Insomnia in breast cancer: a prospective observational study

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ABSTRACT

STUDY OBJECTIVES - Insomnia in cancer patients is prevalent, persistent and confers risk for physical and psychological disorder. We must better understand how insomnia develops in cancer patients and explore the main contributors to its chronicity so that insomnia management protocols can be integrated more effectively within cancer care. This study monitors the etiology of insomnia in breast cancer patients and identifies risk factors for its persistence.

METHODS – 173 females with newly diagnosed, non-metastatic breast cancer were tracked from diagnosis for 12-months. Participants completed monthly sleep assessments using the Insomnia Severity Index (ISI) and 3-monthly health-related quality-of-life assessments using the European Organisation for Research and Treatment of Cancer - Breast (EORTC QLQ-C30-BR23) scale. Clinical data on disease status and treatment regimens were also assessed.

RESULTS – Prior to diagnosis, 25% of participants reported sleep disturbance, including 8% with insomnia syndrome (IS). Prevalence increased at cancer diagnosis to 46% (18% IS) and remained stable thereafter at around 50% (21% IS). We also explored sleep status transitions. The most common pattern was to remain a good sleeper (34%-49%) or to persist with insomnia (23%-46%). 77% of good sleepers developed insomnia during the 12-month period and 54% went into insomnia remission. Chemotherapy (odds ratio=0·08, 95% ci 0·02-0·29, p<·001) and pre-diagnosis ISI scores (odds ratio=1·13/unit increase in pre-diagnosis sleep score, 95% ci 1·05-1·21, p=·001) were identified as the main risk factors for persistent insomnia.

CONCLUSIONS – These data advance our understanding of insomnia etiology in cancer patients and help identify those who should be prioritised for insomnia management protocols.

KEYWORDS – Insomnia, Cognitive Behavioral Therapy, Epidemiology, Mental Health

STATEMENT OF SIGNIFICANCE –

This study explores the longitudinal course of insomnia in women with a diagnosis of breast cancer. Results demonstrate that insomnia is a persistent condition following breast cancer diagnosis that results in significant adverse outcomes, particularly in those patients receiving chemotherapy. Effective insomnia treatment programmes such as Cognitive Behavior Therapy for insomnia (CBT-I) should be initiated at the earliest possible opportunity following cancer diagnosis in order to reduce the prevalence and impact of sleep disturbance during cancer treatment. In addition, patients with a history of sleep disturbance and/or those scheduled to receive chemotherapy should be closely monitored throughout the cancer treatment and rehabilitation phases and if required, offered more intensive forms of CBT-I following completion of active cancer treatment.

INTRODUCTION

Breast cancer survival has doubled in the last forty years and UK net five year survival is 87%. Improving life quality amongst breast cancer survivors has thus become increasingly important. Insomnia is the most commonly reported mental health complaint in the UK [1] and as such, is a significant public health concern. Around 25% of adults report poor sleep, with an estimated 8-10% meeting diagnostic criteria for insomnia syndrome.[2] These rates are considerably higher amongst those with chronic health conditions. Data from cancer populations report that 25-69% have difficulty sleeping, with 18-29% reporting insomnia disorder.[3–5] The highest prevalence rate is found in breast cancer patients, where approximately half of all those diagnosed report poor sleep. A previous study of three hundred breast cancer survivors reported that 51% experienced insomnia symptoms and 19% met diagnostic criteria for insomnia disorder.[6] However, despite increasing awareness of the pervasiveness of insomnia within cancer groups, scientific reports of insomnia prevalence remain variable and wide-ranging.[7] This is partly due to studies utilizing different insomnia definitions, measurements and timing of assessments.[5]

A previous report by Savard (2011) on the natural history of insomnia in cancer patients (mixed sites) reported data on incidence[a], persistence[b], remission[c] and relapse[d] over the eighteen month period following diagnosis.[8] [[a]change of status from good sleep (at one time point) to insomnia symptoms or syndrome (at the next time point), [b]presence of insomnia (symptoms or syndrome) at two consecutive time points, [c]change in status from insomnia (symptoms or syndrome) to good sleep at the subsequent time point, [d]resurgence of insomnia following remission]. The study revealed high rates of insomnia at baseline (59%), including 28% with insomnia syndrome. Insomnia became less prevalent over the eighteen-month assessment period but remained pervasive at the end of the study (36%). Approximately 15%

of patients experienced a first incidence of insomnia during the study and around 20% experienced relapse. Patients with insomnia syndrome were much less likely to experience remission than those with insomnia symptoms and those with insomnia syndrome at baseline retained that sleep status throughout the study.

Using operational diagnostic criteria to distinguish between insomnia syndrome and symptoms is an important differentiation, particularly in prospective studies. However, previous work in this area has included diverse cancer sites, which has led to significant differences between participant characteristics and characteristics of those who declined to participate. Similarly, due to the diversity of cancer treatment regimens across mixed cancer sites, cross-comparison between groups is difficult. Therefore, the exploration of insomnia evolution in a large cohort of breast cancer patients, encompassing active and follow-up treatment phases, permits a useful assessment of the progression from normal sleep to acute, then (potentially) persistent insomnia within a single, homogeneous group. Exploring the evolution of insomnia within breast cancer also helps to inform sleep management protocols, specifically with regard to when and how they would be most useful for patients. Therefore, study aims are (i) describe the natural history of insomnia in breast cancer patients by measuring rates of insomnia incidence, persistence, remission and relapse and (ii) identify potential demographic, clinical and psychological factors that contribute to persistent insomnia after cancer treatment.

