related QOL, and cancer-related symptoms across follow-up (p's ≤ 0.05). Baseline AAS-WASO was positively associated with anxiety and negatively associated with physical health-related QOL at the 3-month follow up (p's ≤ .001). Baseline AAS-WASO and AAS-SE were associated with mental health-related QOL at the 6-month follow up (p's ≤ .05).

Conclusions: In keeping with previous health disparity research, racially/ethnically underserved populations, lower household income, and higher BMI were associated with increased risk for disturbed sleep. Sleep disturbance may have long-term effects on multiple aspects of QOL for women undergoing treatment for breast cancer. Results may inform strategies to identify patients at greatest risk for disturbed sleep and its sequelae.

Keywords

breast cancer; sleep; actigraphy; PSQI; quality of life; health disparities

Introduction

Sleep disturbances are a common and challenging experience for individuals with breast cancer throughout the treatment trajectory and into survivorship [1]. An estimated 30–60% of newly diagnosed or recently treated breast cancer patients experience symptoms of insomnia [2-3], much higher than the 9-15% reported by the general population [4]. A better understanding of patient factors that predict poor sleep during and after treatment for breast cancer would allow targeted strategies to prevent disturbed sleep and, thus, improve patients' quality of life.

Sleep quality can be assessed using subjective measures, such as self-report questionnaires, or objective measures, such as polysomnography or actigraphy. Actigraphy data is a common behavioral measure of sleep derived by analyzing movement recorded by an accelerometer worn for several days on patients' wrists. Sleep difficulties, assessed via self-report and actigraphy, are associated with a variety of quality of life (QOL)-related outcomes important to breast cancer patients, their families, and their healthcare providers [5]. Breast cancer survivors who report significantly disturbed sleep are more likely to report poorer physical functioning, experience greater fatigue, pain, and numbness, and be sedentary compared to their counterparts without sleep disturbances [3, 6-9]. Self-reported poor sleep quality has also been associated with breast cancer survivors' mood, including greater depression [7, 10], anxiety [7], and general distress [8]. In fact, in a study of over 2,600 women with breast cancer, depression was identified as the strongest correlate of self-reported sleep disturbance [3]. Additionally, greater actigraphy-assessed sleep disturbance may be associated with greater depression and anxiety among breast cancer survivors [11], though these findings have not been consistent [6, 12-15].

Some breast cancer patients may be at particular risk for experiencing sleep disturbance during cancer treatment and beyond. For example, lower income and less education may

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increase breast cancer patients' risk of poor self-reported sleep disturbance [3,7]. Additionally, Black/African American and Hispanic women with breast cancer have been found to have shorter sleep duration compared to White non-Hispanic women with breast cancer [16] and the same is true for non-cancer populations [17]. Moreover, actigraphy-assessed sleep disturbances may be more strongly associated with depression and fatigue for Hispanic and Black/African American women compared to White non-Hispanic breast cancer survivors [16]. Unmarried women with breast cancer appear to experience poorer sleep, assessed via polysomnography, compared to their married counterparts [18]. Furthermore, early stage disease, premenopausal status, younger age, and higher BMI have been associated with higher risk of disturbed sleep among women with breast cancer [14, 19-23]. Thus, certain sociodemographic and clinical characteristics may help identify patients who are especially vulnerable to experiencing disturbed sleep during the cancer treatment trajectory. However, the relatively small sample sizes of most previous studies, particularly among those assessing sleep using actigraphy, have limited researchers from drawing conclusions about which patients may be most vulnerable to the detrimental impact of poor sleep on cancer-related QOL.

The present study represents the largest sample to date of both self-reported and actigraphy-assessed sleep quality in women undergoing neoadjuvant or adjuvant chemotherapy (CT) for stage I-III breast cancer (86% of the sample). This is a secondary analysis of a randomized controlled trial assessing the impact of a Tibetan Yoga program compared to stretching or waitlist control conditions on sleep and fatigue [24]. Previously published findings from this dataset demonstrated that yoga was associated with the "daily disturbance" subscale of the PSQI; specifically, participants in the yoga condition self-reported fewer difficulties staying awake and maintaining enthusiasm in daily tasks across the follow up period compared to those in a stretching or usual care control group. Additionally, women in the yoga condition exhibited shorter actigraphy-assessed wakefulness after sleep onset (WASO) and higher actigraphy-assessed sleep efficiency (SE) at the 3-month follow up compared to the stretching group. There were no group differences in self-reported global sleep disturbance (i.e., PSQI global score), self-reported fatigue (i.e., BFI), or actigraphy-assessed total sleep time (TST) across the follow up period [24].

