Psycho-Oncology
Psycho-Oncology **23**: 679–684 (2014)
Published online 23 January 2014 in Wiley Online Library (wileyonlinelibrary.com). **DOI**: 10.1002/pon.3468

Does cognitive behaviour therapy for insomnia reduce clinical levels of fatigue, anxiety and depression in cancer patients?

Leanne Fleming[1]*, Kate Randell[1], Christopher-James Harvey[2] and Colin A. Espie[3]
[1]*Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK*
[2]*Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford, UK*
[3]*Sleep and Circadian Neuroscience Institute, Nuffield Department of Clinical Neuroscience, University of Oxford, Oxford, UK*

**Correspondence to: Mental Health and Wellbeing, Gartnavel Royal Hospital, University of Glasgow, 1055 Great Western Road, Glasgow, UK, G12 0XH. E-mail: leanne.fleming@glasgow.ac.uk*

Received: 15 March 2013
Revised: 27 November 2013
Accepted: 1 December 2013

Abstract

***Objectives*: This secondary analysis of data from a randomised controlled trial explores associations between common symptom clusters and evaluates pre-treatment to post-treatment changes in clinical levels of these symptoms following cognitive behaviour therapy for insomnia (CBT-I).**

***Methods*: Baseline data from 113 participants with insomnia were explored to establish rates of and associations between clinical levels of fatigue, anxiety and depression across the sample. Effects of CBT-I on this symptom cluster were also explored by examining changes in pre-treatment to post-treatment levels of fatigue, anxiety and depression.**

***Results*: At baseline, the most common symptom presentation was insomnia + fatigue, and 30% of the sample reported at least three co-morbid symptoms. Post-CBT, the number of those experiencing clinical insomnia and clinical fatigue decreased. There were no changes in anxiety rates from baseline to post-treatment in the CBT group and modest reductions in rates of those with clinical depression. Seven individuals (9.6%) from the CBT group were completely symptom free at post-treatment compared with 0% from the treatment as usual condition. Chi-square analysis revealed a significant relationship between group allocation and changes in symptoms of insomnia and fatigue. No such relationship was found between group allocation and mood variables.**

***Conclusions*: These findings confirm the high rate of symptom co-morbidities among cancer patients and highlight strong associations between sleep and fatigue. CBT-I appears to offer generalised benefit to the symptom cluster as a whole and, specifically, is effective in reducing fatigue, which exceeded clinical cut-offs prior to implementation of the intervention. This has implications for the diagnosis/management of common symptoms in cancer patients.**

Introduction

Disturbed sleep is a common and distressing problem affecting more than one-third of cancer patients both during and after completion of active treatment [1,2]. Despite its prevalence, insomnia is frequently rationalised as a transient side effect of diagnosis-related stress or cancer treatment [3–5]. Incidence data show, however, that more than one-quarter of cancer patients with sleep disturbance experience chronic insomnia, which fails to remit even when active cancer treatment has ceased [4].

Sleep disturbance is often associated with other symptoms such as fatigue, anxiety and depression [5–9]. Portenoy *et al*. demonstrated that this cluster was highly prevalent (40–80%) across different tumour types [10], and recent work by Liu *et al*. found that the presence of pre-treatment symptom clusters in breast cancer patients was associated with poorer sleep, increased fatigue and lower mood during active treatment [11]. Therefore, each symptom seems to maintain and exacerbate the others, resulting in further impairment to quality of life.

Such interrelationships have also been studied in the general population. For example, psychiatric epidemiology indicates that insomnia is an independent risk factor for the development of first-episode depressive disorder in adults of all ages [12]. Similarly, people with cancer and insomnia report decreased functioning, more pain and higher levels of fatigue than those sleeping well [13,14]. Sharma *et al*. [15] found that nearly a third of patients attending a regional cancer centre reported sleep problems of clinical significance that were strongly associated with symptoms of emotional distress. The nature of these associations requires further study.