PATIENTS AND METHODS

Participants and Recruitment

173 female breast cancer patients participated. Inclusion criteria included confirmed diagnosis of non-metastatic breast cancer, diagnosis < three months and prognosis > six months. Exclusion criteria were (i) untreated/unstable psychiatric illness, diagnosis of another sleep disorder and male gender. We excluded male breast cancer patients because they are few in number and as such, are likely to have different psychological characteristics. To avoid selection bias and priming effects, participants were advised that they were contributing to a study monitoring general wellbeing and health-related symptoms.

Recruitment took place across multiple hospital sites in west central Scotland. Clinical teams identified eligible patients and the project researcher met with them at a scheduled clinic visit to provide further information and complete consent, eligibility and screening procedures. Recruitment was not restricted to individuals who met criteria for insomnia. Rather, we enrolled a cohort, some of whom would develop clinical insomnia or experience exacerbation of pre-existing clinical insomnia since diagnosis (Insomnia Syndrome), some of whom would display symptoms of insomnia without fulfilling all diagnostic criteria of insomnia syndrome (Insomnia Symptoms), and some of whom would continue to sleep well (Good Sleepers).

Study Design

We adopted a prospective quantitative approach in which females with newly diagnosed breast cancer were tracked during their cancer care. The planned study sample size calculation was based on the scenario of detecting a 20% difference in incidence of persistent insomnia post treatment (30% v 50%) between two categories of a predictive variable (e.g. XRT yes/no) with 75% of patients falling into the category with the smaller persistent insomnia rate.[9] This required 250 patients (80% power, 5% level of statistical significance). In practice, the persistent insomnia rate was lower (15%) and only 173 patients were recruited within the study period. On this basis, the study provides approximately 85%

power to detect a difference from 5%-25% in persistent insomnia rates between groups as outlined above. If the split of patients between categories of a prognostic variable is closer to 50:50 than 25:75, the power to detect associations of this magnitude will be greater than 85% (equivalently, associations of a smaller magnitude can be detected with the same power). For variables such as age (examined as continuous variables), the power should also be greater than 85%.

Measures and Procedure

Prior to enrollment, interested patients were assessed for eligibility using the Glasgow Sleep Centre Screening Interview (GSCSI). This comprises assessments of sleep history, screening for other sleep disorders and a full history of physical and psychological health. Those who met inclusion criteria were enrolled and completed monthly sleep status assessments. These monthly assessments were completed from month 0 (baseline) to month 12 using the Insomnia Severity Index (ISI). The ISI is a seven item measure, validated for cancer patients, which is considered a core assessment tool for insomnia research studies.[10] Based on criteria outlined in Savard (2011), data from the ISI was combined with data on sleep medication use and duration of sleep problem, to classify patients into one of three sleep status groups at each assessment point; Insomnia Syndrome (IS), Insomnia Symptoms (ISym) or Good Sleepers (GS). These groups were defined as follows: IS group – patient meets criteria for insomnia, presents symptoms of initial, maintenance or late insomnia at least 3 nights per week for minimum of 1 month, is dissatisfied with sleep, reports psychological distress or daytime impairment related to sleep difficulties. If prescribed medication is used as a sleep-promoting agent at least 3 nights per week, patients are automatically classified as IS regardless of the above; ISym group – patient presents symptoms of initial, maintenance or late insomnia at least 3 nights per week without fulfilling all criteria of IS (i.e. may be

satisfied with sleep, not report distress or daytime consequences, or sleep difficulties could last for < 1 month) or, will be dissatisfied with sleep quality but without symptoms of initial, maintenance or late insomnia. If prescribed medication is used as a sleep promoting agent less than three nights per week or over-the-counter medication at least one night per week participants are automatically classified as ISym regardless of the above; GS group – patients is satisfied with sleep, does not report symptoms of initial, maintenance or late insomnia, does not use prescribed or over-the-counter medication as a sleep-promoting agent.

Alongside monthly sleep assessments, patients also completed an additional, retrospective ISI at month 0. Given the potential impact of diagnosis upon sleep, the purpose of this retrospective account was to establish sleep status 3 months prior to this event. However, due to the potential unreliability of retrospective accounts, we assessed the validity of these pre-diagnosis ISI scores. Patients completed a second retrospective ISI at month 12, which we then correlated with the actual month 9 ISI assessment. The correlation between the retrospective and the actual ISI was 0·91 with 94% scores being within five points of each other. This suggests that these retrospective accounts were reliable.

Patients also completed the European Organisation for Research and Treatment of Cancer - Breast (EORTC QLQ-C30-BR23) scale. This is a cancer-specific measure of health-related quality of life comprising three symptom scales (fatigue, pain, and nausea and vomiting). This measure also includes a breast cancer specific module that assesses body image, sexual functioning, future perspective, systemic therapy side effects and breast symptoms. Patients completed this measure every three months from month 0 to month 12. Once all assessments were completed, individuals who continued to have difficulty sleeping had the option of receiving CBT. Patients had the option of completing these assessment online or via postal return. 52% of the sample opted for postal return.

Statistical Analyses

In order to describe the natural history of insomnia in breast cancer patients, descriptive tabulations, associated histograms and bar charts are primarily used. To examine insomnia persistence and remission duration, Kaplan-Meier techniques were employed. To identify factors that predict susceptibility to developing persistent insomnia over a twelve month period, we examined the relationship between patient, tumor and treatment characteristics and the proportion of patients who developed persistent insomnia syndrome (PIS) during the post cancer-treatment phase. PIS is defined as a sleep status of IS present on 3 separate occasions, during the post treatment follow-up phase (T8 – T12). The post treatment follow-up phase was defined as months 8-12 in this study, as all patients had completed chemotherapy by month 7. Patients who completed less than 3 ISI assessments during this period were excluded from the analysis (n=3). We also examined the influence of worst recorded symptom scores (from month 0-6 EORTC QLQ-C30/BR23 data) on the development of PIS.