The present study had three aims. First, we examined sociodemographic and clinical correlates of sleep at study entry, which was just before beginning CT for 25% of participants, within the first 2-months of beginning CT for 61% of study participants, and within 12 months of completing CT for 14% of participants. Second, we examined the association of sociodemographic and clinical characteristics on sleep throughout the 15-month follow up period, controlling for sleep at study entry. These analyses aimed to identify breast cancer patients at increased risk of experiencing disturbed during and after active treatment for breast cancer. Based on previous studies, we hypothesized that younger age, racially/ethnically underserved populations, unmarried status, lower income, early stage of disease, and premenopausal status would be associated with greater self-reported and actigraphy-assessed sleep problems throughout the 15-month follow up period. Third, we examined the effect of sleep disturbances at study entry on physical and mental health aspects of QOL (i.e., depression, anxiety, fatigue, health-related QOL, and cancer-related symptoms) measured throughout the 15-month follow-up period. We hypothesized that self-

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reported and actigraphy-assessed sleep disturbances at study entry would be associated with worse QOL across the follow-up period, independent of sociodemographic and clinical covariates. Results from these analyses may help suggest targets for future interventions delivered during active treatment for breast cancer (e.g., targeting sleep quality during active treatment may be one way to improve QOL during the months following treatment).

Methods

Participants

Participants were women with stage I-III breast cancer who were undergoing neoadjuvant or adjuvant chemotherapy or within 12-months of completing chemotherapy, over 18 years old, and proficient in English. Patients were excluded if they had lymphedema, a documented diagnoses of a formal thought disorder, a Mini-Mental State Examination score ≤ 23, were currently engaged in psychiatric or psychological counseling or support groups, or reported the need for psychological services. The narrow inclusion criteria were in order to maintain a relatively homogenous sample of women for the parent clinical trial.

Procedures

A full description of study procedures can be found in the primary outcome paper [24]. Potential participants were approached during clinic appointments and asked to participate in a study investigating the effects of a Tibetan Yoga intervention. Participants who provided informed consent were randomized into one of three conditions: yoga, stretching, or waitlist control. Those in the yoga or stretching conditions attended 4 weekly sessions or 3 sessions every 3 weeks for 12 weeks, depending on chemotherapy regimen. The small proportion (14%) of participants who had completed CT within the previous 12-months, and were currently receiving either radiotherapy or hormone therapy, attended yoga or stretching sessions at similar intervals. Participants completed the measures below at study entry, at the end of the yoga/stretching intervention period (approximately 3 months after study entry), and 3, 6 and 12 months later (i.e., 6, 9, 15 months after study entry). In the present study, these time points will be referred to as baseline and 3-, 6-, 9-, and 15-month follow ups. The study was approved by MDACC Institutional Review Board.

Measures

Sleep—Four prevalent and debilitating indices of sleep in cancer patients were selected for investigation: 1) subjectively-assessed *sleep quality complaints* (i.e., Pittsburgh Sleep Quality Index Global scale; PSQI) and actigraphy-assessed 2) *sleep continuity* (i.e., wakefulness after sleep onset; WASO), 3) *sleep duration* (i.e., total sleep time; TST), and 4) *sleep efficiency* (i.e., the percent of time spent sleeping during the nocturnal period; SE) [25].

Subjective sleep quality complaints were assessed with the Pittsburgh Sleep Quality Index (PSQI), a 19-item questionnaire in which participants report on seven dimensions of sleep (i.e., quality, duration, efficiency, latency, disturbances, medication, and daytime dysfunction) during the previous month [26]. Component scores are summed to create a

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global sleep quality score, with higher scores reflecting poorer subjective sleep quality. Only the global sleep quality score is examined in the present study.

Behavioral indices of fragmentation and duration were assessed by wrist actigraphy (Actiwatch, Philips Inc., Bend, Oregon). Participants were instructed to wear the Actiwatch on their non-dominant arm 24 hours a day for seven consecutive days. The Actiwatch (Actiwatch 2 model) contains a uniaxial accelerometer that records movement. Each device was set to an epoch length of 30 seconds and medium level of sensitivity. Actigraphy data were edited by a research associate trained by co-author (M.H.H.) to remove artifacts and identify the start and stop of each nocturnal sleep period. The Actiwatch data were then analyzed using the manufacturer's software (Actiwatch Activity and Sleep Analysis 5, version 5.32, Cambridge Neurotechnology). Actigraphy-assessed outcomes included wakefulness after sleep onset (WASO; total minutes of wakefulness between nocturnal sleep onset and the end of the sleep period), total sleep time (TST; total minutes of sleep during the nocturnal sleep period), and sleep efficiency (SE; the percent sleep obtained during the nocturnal sleep period (TST/time in bed x 100)). These three outcomes are typically included in actigraphy studies, as they provide a relatively full picture of objectively-assessed sleep quality [25, 27]. The cutoff for number of nights and days for actigraphy variables was six days. Each outcome was measured as a continuous variable, with higher WASO indicating greater sleep continuity, shorter TST indicating shorter sleep duration, and lower SE indicating poorer sleep efficiency.

Quality of Life

Depressive symptoms were assessed using the Centers for Epidemiological Studies – Depression measure (CES-D), a 20-item self-report measure of depression symptoms over the past week [28]. In the present study, the item assessing sleep was removed from the scoring of the CES-D in order to assess depressive symptoms apart from sleep disturbance.

Anxiety symptoms were assessed using the STATE scale of the Speilberger State/Trait Anxiety Inventory (STAI Form Y-1), a 20-item scale that provides information about a person's current level of anxiety [29].

Fatigue was measured using the Brief Fatigue Inventory (BFI) a 9-item questionnaire that is designed to assess fatigue severity over the past week [30].