Implementing a programme of cognitive behaviour therapy for insomnia (CBT-I) in cancer patients yields generalised improvements in other symptoms including fatigue, quality of life and daytime functioning [16,17], suggesting that these symptoms share common pathways [8,18,19].

The aims of this paper are as follows: (i) to report on the rates of and associations between co-morbid clinical symptoms of insomnia, fatigue, anxiety and depression in a sample of cancer patients; (ii) to investigate potential generalised effects on these symptoms following CBT-I; and (iii) to assess the clinical significance of any such improvement.

Methods

Experimental design

This is a secondary analysis of data from 113 patients, derived from a randomised controlled clinical effectiveness trial of CBT-I versus treatment as usual (TAU) for insomnia in cancer patients [16]. CBT comprised five, small group sessions across consecutive weeks, following a manualised protocol. TAU represented normal clinical practice, the appropriate control for a clinical effectiveness study. The trial conformed to a pragmatic, two-centre design comparing CBT-I with TAU. Major assessments were at baseline, post-treatment and follow-up 6 months later (6-month assessment is not reported because of missing data). Suitable participants were randomly allocated to either CBT-I or TAU by means of a centralised computer-based registration/randomisation service available within the Cancer Research UK Clinical Trials Unit, Glasgow. The study was stratified for centre, existing treatment for insomnia and tumour type using the minimisation method. A 2:1 treatment allocation, in favour of the intervention, was selected because this would make more efficient use of available CBT-I sessions and would minimise the time a patient had to wait before being able to start a CBT-I course, thereby reducing patient dropout. Because of the nature of the intervention, it was not possible to blind participants or therapists to allocation. No adverse events were reported with either CBT-I or TAU. Full details of the CBT therapists, integrity–fidelity of treatment allocation and attrition rates can be found in Espie *et al.* [16].

Recruitment of participants

Participants (18 years and older) were attending follow-up oncology clinics at either the Glasgow Beatson Oncology Centre (BOC) or the Aberdeen Royal Infirmary (ARI). Included participants had been diagnosed with breast, prostate, bowel or gynaecological cancer and had satisfied the diagnostic criteria for chronic insomnia, defined as mean value >30 min for the complaint of delayed sleep-onset latency and/or wake time after sleep onset, insomnia occurring three or more nights per week for at least 3 months and affecting daytime function [20,21]. Participants had also scored 5 or more on the Pittsburgh Sleep Quality Index [22,23], a psychometrically robust instrument that identifies clinically significant sleep disturbance. Thus, acute insomnia and transient side effects associated with cancer treatment were excluded. Participants had completed anticancer therapy (radiotherapy/chemotherapy) by ≥1 month and had no further anticancer therapy planned (excepting adjuvant hormone therapy for breast and prostate cancer patients). Participants were excluded if they had acute illness, estimated prognosis <6 months, another sleep disorder, confusional problems or untreated and unstable psychiatric disorder (screening procedures did not identify anyone with untreated/unstable psychiatric disorder; therefore, no one was excluded on the basis of their psychiatric history).

Potential participants were notified of the study by posters/leaflets in clinic waiting areas, by mailing information to those attending upcoming clinics or directly by staff upon attendance at clinics. All participants provided written informed consent, and their medical consultant agreed to their participation. The protocol was approved by local National Health Service research ethics committees.

Measures

We conducted a secondary analysis of sleep-onset latency and wake time after sleep onset, anxiety and depression, and fatigue (severity and interference), using a 10-day sleep diary [24], the Hospital Anxiety and Depression Scale (HADS) [25] and the Fatigue Symptom Inventory (FSI) [26].

Sleep diaries are the staple tool of insomnia assessment practice and offer a valid, relative index of sleep disturbance when used as repeated measures [27]. Participants were trained to complete sleep diaries using the established criteria for accurate completion [28]. The HADS has been validated for use in cancer patients to screen for anxiety and depressive symptoms [29,30]. It is a particularly useful measure for assessing mood in sleep research, as unlike many other anxiety/depression questionnaires, the HADS does not contain a sleep-specific item. The FSI is also recommended for use with cancer patients, as a brief measure with good validity and internal consistency [26,31]. Median values for these scales (and subscales) are presented in Table 1.