The association of each variable with the development of PIS was examined in a univariate fashion based on Pearson's chi-square test (exact version) for categorical variables or the Mann-Whitney U-test for continuous variables. Those variables with a significant association at the 25% level were entered in a stepwise fashion into a multivariable logistic regression model to determine a set of variables that were significantly associated with the development of PIS. Variables were retained if they were statistically significant at the 5% level. The final logistic regression model was assessed for goodness of fit using the Hosmer-Lemeshow test. In table 1, Pearson's chi-square test (exact version) was used to determine the association with first major assessment point completed. All analyses were done using SPSS v22.0 (Chicago, IL).

RESULTS

Of the 393 patients approached, 42 were excluded and 178 declined to participate, resulting in a participation rate of 49% (n = 173) (refer to Figure I for full exclusion/refusal details). As previously stated, patients were eligible to enroll on the study if their diagnosis was within the previous three month period. For clarity, these patients are presented separately as 'recruited at month 0' or 'recruited at month 3', depending on which assessment point was closest to their date of written consent. As outlined in Figure 1, 80 (46%) patients were enrolled at month 0 (diagnosis) and 93 (54%) were enrolled at month 3.

Insert Figure 1

The mean age of the sample was 58 years. Most patients were married (53·2%) and either retired (35·8%) or on sick leave from work (36·4%). The majority of patients had a stage I (38·2%) or stage II (26·0%) disease, consistent with study inclusion criteria. 67·6% of the sample had breast-conserving surgery. The remaining 26·6% had a mastectomy, 37·0% of whom also had breast reconstruction. In terms of anti-cancer therapy, 46·2% of patients received chemotherapy, 93·6% received radiotherapy and 84·4% received adjuvant hormonal therapy. There were minimal differences between patients recruited at month 3 and those recruited at month 0. The only statistically significant difference was in T-stage where month 0 patients tended to have smaller tumours (T1 58·8% vs 39·8%, p=·028). This difference was partially reflected in the overall stage of disease where month 0 patients tended to have earlier disease (stage I 47·5% v 30·1%, p=·059). Both the pre-diagnosis [Mean=4·4, S.D=5·7

(patients recruited at month 0); M=3·9, S.D=5·7 (patients recruited at month 3)] and month 3 [M=9·0, S.D=6·9 (patients recruited at month 0); M=8·9, S.D=6·6 (patients recruited at month 3)] ISI scores were very similar at the two recruitment time-points. Full details on patient demographics are presented in Table 1

Insert Table 1

Prevalence of Insomnia over Time

Prior to cancer diagnosis, 75·1% *[se=3·2%]* of patients were good sleepers (GS), 16·8% *[2·8%]* reported symptoms of insomnia (ISym) and 8·1% *[2·0%]* reported insomnia syndrome (IS), using recognized ISI criteria. Therefore, the point prevalence of insomnia (combining those with IS and ISym) at pre-diagnosis was 24·9% *[3·3%]*. This rate increased at diagnosis (month 0) to 46·1% *[5·6%]*, with rates remaining stable at around 50% thereafter (46·1% - 56·3%). When looking at prevalence of IS separately over this same period, 8·1% of patients reported IS at pre-diagnosis. This figure rises to 17·9% *[4·3%]* at diagnosis and remains at around 21% (18·2% - 24%) until month 11. At month 11, rates of IS dropped to 14·9% before increasing again to 18·5% at month 12. At pre-diagnosis, 16·8% of patients report ISym, which rises to 28·2% *[5·1%]* at diagnosis and remains at approximately 30% thereafter (28·1% - 3·9%). Figure II shows rates of insomnia (both IS and ISym) double at diagnosis and remain relatively steady across the following 12-month period with half of the total sample reporting chronic, unremitting insomnia.

Insert Figure 2

Sleep Status Transitions

The analysis of insomnia incidence, remissions and relapse data over the 12-month period, is based on the cohort recruited at month 0 who had no more than one missing assessment (68 patients; 85·1% of month 0 cohort). In terms of incidence, 64·7% (n=44) of these patients reported being GS at pre-diagnosis. However, 77·3% *[6·3%]* of these had a first incidence of insomnia (where ISI score >7) at some point during the 12-month study period. In terms of remission, 55·9% of the total cohort (n=38) developed insomnia at some point over the assessment period (including the pre-diagnosis assessment) and of these patients, 44·8% *[8·1%]* experienced a subsequent insomnia remission. The persistence and remission durations of insomnia were estimated using data on all patients without a missing assessment (n=132). Of these, 106 developed insomnia at some point and insomnia persisted for a median of four months (95% confidence interval 2-6 months). 71 (54%) patients experienced insomnia remission at some point during the study and remission persisted for some time, providing there was no immediate relapse at the next assessment. The median remission duration was nine months (95% confidence interval 2-9 months).