Health-related QOL was measured using the Medical Outcomes Study 36-item short form survey (SF-36) which assesses physical functioning, role-physical, bodily pain, general health perceptions, vitality, social functioning, role-emotional, and mental health [31]. The RAND scoring method was used (0 [worst] to 100 [best]), and physical component summary (PCS) and mental component summary (MCS) scores were computed.

Cancer-related symptoms were measured using the MD Anderson Symptom Inventory (MDASI) [32]. Patients rated the intensity and interference of cancer symptoms, including pain, nausea, difficulty remembering, dry mouth, and numbness/tingling. Symptom intensity and interference are combined for the MDASI total score. In the present study, the item

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assessing sleep was removed from the scoring of the MDASI in order to assess cancer-related symptoms apart from sleep disturbance.

Sociodemographic and Clinical Characteristics

Sociodemographic information including age, ethnicity/race, marital status, education, and income was provided via self-report. Ethnicity/race was categorized as White/European American, Black/African American, Latina, Asian American, or Native American. Race/ethnicity was maintained as multi-categorical for multivariate analyses, but was dichotomized as racial/ethnic majority (i.e., White/European American) or racially/ethnically underserved (i.e., Black/African American, Latina, Asian American, or Native American) populations to compute effect size. Marital status was categorized as partnered or not partnered. Income was categorized into two levels (annual household income ≤$75,000 or >$75,000).

Clinical characteristics included stage of disease (stage I, II, or III), treatment type during the study period (CT, radiotherapy, or hormone therapy), CT timing (if on CT during the study period; categorized as “began CT in the last 6-months” or “will begin CT in the next 1 month”), menopausal status (pre/post), and BMI (calculated using height and weight from patients’ medical records).

Statistical Analysis

To determine the independent association of sociodemographic or clinic characteristics with baseline sleep, we conducted multivariate ANOVAs (PROC GLM in in SAS v9.2) examining the associations of seven sociodemographic and clinical characteristics (age, ethnicity/race, marital status, income, stage of disease, menopausal status, or BMI) with four sleep indices (baseline PSQI total score, WASO, TST, and SE), covarying for treatment type (chemotherapy, radiation, hormone therapy). Education was not included in any analyses due to its strong correlation with income.

To determine the independent association of sociodemographic or clinic characteristics with sleep across the follow up period, we conducted multilevel modeling analyses (PROC MIXED in in SAS v9.2) examining the association of seven sociodemographic and clinical characteristics (age, ethnicity/race, marital status, income, stage of disease, menopausal status, or BMI), time, and the sociodemographic or clinical characteristic-by-time interaction effects on each of the four sleep indices (PSQI total score, WASO, TST, and SE). All analyses controlled for the baseline level of the sleep outcome variable, treatment type (chemotherapy, radiation, or hormone therapy), and group (yoga, stretching, or waitlist control). Time was treated as a categorical variable, the intercept as a random effect, and an unstructured covariance structure was specified. Pairwise comparisons were conducted to follow up on significant time-by-sociodemographic or clinical characteristic interactions.

To determine the association of baseline sleep with QOL outcomes across the follow-up period, we examined the sleep, time, and sleep-by-time effects on each of the six dependent variables (CES-D, STAI-State, BFI, SF-36 PCS and MCS, MDASI) using PROC MIXED in SAS v9.2. We controlled for the respective baseline outcome as well as sociodemographic

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and clinical characteristics, treatment type (chemotherapy, radiation, or hormone therapy), and group (yoga, stretching, or waitlist control). We treated time as a categorical variable and the intercept as a random effect. We specified an unstructured covariance structure. Pairwise comparisons were conducted to follow up on significant 2-way interactions.

Results

Of the 820 eligible women approached for the study, 452 (55.1%) consented and 415 (92%) provided some baseline data. Most (86%) women were undergoing chemotherapy during the study period, with some undergoing radiotherapy (9%) or hormone therapy (5%). Of those undergoing chemotherapy, most had begun chemotherapy within the six months prior to baseline (71%) and some began chemotherapy after baseline (29%).

A total of 375 participants (90%) returned the packet of self-report measures (containing the PSQI, CES-D, STAI-State, BFI, SF-36 PCS and MCS, MDASI). However, some participants left questions or full measures blank, resulting in a different N for each self-report measure (as noted in Table 2). Complete PSQI total score at baseline was available for 344 participants, and six-night actigraphy data at baseline was available for 388 participants. Participant characteristics can be seen in Table 1 and means for each of the sleep and QOL indices across the follow-up can be seen in Table 2. Fifty-eight percent of the sample reported disturbed sleep (PSQI ≥5) and 38% reported very disturbed sleep (PSQI ≥8) at baseline [26]. Women experienced relatively long WASO (48 minutes), poor SE (81%), and short TST (7.11 hours) at baseline compared to non-clinical samples [33]. Self-reported and actigraphy-assessed sleep had small-to-moderate correlations. Specifically, PSQI was correlated with WASO baseline ($r_{(304)} = .11$, $p = .049$), and 3- ($r_{(186)} = .19$, $p = .009$), 6- ($r_{(135)} = .33$, $p < .001$), and 15- ($r_{(63)} = .26$, $p = .034$) follow ups, and with SE at baseline ($r_{(304)} = -.142$, $p = .0135$), and 3- ($r_{(186)} = -.15$, $p = .043$) and 6- ($r_{(135)} = -.18$, $p = .037$) follow ups. PSQI scores were not correlated with TST at any time point (p's >.4).