In order to understand polysymptomatic associations between insomnia and clinical-level symptoms of fatigue, anxiety and depression, baseline data were reanalysed to isolate only those participants scoring beyond recognised clinical cut-offs for insomnia and at least one other domain. Therefore, 'anxiety' refers to HADS anxiety scores of ≥11 [29,30], 'depression' refers to HADS depression scores of ≥11 [29,30] and 'fatigue' refers to FSI fatigue severity and/or interference scores of ≥3 [31,32]. Applying these criteria[1] to the data meant that 37 participants, who were included in the analyses for the original trial, were excluded from this secondary analysis. This means that the proportions presented in the

DOI: 10.1002/pon

Table 1. Baseline demographic and clinical information on the sample

	CBT group ($n = 73$)	TAU group ($n = 40$)
Age (years)	63 (55–69)	58 (54–66)
Gender		
Male	23 (32%)	12 (30%)
Female	50 (68%)	28 (70%)
Civil status		
Married	51 (70%)	27 (68%)
Single	8 (11%)	7 (17%)
Separated	1 (1%)	0
Divorced	7 (10%)	4 (10%)
Widowed	6 (8%)	2 (5%)
Employment status		
Employed	27 (37%)	18 (45%)
Unemployed	2 (3%)	1 (2%)
Retired	44 (60%)	21 (53%)
Tumour site		
Breast	46 (63%)	22 (55%)
Prostate	18 (25%)	9 (23%)
Bowel	8 (11%)	8 (20%)
Gynaecological	1 (1%)	1 (2%)
Cancer diagnosis—screening (months)	22 (9–52)	25 (10–68)
Current treatment for depression		
Yes	10 (14%)	7 (17%)
No	63 (86%)	33 (83%)
Insomnia duration (months)	30 (12–60)	27 (10–60)
Insomnia pattern		
Constant	49 (67%)	25 (63%)
Episodic	24 (33%)	15 (37%)
Sleep medication		
Yes	18 (25%)	6 (15%)
No	55 (75%)	34 (85%)
PSQI	13 (11–16)	13 (11–15)
Sleep		
SOL (min)	41 (20–59)	27 (23–50)
WASO (min)	69 (47–118)	47 (30–81)
Fatigue		
Severity	5 (4–6)	5 (4–6)
Interference	4 (2–5)	4 (2–5)
Anxiety	7 (4–10)	8 (5–10)
Depression	4 (2–8)	5 (2–7)

Data are categorical or median (IR). There are no between-group differences.
CBT, cognitive behaviour therapy; TAU, treatment as usual; SOL, sleep-onset latency; WASO, wake time after sleep onset; PSQI, Pittsburgh Sleep Quality Index.

Results section relate only to patients who presented with co-morbidity at baseline.

Statistical methods

The randomised control trial was designed to have 80% power to detect a standardised difference of 0.5 between the treatments in the primary sleep outcome measures at post-treatment. A significance level of 0.0125 was chosen to adjust for multiple comparisons. These criteria implied recruiting 204 participants. In practice, slow recruitment meant that a total of 150 patients were randomly assigned, giving 80% power to detect a slightly larger standardised difference of 0.59.

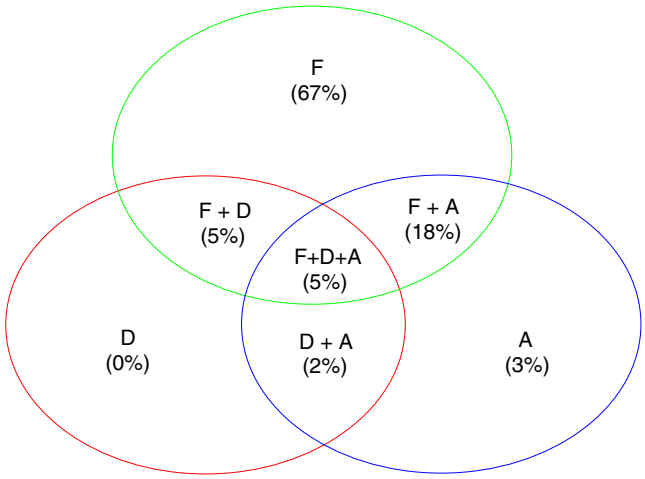

Figure 1. Venn diagram representing baseline associations between fatigue (F), anxiety (A) and depression (D) scores across the sample ($N = 113$). All participants met the criteria for insomnia