At every time interval, with the exception of pre-diagnosis to month 0, the most common sleep status transitions are either to persist with insomnia or to remain a good sleeper. As illustrated in Figure 3, rates for remaining a good sleeper range from 34·2% *[5·4%]* to 49·0% *[4·0%]*. Rates for insomnia persistence range from 23·1% *[4·8%]* to 46·1% *[3·9%]* (from 40% *[5·7%]* to 46·1% excluding the pre-diagnosis to month 0 transition). Insomnia incidence rates range from 4·5% *[1·7%]* to 23·1% *[4·8%]* (from 4·8% *[1·7%]* to 13·2% *[3·9%]* excluding the pre-diagnosis to month 0 transition) and rates for insomnia remission range from 3·8% *[1·5%]* to 11·2% *[2·6%]*. Overall, the most probable current sleep status

corresponds to retaining the previous sleep status in every instance except one (pre-diagnosis to diagnosis transition).

Insert Figure 3

Common Sleep Trajectories

This analysis is based on the cohort of patients who were recruited at month 0 who had no more than one missing assessment (68 patients; 85·1% of cohort). To reduce the number of possible sleep trajectories, the categories 'IS and 'ISym' were merged. There were six distinct trajectories that accounted for 43% of the patients; 12 patients (17·6%) with the trajectory 'good sleeper' throughout, 6 patients (8·8%) with the trajectory 'insomnia' throughout, 5 patients (7·4%) who were good sleepers at pre-diagnosis and then had insomnia for the subsequent twelve months. There are three trajectories, which have 2 patients each (1 with 11 months 'good sleeper' and 'insomnia' once at month 5; 2 with insomnia throughout apart from 1 month). The remaining thirty nine trajectories are distinct to single patients.

Insert Table 2

Risk Factors for Developing Persistent Insomnia Syndrome Post Cancer Treatment

As described above, patients with PIS during the post cancer treatment phase are defined as having a sleep status of IS present on three separate occasions, during the post treatment follow-up phase. Specifically, in our analysis, insomnia syndrome was identified by examining ISI scores over months 8-12 of the study, excluding those patients with less than

three scores (n=3). One-hundred and fifty patients had all 5 ISI scores assessed over months 8-12, 12 were missing 1 ISI score and 8 were missing 2 ISI scores. Of these 20 patients with one or two missing scores the presence/absence of persistent insomnia was ambiguous in 5 (IS present on at least one assessment), but for the purposes of the analysis this small percentage of the total patient number has been assumed not to have persistent insomnia. Of the 170 patients included in the analysis, 26 (15%) met criteria for persistent insomnia syndrome post cancer treatment. The association of persistent insomnia with individual patient demographic, disease and treatment details is presented in table 2. A multiple logistic regression analysis examining demographic, clinical and treatment factors shows that the key parameters associated with insomnia syndrome after cancer treatment are pre-diagnosis sleep score and whether the patient receives chemotherapy. Patients who had no chemotherapy were much less likely to develop insomnia syndrome (3·3%, 3/91) compared to those receiving chemotherapy (29·1%, 23/79) (odds ratio=0·08, 95% ci 0·02-0·29, p<·001). A higher pre-diagnosis sleep score was associated with a higher chance of developing insomnia syndrome (odds ratio=1·13/unit increase in pre-diagnosis sleep score, 95% ci 1·05-1·21, p=·001). The chance of developing persistent insomnia in those with a pre-diagnosis ISI score $\geq$ 8 was 32·4% (11/34) compared to 11·0% (15/136) for those with lowers scores. In the 16 patients who received chemotherapy and had a pre-diagnosis ISI score $\geq$8, the persistent insomnia rate was 62·5%. When data on patients' worst symptoms over the first six months were entered into the regression, the worst recorded systemic therapy side effect and arm symptom scores completely replaced chemotherapy and pre-diagnosis sleep score in the model. Patients who had a high systemic therapy side effect score had a much higher chance of developing insomnia syndrome (odds ratio=1·04/unit increase in worst systemic therapy side effect score, 95% ci 1·01-1·07, p=·010), as did patients with high arm symptom scores (odds ratio=1·05/unit increase in worst arm symptom score, 95% ci

1·02-1·08, p<·001). Of the 47 patients who had worst arm symptom scores >33, 19 (40·4%) developed persistent insomnia compared to 4/103 (3·9%) with lower scores. Similarly, of the 76 patients who had worst systemic therapy side effect scores >33, 22 (28·9%) developed persistent insomnia compared to 1/74 (1·4%) with lower scores. In the 37 patients who had both these symptom scores >33, the persistent insomnia rate was 51·4% (19/37).

DISCUSSION

Breast cancer patients frequently report disturbed sleep during diagnosis/treatment, and persistently after discharge from anti-cancer therapy. However, the evolution of insomnia over time is not well established in this population. Therefore, this study explored the naturally occurring trajectory of insomnia, in a sample of newly diagnosed breast cancer patients, over a 12-month period. Monthly data on insomnia incidence, persistence, remission and relapse were examined and factors that contributed to these pathways were identified.

The point prevalence of insomnia at pre-diagnosis was 25%, comprising 8% with IS and 17% with ISym. This prevalence increased at diagnosis to 46% (18% IS and 28% ISym) and remained relatively stable thereafter at around 50% (21% IS and 30% ISym). This elevated prevalence of IS throughout the 12-month study period is considerably greater than the prevalence reported by the general population (8%-10%).[11,12] Also, the stability of insomnia over time challenges Savard's (2011) findings, where prevalence significantly decreased throughout the cancer trajectory. 77% of those who were good sleepers prior to cancer developed insomnia at some point during the 12-month assessment period. In addition, most patients who met criteria for IS retained that status throughout the 12-month period, which is contrary to findings reported in population based samples.[13,14] Our data suggest that cancer is

a precipitating factor for insomnia and once insomnia develops, it remains persistent over time.