Sociodemographic and Clinical Correlates of Baseline and Follow-up Sleep

Baseline: The associations of sociodemographic and clinical characteristics with baseline sleep are presented in Table 3. No sociodemographic or clinical characteristics were associated with PSQI-assessed sleep quality complaints at baseline. Women with lower income (i.e., < $75,000/year) experienced longer WASO than those with higher income (i.e., >$75,000/year; 49.68 min vs. 46.24 min, $F_{(1, 263)} = 5.83$, $p = .016$). BMI was negatively associated with baseline SE ($B = -0.20$, $SE = .06$, $F_{(1, 263)} = 13.98$, $p < 0.001$). Race/ethnicity was associated with SE ($F_{(4, 263)} = 2.92$, $p = .020$) and TST ($F_{(4, 263)} = 2.62$, $p = .035$). Specifically, Black/African American participants experienced the poorest SE and shortest TST (79.24%, 6.67 hours), followed by Latina (81.06%, 6.75 hours) and Asian American (76.93%, 7.18 hours) participants, with Native American (81.73%, 7.22 hours) and White/European Americans (81.89%, 7.14 hours) participants experiencing relatively better SE and TST. Pairwise comparisons indicated that Black/African Americans experienced significantly poorer SE ($p = 0.022$) and shorter TST ($p = 0.008$) compared to White/European Americans, and Latinas experienced significant shorter TST compared to White/European Americans ($p = 0.026$).

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Follow-up: The associations of sociodemographic and clinical characteristics with sleep across the follow up period are presented in Table 3. There was a significant race/ethnicity-by-time interaction effect on PSQI-assessed sleep quality complaints ($F_{(12, 421)} = 2.38$, $p = .006$). Specifically, at 3-months, Black/African American participants reported higher PSQI scores ($LSM = 7.98$) compared to White/European American ($LSM = 6.35$, $p = 0.053$) and Asian American ($LSM = 5.05$, $p = 0.050$) participants. Latina participants reported higher PSQI scores compared to White/European American participants at 6- ($LSM = 7.93$ vs. 5.88, $p = 0.014$) and 15-month follow ups ($LSM = 6.97$ vs. 5.31, $p = .056$). There was a main effect of income on PSQI, with women with lower income reporting higher PSQI than those with higher income ($LSM = 6.83$ vs. 5.37, $F_{(1, 212)} = 8.39$, $p = .004$).

There was a main effect of race/ethnicity on WASO over time ($F_{(4, 188)} = 3.03$, $p = .019$), with Black/African American experiencing longer WASO compared to Latina (54.11 min vs. 43.02 min, $p = 0.007$) and White participants (54.11 min vs. 42.61 min, $p < 0.001$). There was an income-by-time interaction effect on WASO ($F_{(1, 226)} = 4.24$, $p = 0.006$). Specifically, women with lower income reported greater WASO compared to women with higher income only at the 6-month follow up (49.38 min vs. 38.02 min, $p < 0.001$). There was a significant stage-by-time interaction on WASO ($F_{(6, 225)} = 3.74$, $p = .002$), such that, at 3-months, women with stage 1 disease experienced shorter WASO than those with stage 2 (42.40 min vs. 48.96 min, $p = 0.027$) or stage 3 disease (42.40 min vs. 50.10 min, $p = 0.026$), but this pattern was reversed 9-months, with stage 1 disease being associated with longer WASO compared to stage 2 (54.32 min vs. 41.97 min, $p = 0.002$) or stage 3 disease (54.32 min vs. 41.20 min, $p = 0.008$). There was a BMI-by-time interaction effect on SE ($F_{(3, 239)} = 3.24$, $p = .023$), with BMI being significantly negatively associated with SE only at the 3-month follow up ($B = -0.28$, $SE = 0.10$, $p = .004$). There were no significant main effects or interaction effects of any sociodemographic or clinical characteristic with TST across the follow up period.

Association of Baseline Sleep with QOL Over 15 Months

The associations of baseline sleep with QOL across the follow up period are presented in Table 4. There were significant main effects for PSQI-assessed sleep quality complaints on CES-D ($F_{(1, 186)} = 4.13$, $p = 0.043$), BFI ($F_{(1, 197)} = 23.59$, $p < 0.001$), PCS ($F_{(1, 198)} = 40.81$, $p < .0001$) MCS ($F_{(1, 196)} = 3.71$, $p = .056$), and MDASI ($F_{(1, 194)} = 4.24$, $p = .041$) in the expected directions. There were also significant PSQI-by-time interaction effects on MCS ($F_{(3, 445)} = 5.27$, $p = 0.001$) and MDASI ($F_{(3, 452)} = 2.68$, $p = 0.047$). Specifically, PSQI was positively associated with MDASI at only at the 3- ($B = 1.41$, $SE = 0.57$, $p = 0.014$) and 6-month follow ups ($B = 1.99$, $SE = 0.56$, $p < 0.001$). Though post hoc test of the association between baseline PSQI and MCS at each time point did not reveal any significant associations, the association between PSQI and MCS was strongest at the 15 months follow up ($B = -0.23$, $SE = 0.19$, $p = 0.230$).