In terms of predicting those most at risk of developing persistent insomnia syndrome, analyses identified two main factors; chemotherapy and pre-diagnosis ISI score. Patients who received chemotherapy were much more likely to develop persistent insomnia syndrome post-cancer treatment, than those who did not receive chemotherapy. This is an important finding because, to the best of our knowledge, no longitudinal studies have demonstrated the predictive value of chemotherapy on insomnia syndrome after the completion of active cancer treatment. Studies that have explored the relationship between chemotherapy and sleep have demonstrated that chemotherapy is associated with increased insomnia symptoms during the delivery of chemotherapy treatment and report a deleterious effect of chemotherapy on insomnia symptoms over time.[15-19] Similarly, and unsurprisingly, poorer pre-diagnosis sleep was associated with a greater chance of developing persistent insomnia syndrome post-cancer treatment. However, when treatment side-effects and breast-specific symptoms were explored, these superseded chemotherapy and pre-diagnosis ISI score as best predictors of persistent insomnia syndrome, post-cancer treatment. Patients who had high systemic therapy side-effect scores and high arm symptom scores, had a much higher chance of developing IS than those who did not.

These data are helpful in identifying patients most likely to experience sleep disturbance, whilst minimizing confounding factors related to mixed cancer sites and diverse treatment regimens. However, although focusing on the evolution of insomnia in breast cancer specifically permits clearer within-groups comparisons, variation does still exist in terms of disease characteristics, treatment regimens and follow-up/after-care support. This diversity may explain why symptom management strategies within oncology services are often

piecemeal and unsystematic. It may also explain the well documented absence of effective sleep management programs for cancer patients, despite the considerable evidence supporting cognitive behavioral therapy (CBT) as a first-line treatment for insomnia associated with cancer.[20–23] This absence may be explained by a lack of appreciation for the extent to which episodes of insomnia will persist or remit over time. Therefore, the importance of assessing insomnia evolution in cancer patients is clear. Insomnia is a well-known risk factor for impaired function and for development of other medical and mental disorders, resulting in increased health care utilization.[24] Given the increasing number of breast cancer survivors (currently 22% of all cancer survivors) who are likely to have comorbid symptoms (including insomnia), there is considerable burden on healthcare providers to implement symptom management strategies to cope with these increasing demands. Data that facilitate the improved understanding of insomnia evolution over time will undoubtedly lead to more tailored and accessible insomnia treatment.

Strengths of this study include the recruitment of a clinical sample of breast cancer patients directly from oncology clinics, utilizing very few exclusion criteria. This emphasizes the generalizability of study outcomes. We conducted monthly sleep assessments, providing a very clear picture of sleep status variability during active cancer treatment and post-treatment rehabilitation phases. Despite this rigorous data collection protocol, retention rate was very high throughout the study. However, several limitations exist in the study. First, we recruited only females with breast cancer. Therefore it is unclear whether our findings would extend to patients with other cancer types. A second limitation of the study is the absence of a diagnostic interview/questionnaire for assessing insomnia. Sleep status categories were determined by ISI data and sleep medication use. However, we acknowledge that utilising DSM-V criteria to make this assessment would have enhanced the validity of the study. The

relatively high refusal rate also limits the external validity of the study. This is mainly due to the number of eligible patients (n = 178) who declined to participate. Reasons given for non-participation varied, with the largest number (n=69) giving no reason. Most commonly, patients said they felt too unwell (n=41) had too much going on (n=34) or didn't want to commit to a 1-year assessment protocol (n=27). Therefore it is possible that our sample represents those patients who are comparably high-functioning.

This work is of significant clinical importance. In our experience, cancer patients with sleep difficulties value those difficulties being appropriately addressed. Evidence suggests that improving sleep enhances engagement with cancer treatment and contributes to a reduction in co-morbid mental health complaints.[25] Currently, the psychological care of cancer patients during cancer treatment and rehabilitation fails to include appropriate sleep management strategies. This study emphasizes the importance of reconsidering the priority given to sleep within cancer care.

DISCLOSURE STATEMENT

The authors gratefully acknowledge funding support from Breast Cancer Now (Ref. 2010MayPR07).

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Figure Captions

Figure 1 – Participant demographic, disease and treatment details

Figure 2 - Prevalence of Insomnia by Assessment Time-Point

Figure 3 - Sleep Status Transitions

Table 1 – Patient demographic, disease and treatment details

		First major assessment point completed (month of entry)					
		0 (n=80)		3 (n=93)		Total (n=173)	
		Column N %	Count	Column N %	Count	Column N %	Count
Employment Status at recruitment (p=.558)	Employed	18.8%	15	20.4%	19	19.7%	34
	Unemployed	3.8%	3	7.5%	7	5.8%	10
	Sick leave	33.8%	27	38.7%	36	36.4%	63
	Retired	40.0%	32	32.3%	30	35.8%	62
	Missing	*3.8%*	*3*	*1.1%*	*1*	*2.3%*	*4*
Marital status (p=.752)	Married	46.3%	37	59.1%	55	53.2%	92
	Single	12.5%	10	14.0%	13	13.3%	23
	Divorced	13.8%	11	8.6%	8	11.0%	19
	Widowed	13.8%	11	10.8%	10	12.1%	21
	Living with partner	5.0%	4	4.3%	4	4.6%	8
	Separated	2.5%	2	2.2%	2	2.3%	4
	Missing	*6.3%*	*5*	*1.1%*	*1*	*3.5%*	*6*
Menopausal Status (p=.293)	Pre-menopause	23.8%	19	22.6%	21	23.1%	40
	Peri-menopause	3.8%	3	9.7%	9	6.9%	12
	Post-menopause	53.8%	43	47.3%	44	50.3%	87
	Missing	*18.8%*	*15*	*20.4%*	*19*	*19.7%*	*34*
Ductal carcinoma in situ (p=1.00)	No	90.0%	72	89.2%	83	89.6%	155
	Yes	10.0%	8	10.8%	10	10.4%	18
Neoadjuvant treatment (p=.081)	No	83.8%	67	93.5%	87	89.0%	154
	Yes	15.0%	12	6.5%	6	10.4%	18
Overall stage of disease (p=.059)	I	47.5%	38	30.1%	28	38.2%	66
	II	20.0%	16	31.2%	29	26.0%	45
	III	20.0%	16	18.3%	17	19.1%	33
	IV	2.5%	2	9.7%	9	6.4%	11
	DCIS	10.0%	8	10.8%	10	10.4%	18
T-stage (p=.028)	T1	58.8%	47	39.8%	37	48.6%	84
	T2	27.5%	22	44.1%	41	36.4%	63
	T3	1.3%	1	5.4%	5	3.5%	6
	T4	1.3%	1	.0%	0	.6%	1
	DCIS	10.0%	8	10.8%	10	10.4%	18
	Missing	*1.3%*	*1*	*.0%*	*0*	*.6%*	*1*
Nodes staging (p=.808)	N0	68.8%	55	63.4%	59	65.9%	114
	N1	5.0%	4	7.5%	7	6.4%	11
	N2	.0%	0	1.1%	1	.6%	1

	N3	1.3%	1	2.2%	2	1.7%	3
	Missing	*25.0%*	*20*	*25.8%*	*24*	*25.4%*	*44*
Metastatic staging (p=.498)	M0	95.0%	76	88.2%	82	91.3%	158
	M1	.0%	0	2.2%	2	1.2%	2
	Missing	*5.0%*	*4*	*9.7%*	*9*	*7.5%*	*13*
Oestrogen receptors (p=1.000)	Negative	10.0%	8	8.6%	8	9.2%	16
	Positive	86.3%	69	79.6%	74	82.7%	143
	Missing	*3.8%*	*3*	*11.8%*	*11*	*8.1%*	*14*
Progesterone receptors (p=.372)	Negative	22.5%	18	26.9%	25	24.9%	43
	Positive	73.8%	59	60.2%	56	66.5%	115
	Missing	*3.8%*	*3*	*12.9%*	*12*	*8.7%*	*15*
HER receptors (p=.612)	Negative	88.8%	71	78.5%	73	83.2%	144
	Positive	8.8%	7	10.8%	10	9.8%	17
	Missing	*2.5%*	*2*	*10.8%*	*10*	*6.9%*	*12*
Surgery type (p=.327)	Wide Local Excision	8.8%	7	3.2%	3	5.8%	10
	Mastectomy	25.0%	20	28.0%	26	26.6%	46
	Quadrantectomy	.0%	0	.0%	0	.0%	0
	No surgery	.0%	0	.0%	0	.0%	0
	Lumpectomy	62.5%	50	61.3%	57	61.8%	107
	Other	3.8%	3	7.5%	7	5.8%	10
Reconstructive surgery (p=.320)	No	92.5%	74	87.1%	81	89.6%	155
	Yes	7.5%	6	12.9%	12	10.4%	18
Chemotherapy Treatment (p=.284)	No	58.8%	47	49.5%	46	53.8%	93
	Yes	41.3%	33	50.5%	47	46.2%	80
Radiotherapy treatment (p=.228)	No	3.8%	3	8.6%	8	6.4%	11
	Yes	96.3%	77	91.4%	85	93.6%	162
Hormonal treatment (p=153)	No	7.5%	6	15.1%	14	11.6%	20
	Yes	88.8%	71	80.6%	75	84.4%	146
	Missing	*3.8%*	*3*	*4.3%*	*4*	*4.0%*	*7*

Table 2 – Association of patient demographic, disease and treatment details with the presence of persistent insomnia syndrome post cancer treatment