There was a significant main effect of SE on MCS ($F_{(1, 146)} = 3.72$, $p = 0.056$) in the expected direction. There were significant WASO-by-time interaction effects on STAI-state ($F_{(3, 79)} = 5.91$, $p = .001$), PCS ($F_{(3, 180)} = 6.41$, $p < .001$), and MCS ($F_{(3, 180)} = 3.83$, $p = 0.012$). Specifically, baseline WASO was significantly associated with STAI-state ($B = 0.24$,

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SE = 0.10, *p* = .014) and PCS (*B* = −0.12, *SE* = 0.04, *p* = .003) at 3-months and no other time points and was associated with MCS at 6-months (*B* = −0.14, *SE* = 0.05, *p* = .005) and no other time points. Baseline TST was not associated with any index of QOL at baseline or over time.

Exploratory Analyses

Due to the large number of participants undergoing CT, all analyses were run on only participants undergoing CT (n = 358), controlling for timing of CT. Results were identical in terms of significance to those reported above with three exceptions: the association of income with baseline WASO (*p* = .10), the association of race/ethnicity with baseline TST (*p* = .12), and the association of BMI with SE at 3 months (*p* = .40). In each case, the effect was in the same direction.

Discussion

This study sought to determine sociodemographic and clinical characteristics associated with increased risk of disturbed sleep during active breast cancer treatment as well as over the following 15 months, and the effect of baseline sleep disturbances on subsequent QOL in a large and diverse sample of women undergoing active treatment for breast cancer.

As hypothesized, breast cancer survivors from racially/ethnically underserved populations were at increased risk for poorer sleep at baseline, and at various points in the 15-month follow-up period, independent of other sociodemographic characteristics. For example, Black/African American participants got an average of 28 minutes less sleep and Latina participants got an average of 23 minutes less sleep each night at study entry compared to White/European American participants. Additionally, Black/African American participants spent an average of 12 more minutes awake after sleep onset compared to White/European Americans during the follow up period, and Black/African American and Latina participants self-reported greater sleep disturbances at various points during the 15-month follow-up compared to their White/European American counterparts. Indeed, race/ethnicity was the only sociodemographic or clinical characteristic included in this study that was associated with all four indices of sleep at some point during the study period. This is consistent with previous literature, as many studies have reported that racially/ethnically underserved groups, particularly Black/African American women, both with and without a diagnosis of breast cancer, experience poorer self-reported and actigraphy-assessed sleep compared to White/European American women [16-17, 34-36].

The present study also found that income was associated with two indices of sleep, and BMI was associated with one index of sleep. Specifically, women with household incomes below $75,000/year self-reported poorer sleep throughout the follow-up period and spent slightly more minutes awake after sleep onset compared to those earning above $75,000/year at study entry and the 6-month follow up, though the absolute difference in minutes was small and likely not clinically significant (<5 minutes). Though, to our knowledge, income has not been examined in relation to sleep, fewer years of education (a related construct) have been associated with risk of insomnia among breast cancer patients [3, 10]. This study suggests that income has a modest association with sleep quality during breast cancer treatment.

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Additionally, actigraphy-assessed baseline SE decreased one percentage point, on average, for every five-point increase in BMI, and this association was even stronger at the three-month follow-up. This echoes findings in cancer and non-cancer samples [7, 23]. However, contrary to hypothesis, BMI was only associated with one index of sleep quality, and was not related to WASO, TST, or self-reported sleep quality.

Poorer sleep among breast cancer patients who are from racially/ethnically underserved populations and who have lower income and higher BMI is best understood within the context of health disparities research. Health disparities, including differences in sleep quality, arise from multiple social, economic, and environmental risk factors; factors which are often entwined with ethnicity/race [34, 37]. Thus, rather than pointing to race or ethnicity as a biological risk factor for poor sleep, these findings must be interpreted within the social context. Rather, race/ethnicity, income, and even BMI [38] may instead be a proxy for social, cultural, and economic risk factors for health disparities in general, and sleep quality disparities specifically.

The present study also found that stage was associated with actigraphy-assessed sleep continuity (WASO), but the direction of the effect depended on the follow-up time, with stage 1 being associated with greater WASO early in the follow up period, and less WASO later in the follow-up period. Women with stage 1 disease may have increased stress early in the follow-up period, perhaps due to adjusting to a new diagnosis, whereas women with later stage disease may experience greater stress later in the follow-up period.

As hypothesized, poor subjective sleep quality (i.e., PSQI) predicted higher depression symptoms, fatigue, physical and mental health-related QOL, and cancer-related symptoms during the 15-month follow up period. This is keeping with previous literature demonstrating a connection between subjective sleep quality and health-related QOL, particularly depression, in cancer and non-cancer samples [3, 6-8, 39]. Baseline WASO was associated with greater anxiety and poorer physical health-related QOL three months later and poorer mental health-related QOL six months later. Additionally, baseline SE was also associated with poorer mental health-related QOL six months later. TST, however, was not related to any QOL indices during the follow-up period. These mixed findings regarding actigraphy data are in keeping with the literature, in which some studies report an association of actigraphy-assessed sleep quality with QOL [11] and even mortality [40] among breast cancer survivors, while others do not [12-14, 41]. Thus, further examination of the complex association between actigraphy-assessed sleep and QOL is warranted.

In addition to the significant results found, the present study also examined many associations that did not reach statistical significance. Indeed, most sociodemographic and clinical characteristics were unrelated to sleep. For example, results suggest that marital status, menopausal status, age, and possibly even income, stage, and BMI may have little to do with sleep. Additionally, two actigraphy-assessed sleep indices (SE and TST) were largely unrelated to measures of quality of life. The lack of associations among these variables are also important to consider when developing future research on the predictors and consequences of disturbed sleep during treatment for breast cancer.

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This study does have some limitations. First, this paper represents an exploration of data collected as a part of a larger study, not an examination of the original study's primary hypotheses, so findings must be interpreted with caution. Additionally, this exploratory paper examined the associations between many variables, which increases the risk of false-positive findings (i.e., finding a result that is statistically significant by chance and does not represent a true association in the population). Thus, it is important to view these findings as exploratory, hypothesis-generating, and warranting replication. It is also important to note that, because this is a secondary analysis of a randomized controlled trial, it is possible that longitudinal analyses could be confounded by participation in the intervention. However, all analyses included group assignment as a covariate to mitigate this risk as much as possible. Additionally, it is important to note that, though actigraphy is commonly used to approximate sleep, it is a measure of movement, not sleep.

There are also limitations related to the generalizability of these findings. First, the research participants may not reflect the general population, as just over half of patients approached for the study consented to participate. Indeed, it is possible that patients who opted to participate may have been particularly well-adjusted, as indicated by the relatively high QOL reported throughout the follow-up period, which may have introduced a ceiling effect. Additionally, the study's inclusion criteria were relatively narrow in order to maintain a relatively homogenous sample of women for the parent clinical trial, which may have also limited generalizability. For example, women who reported the need for psychological services or were currently engaged in counseling or support groups or who had lymphedema were excluded, which may have restricted the range of mental and physical health symptom severity. Furthermore, though the sample relatively diverse, it was predominantly White/European American (60%), and future research is needed to tease out differences among racially/ethnically underserved groups. Similarly, the sample was relatively affluent, with nearly half of the sample reporting a household income of $75,000, well above the national average of $57,000 [42].

Conclusion

This represents the largest sample to date of sleep quality (assessed via self-report and actigraphy) in women undergoing active treatment for stage I-III breast cancer. Taken together, these findings suggest that 1) health disparities in sleep quality during and after treatment for breast cancer exist, with ethnicity/race and possibly income and BMI likely serving as proxies for larger societal and economic forces, and 2) sleep disturbance, assessed via self-report and via some aspects of actigraphy (i.e., WASO), is associated with important, often difficult to address aspects of QOL during and after treatment for breast cancer. These findings may help inform screening measures to identify patients that may derive particular benefit from participating in an intervention to improve sleep, such as cognitive behavioral therapy for insomnia (CBT-I), which has been shown to have both statistical and clinical significance for improving sleep in cancer survivors [43]. Future research should continue to examine these associations, explore interventions for the modifiable risk factors, and consider these factors when screening for patients who may benefit from psychosocial intervention to improve sleep.

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Table 1.

Demographic and clinical characteristics

Characteristic	M/n	SD/%
Sociodemographic Factors		
Age (n=415)	49.82	10.09
BMI (n=389)	28.63	6.81
Ethnicity/Race (n=377), n%		
White /European American	227	60.21
Latina	58	15.38
Black/African American	59	15.65
Asian American	20	5.31
Native American	13	3.45
Marital Status (n = 375), n% Partnered	233	62.13
Education, (n=356), n%		
High School	67	18.82
College	183	51.40
Graduate School	106	29.78
Income (n=346), n%		
≤75K	178	51.45
>75K	168	48.55
Clinical Factors		
Stage (n=415), n%		
I	91	21.93
II	220	53.01
II	104	25.06
Treatment Plan (n=415)		
Chemotherapy	358	86.27
Radiation	38	9.16
Hormone Therapy	19	4.58
Chemotherapy Timing (n=358), n%		
On Chemotherapy at Baseline	254	70.95
Began Chemotherapy after Baseline	104	29.05
Menopausal (n=415), n%		
Pre-Menopausal	182	43.86
Post-Menopausal	233	56.14

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Table 2.

Cancer-Related Quality of Life Across Follow Up Period

	Baseline Self-Report N=375* Actigraphy N = 388		3-Months Self-Report N=252 Actigraphy N=215		6-Months Self-Report N=237 Actigraphy N=152		9-Months Self-Report N=198 Actigraphy N=108		15-Months Self-Report N=194 Actigraphy N=74	
	M	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**
PSQI	8.28	3.99	7.64	4.06	7.24	4.10	6.73	3.84	6.25	3.84
Efficiency (%)	80.62	6.52	80.15	9.10	80.59	7.19	80.65	9.24	83.22	9.24
TST (hours)	7.11	1.00	7.19	1.24	7.20	1.09	7.08	1.16	7.30	1.16
WASO (min)	48.39	21.73	50.75	18.45	45.53	19.56	46.36	20.69	41.49	20.69
CES-D†	12.01	8.422	11.49	8.44	11.16	8.92	9.65	8.92	8.81	7.94
STATE	32.03	34.92	35.12	12.16	34.73	11.96	32.88	11.50	33.01	11.50
BFI	2.79	2.22	3.31	2.35	2.88	2.33	2.34	2.09	2.21	2.09
SF-36 PCS	22.49	3.86	41.57	9.79	43.43	9.85	46.29	9.59	47.92	9.59
SF-36 MCS	36.37	12.44	47.70	9.93	48.19	10.83	49.57	10.84	51.32	10.84
MDASI†	35.46	29.08	40.30	33.56	34.72	30.78	26.97	28.58	25.66	28.58