		Insomnia syndrome?				P-value
		No (N=144)		Yes (N=26)		
		Row N %	Count	Row N %	Count	
First major assessment point completed (month of entry)	0	85.7%	66	14.3%	11	.832
	3	83.9%	78	16.1%	15	
Marital status	Married	86.8%	79	13.2%	12	.269
	Single	86.4%	19	13.6%	3	
	Divorced	77.8%	14	22.2%	4	
	Widowed	76.2%	16	23.8%	5	
	Living with partner	87.5%	7	12.5%	1	
	Separated	75.0%	3	25.0%	1	
	Missing	*100.0%*	*6*	*.0%*	*0*	
Employment Status at recruitment	Employed	94.1%	32	5.9%	2	<.001
	Unemployed	60.0%	6	40.0%	4	
	Sick leave	72.1%	44	27.9%	17	
	Retired	95.1%	58	4.9%	3	
	Missing	*100.0%*	*4*	*.0%*	*0*	
Menopausal Status	Pre-menopause	75.0%	30	25.0%	10	.036
	Peri-menopause	72.7%	8	27.3%	3	
	Post-menopause	90.6%	77	9.4%	8	
	Missing	*85.3%*	*29*	*14.7%*	*5*	
Ductal carcinoma in situ	No	85.5%	130	14.5%	22	.485
	Yes	77.8%	14	22.2%	4	
Neoadjuvant treatment	No	87.4%	132	12.6%	19	.009
	Yes	61.1%	11	38.9%	7	
	Missing	*100.0%*	*1*	*.0%*	*0*	
Overall stage of disease	I	93.7%	59	6.3%	4	.136
	II	82.2%	37	17.8%	8	
	III	78.8%	26	21.2%	7	
	IV	72.7%	8	27.3%	3	
	DCIS	77.8%	14	22.2%	4	
T- stage	T1	88.9%	72	11.1%	9	.215
	T2	82.5%	52	17.5%	11	
	T3	83.3%	5	16.7%	1	
	T4	100.0%	1	.0%	0	
	DCIS	77.8%	14	22.2%	4	
	Missing	*.0%*	*0*	*100.0%*	*1*	
N-stage	N0	91.9%	102	8.1%	9	.157
	N1	72.7%	8	27.3%	3	
	N2	100.0%	1	.0%	0	
	N3	66.7%	2	33.3%	1	
	N4	.0%	0	.0%	0	
	Missing	*70.5%*	*31*	*29.5%*	*13*	
Metastatic staging	M0	86.5%	134	13.5%	21	.261
	M1	50.0%	1	50.0%	1	
	Missing	*69.2%*	*9*	*30.8%*	*4*	
Oestrogen receptors	Negative	81.3%	13	18.8%	3	1.000
	Positive	84.3%	118	15.7%	22	
	Missing	*92.9%*	*13*	*7.1%*	*1*	
Progesterone receptors	Negative	81.4%	35	18.6%	8	.629
	Positive	84.8%	95	15.2%	17	
	Missing	*93.3%*	*14*	*6.7%*	*1*	
HER receptors	Negative	83.0%	117	17.0%	24	.314
	Positive	94.1%	16	5.9%	1	
	Missing	*91.7%*	*11*	*8.3%*	*1*	
Surgery type	Wide Local Excision	90.0%	9	10.0%	1	.014 (p=.001, Mastectomy v Rest)
	Mastectomy	69.6%	32	30.4%	14	
	lumpectomy	90.4%	94	9.6%	10	
	other	90.0%	9	10.0%	1	
Reconstructive surgery	No	85.5%	130	14.5%	22	.485
	Yes	77.8%	14	22.2%	4	
Chemotherapy treatment	No	96.7%	88	3.3%	3	<.001
	Yes	70.9%	56	29.1%	23	
Radiotherapy treatment	No	80.0%	8	20.0%	2	1.000
	Yes	85.0%	136	15.0%	24	
Hormonal treatment	No	85.0%	17	15.0%	3	1.000
	Yes	83.9%	120	16.1%	23	
	Missing	*100.0%*	*7*	*.0%*	*0*	
Age	Mean (sd, N)	59 (9,144)		52 (9, 26)		.003
Prediagnosis ISI score	Mean (sd, N)	3.38 (4.65, 144)		8.15 (8.60. 26)		.006

EORTC* Fatigue score	Mean (sd, N)	42.6 (27.7, 128)	76.3 (23.0, 23)	<.001
EORTC Nausea/Vomiting score	Mean (sd, N)	14.1 (22.6, 128)	29.7 (20.1, 23)	<.001
EORTC Pain score	Mean (sd, N)	27.3 (27.8, 128)	68.1 (27.0, 23)	<.001
EORTC Dysnoea score	Mean (sd, N)	23.4 (28.2, 128)	49.3 (33.1, 23)	<.001
EORTC Insomnia score	Mean (sd, N)	48.2 (31.5, 128)	88.4 (23.8, 23)	<.001
EORTC Appetite loss score	Mean (sd, N)	24.7 (31.9, 128)	43.5 (34.0,23)	.005
EORTC Breast symptoms score	Mean (sd, N)	29.3 (19.9, 127)	51.1 (24.3, 23)	<.001
EORTC Constipation score	Mean (sd, N)	27.3 (31.1, 128)	53.6 (31.4, 23)	<.001
EORTC Body image score	Mean (sd, N)	71.1 (28.4, 127)	38.8 (29.8, 23)	<.001
EORTC Diarrhoea score	Mean (sd, N)	14.3 (23.9, 128)	34.8 (32.5, 23)	.001
EORTC Arm symptoms score	Mean (sd, N)	17.1 (18.8, 127)	54.6 (25.9, 23)	<.001
EORTC Systemic therapy side effects score	Mean (sd, N)	31.2 (21.8, 127)	60.5 (18.9, 23)	<.001
EORTC Upset by hair loss score	Mean (sd, N)	24.5 (35.2, 127)	62.3 (40.6, 23)	<.001

* All EORTC scores range from 0-100 with 0 being “best” and 100 being “worst”, except for Body image where the direction is reversed.

Figure 1

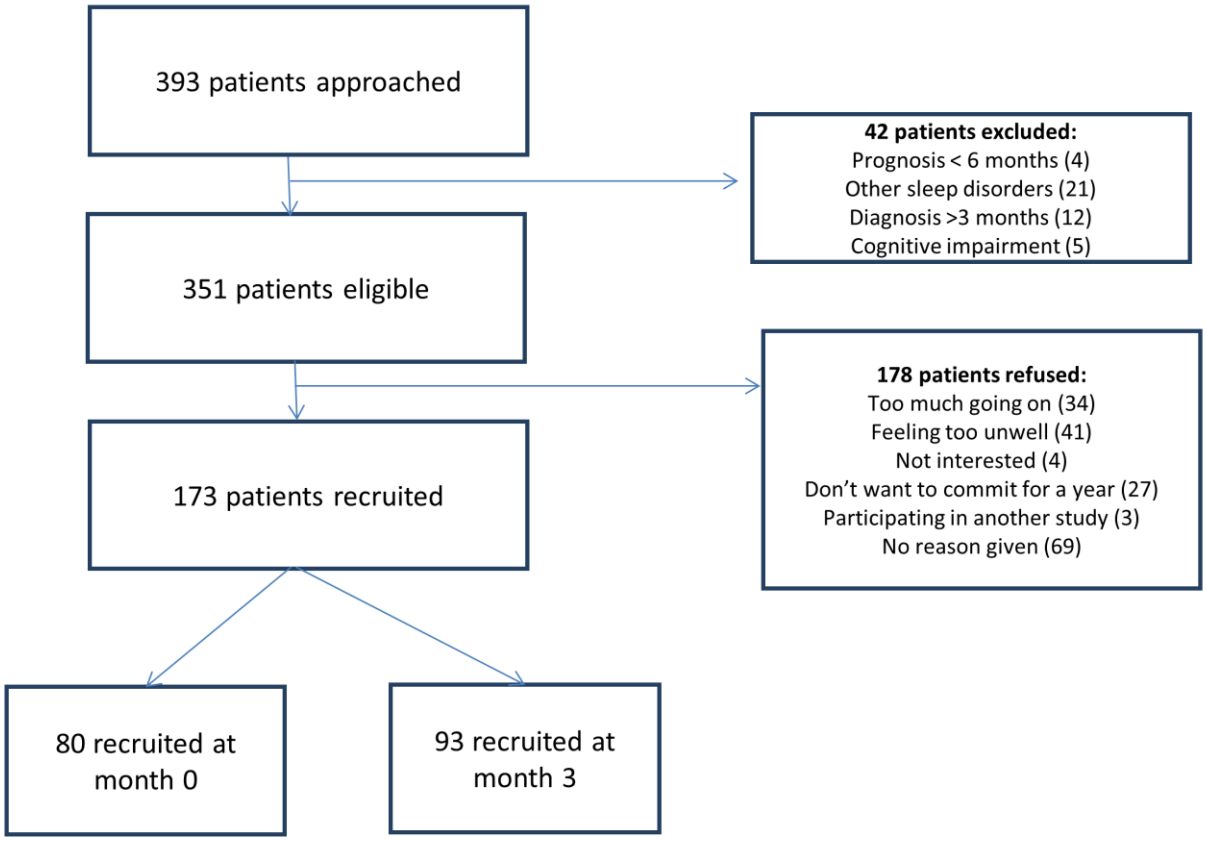

Figure 2

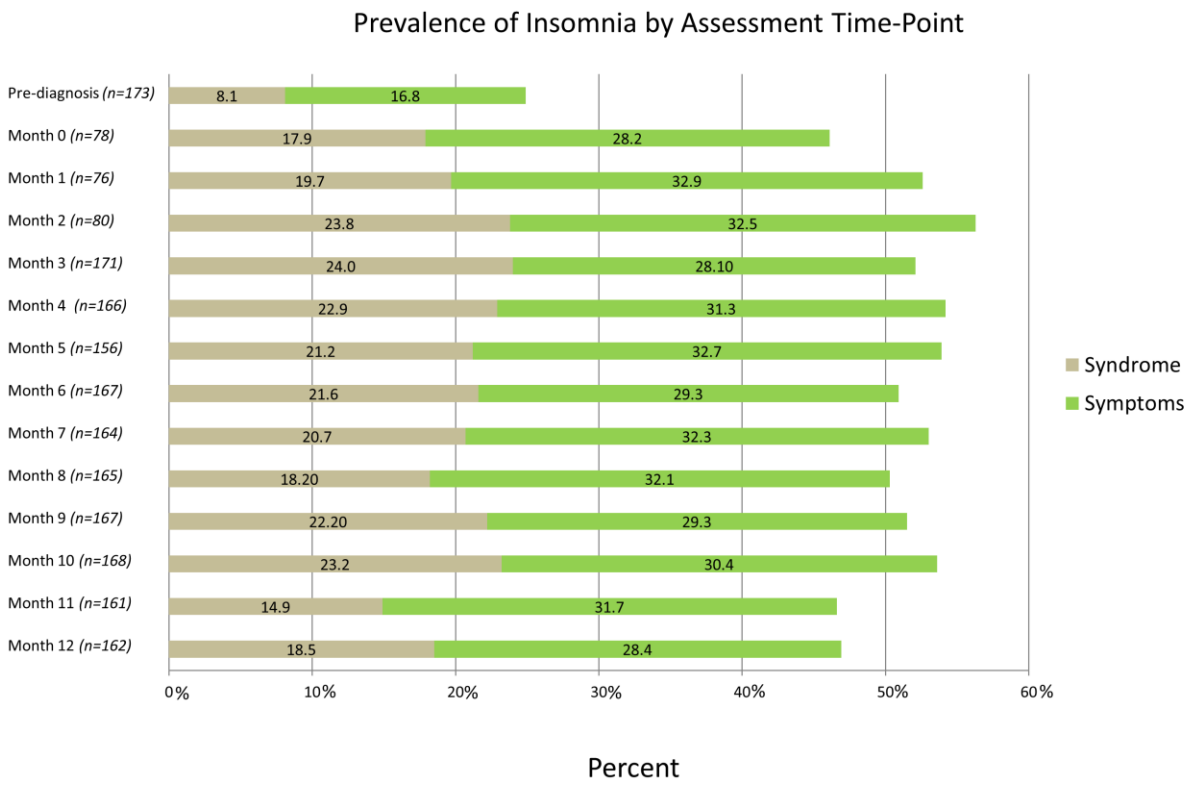

Figure 3