*N's represent total in sample. Some measures were completed by fewer participants. All baseline measures were completed by at least 344 participants.

†Sleep-related items removed from variable

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Table 3.

Sociodemographic and Clinical Characteristics Associated with Sleep at Baseline and Across the Follow Up Period

PSQI Total													
	Baseline					**Main Effects**				**Interaction Effects**			
	F	**p**	**d/ β**	**95% CI/SE**		**F**	**P**	**β**	**SE**	**F**	**p**	**β**	**SE**
Ethnicity/Race	0.59	0.669	−0.14	−0.36	0.08	1.45	0.220	0.16	0.16	**2.38**	**0.006**	**−0.16**	**0.18**
Marital Status	0.31	0.581	0.04	−0.21	0.28	2.92	0.089	0.31	0.16	1.26	0.287	0.05	0.05
Income	1.52	0.219	0.09	−0.16	0.33	**8.39**	**0.004**	**0.39**	**0.16**	1.13	0.339	−0.04	0.04
Stage	1.93	0.147	0.23	−0.02	0.49	0.33	0.720	0.06	0.18	0.61	0.725	0.00	0.05
Menopausal	3.30	0.071	0.02	−0.21	0.24	0.70	0.404	−0.16	0.15	0.58	0.626	−0.05	0.04
BMI	0.66	0.416	0.05	0.06	*	0.04	0.834	0.02	0.08	1.57	0.197	−0.02	0.02
Age	1.91	0.168	−0.12	0.09	*	1.80	0.181	0.09	0.07	1.79	0.149	0.04	0.02
Actigraphy WASO													
	Baseline					**Main Effects**				**Interaction Effects**			
	F	**p**	**d/ β**	**95% CI/SE**		**F**	**P**	**β**	**SE**	**F**	**p**	**β**	**SE**
Ethnicity/Race	1.12	0.347	−0.19	−0.41	0.03	**3.03**	**0.019**	**0.31**	**0.22**	1.63	0.086	0.04	0.07
Marital Status	0.01	0.930	0.01	−0.21	0.23	0.17	0.681	−0.13	0.22	1.34	0.262	−0.11	0.07
Income	**5.83**	**0.017**	**0.28**	**0.05**	**0.50**	1.93	0.166	−0.11	0.22	**4.24**	**0.006**	**−0.11**	**0.07**
Stage	0.76	0.470	−0.01	−0.26	0.25	0.27	0.766	0.07	0.21	**3.74**	**0.002**	**0.23**	**0.07**
Menopausal	1.05	0.306	0.11	−0.10	0.31	0.23	0.632	0.01	0.20	1.49	0.217	0.02	0.06
BMI	2.72	0.100	0.11	0.06	*	1.38	0.242	−0.01	0.12	0.41	0.745	−0.01	0.03
Age	1.20	0.273	−0.10	0.10	*	0.29	0.592	−0.03	0.10	0.83	0.481	0.03	0.03
Actigraphy SE													
	Baseline					**Main Effects**				**Interaction Effects**			
	F	**p**	**d/ β**	**95% CI/SE**		**F**	**P**	**β**	**SE**	**F**	**p**	**β**	**SE**
Ethnicity/Race	**2.98**	**0.020**	**0.32**	**0.09**	**0.54**	0.68	0.608	0.01	0.29	0.75	0.706	0.05	0.09
Marital Status	2.86	0.092	0.19	−0.03	0.41	0.87	0.354	−0.23	0.29	1.06	0.367	−0.10	0.09
Income	2.40	0.123	0.18	−0.05	0.40	0.10	0.757	0.04	0.27	1.99	0.117	0.16	0.09
Stage	1.08	0.343	0.00	−0.25	0.24	0.68	0.509	0.57	0.27	1.66	0.132	0.20	0.09
Menopausal	1.97	0.162	0.15	−0.06	0.35	0.21	0.647	0.00	0.26	1.23	0.298	0.10	0.08
BMI	**13.06**	**0.000**	**−0.20**	**0.06**	*	1.43	0.233	0.05	0.14	**3.24**	**0.023**	**0.07**	**0.04**
Age	0.23	0.635	0.04	0.09	*	0.06	0.805	0.02	0.13	0.03	0.994	−0.01	0.04
Actigraphy TST													
	Baseline					**Main Effects**				**Interaction Effects**			
	F	**p**	**d/ β**	**95% CI/SE**		**F**	**P**	**β**	**SE**	**F**	**p**	**β**	**SE**
Ethnicity/Race	**2.62**	**0.035**	**0.31**	**0.09**	**0.53**	0.65	0.629	−0.07	0.27	0.67	0.782	0.06	0.09
Marital Status	3.33	0.069	0.21	−0.02	0.43	0.56	0.456	−0.03	0.28	1.19	0.314	−0.15	0.09
Income	1.09	0.299	0.12	−0.10	0.34	0.13	0.722	0.12	0.27	0.83	0.480	0.07	0.09
Stage	0.11	0.892	0.01	−0.25	0.27	1.98	0.141	0.43	0.26	1.33	0.243	0.14	0.09

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PSQI Total													
	Baseline					Main Effects				Interaction Effects			
	F	p	d/ β	95% CI/SE		F	P	β	SE	F	p	β	SE
Menopausal	0.92	0.337	0.10	−0.11	0.31	0.11	0.741	−0.13	0.25	0.52	0.670	0.04	0.08
BMI	1.34	0.248	−0.07	0.06	*	0.03	0.857	0.08	0.14	0.56	0.641	0.05	0.04
Age	0.16	0.687	−0.03	0.08	*	0.00	0.964	0.05	0.12	0.47	0.706	0.05	0.04

Note: To calculate effect sizes for the association of sociodemographic and clinical characteristics with baseline sleep and the main effects, Cohen's d was calculated for categorical characteristics and the standardized beta coefficient was reported for continuous characteristics (i.e., BMI and age). To calculate effect sizes associated with main effects and interaction effects, all categorical variables were dichotomized (White/European American vs. All Other Ethnicity/Racial categories; Stage 1 vs. Stages 2 and 3; Chemotherapy vs. Radiation therapy and Hormone Therapy) and standardized beta weights are reported. Additionally, to calculate effect sizes associated with interaction effects, models were run with time as a continuous variable.

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Table 4.

Baseline Sleep Associated with QOL Across the Follow Up Period

PSQI Global								
	Main Effects				**Interaction Effects**			
	F	**p**	**β**	**SE**	**F**	**p**	**β**	**SE**
CES-D**	**4.13**	**0.043**	**0.09**	0.07	1.30	0.274	0.01	0.02
STATE	2.20	0.143	0.07	0.14	1.07	0.365	−0.05	0.03
BFI	**23.59**	**<.001**	**0.27**	0.07	0.99	0.399	−0.02	0.02
SF-36 PCS	**40.81**	**<.001**	**−0.34**	0.07	0.88	0.450	0.01	0.02
SF-36 MCS	**3.71**	**0.056**	**−0.01**	**0.07**	**5.27**	**0.001**	**0.02**	**0.02**
MDASI**	**4.24**	**0.041**	**0.02**	**0.07**	**2.68**	**0.047**	**−0.05**	**0.02**
Actigraphy WASO								
	Main Effects				**Interaction Effects**			
	F	**p**	**β**	**SE**	**F**	**p**	**β**	**SE**
CES-D**	1.54	0.216	0.10	0.14	0.48	0.698	−0.03	0.04
STATE	0.16	0.687	−0.05	0.21	**5.91**	**0.001**	**−0.22**	**0.05**
BFI	1.00	0.319	0.07	0.14	2.45	0.065	−0.09	0.04
SF-36 PCS	0.23	0.635	0.04	0.13	**6.41**	**0.000**	**0.11**	**0.03**
SF-36 MCS	1.02	0.314	0.08	0.14	**3.83**	**0.011**	**0.09**	**0.04**
MDASI**	0.83	0.364	0.01	0.12	1.02	0.385	−0.06	0.03
Actigraphy SE								
	Main Effects				**Interaction Effects**			
	F	**p**	**β**	**SE**	**F**	**p**	**β**	**SE**
CES-D**	0.73	0.395	−0.20	0.14	1.44	0.232	−0.03	0.04
STATE	1.01	0.320	−0.04	0.22	1.43	0.240	−0.03	0.06
BFI	1.42	0.236	−0.11	0.14	0.24	0.867	0.02	0.04
SF-36 PCS	1.12	0.292	0.08	0.08	1.04	0.375	−0.05	−0.05
SF-36 MCS	**3.72**	**0.056**	**0.20**	**0.14**	0.84	0.471	0.02	0.04
MDASI**	0.66	0.417	−0.13	0.12	0.38	0.771	−0.02	0.03
Actigraphy TST								
	Main Effects				**Interaction Effects**			
	F	**p**	**β**	**SE**	**F**	**p**	**β**	**SE**
CES-D**	1.50	0.223	−0.06	0.13	2.06	0.108	−0.05	0.04
STATE	0.50	0.484	−0.04	0.25	1.34	0.267	−0.07	0.06
BFI	0.09	0.771	−0.05	0.14	1.11	0.344	−0.04	0.04
SF-36 PCS	0.42	0.518	0.21	0.13	1.2	0.312	0.04	0.03
SF-36 MCS	1.26	0.263	0.23	0.14	1.24	0.296	0.07	0.04
MDASI**	0.32	0.570	−0.07	0.12	1.88	0.135	−0.07	0.03

Note: To calculate effect sizes, models were run with time as a continuous variable. Standardized beta weights are reported.

* Sleep-related items removed from variable

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