Results

Descriptive analysis of baseline data across the entire sample ($N = 113$) showed that alongside clinical levels of insomnia, 76 participants (67%) also reported levels of fatigue that reached or exceeded clinical cut-offs. This was the most common symptom profile. The next most common presentation was 'insomnia + fatigue + anxiety', reported by 20 individuals (18% of the total sample). Six participants (5%) scored above clinical cut-offs for all symptoms, and 'insomnia + fatigue + depression' also accounted for 5% of the sample. The least common symptom presentations were 'insomnia + anxiety' (three participants), 'insomnia + anxiety + depression' (two participants) and 'insomnia + depression', accounting for 3%, 2% and 0% of the sample, respectively (Figure 1).

In order to explore whether CBT had any effect on the presence or absence of clinical-level symptoms between baseline and post-treatment, the percentage of individuals who met clinical cut-offs for each symptom was calculated. The number of people experiencing clinical-level insomnia at post-treatment was reduced by 52% in the CBT group, compared with a 17.5% reduction in the TAU group. The rate of clinical levels of fatigue was extremely high across both treatment arms at baseline (90.4% CBT and 90% TAU). However, CBT-I resulted in a 10.9% reduction in rates of fatigue compared with a 2.5% increase at post-treatment in the TAU group. There was no change in the anxiety rates from baseline to post-treatment in the CBT group and a 5% increase in those with anxiety at post-treatment in the TAU group. The majority of participants were not depressed at baseline (90.4% CBT and 92.5% TAU), and CBT reduced the rate of those with clinical levels of depression by 5.5% compared with an increase of 5% in TAU. Importantly, seven individuals (9.6%) from the CBT group were completely symptom free at

DOI: 10.1002/pon

post-treatment (compared with 0% in the TAU group). Further inspection of baseline data from this 'symptom-free' group shows that all seven individuals had both clinical-level insomnia and clinical-level fatigue. No one had clinical-level anxiety, but one person had clinical-level depression. Although this group is small, the pattern of symptom change indicates that CBT may be of some benefit when treating clinical-level insomnia and clinical-level fatigue (Table 2).

Change data (baseline to post-treatment) were calculated for each of the four variables of interest, in order to compare differences in symptom trajectories (symptom remission versus maintenance of baseline presentation) between treatment arms. In this case, 'symptom remission' refers to the presence of a symptom exceeding clinical cut-offs at baseline that is then below this cut-off at post-treatment. 'Maintenance' refers to either a symptom exceeding clinical cut-offs at baseline that is still beyond this cut-off at post-treatment or a symptom below clinical cut-offs at baseline that is still below this cut-off at post-treatment.

Insomnia

At post-treatment, 52% of the CBT group showed insomnia remission, compared with only 17.5% of the TAU group. Chi-square analyses were conducted to test the significance of this 'symptom trajectory × group allocation' relationship. Results show that there was a significant association between treatment group allocation and post-treatment change in insomnia symptoms [$\chi^2(1,\ N=113)=12.875,\ p<0.001$].

Fatigue

A total of 17.4% of the CBT group showed fatigue remission at post-treatment, compared with 2.6% of the TAU group. Fatigue symptoms were maintained in 82.6% of the CBT group and 97.4% of the TAU group. Chi-square analysis confirms a significant association between treatment group allocation and post-treatment change in fatigue [$\chi^2(1,\ N=107)=5.002,\ p=0.03$] (using Fisher's exact test).

Table 2. Group allocation × symptom present or absent at BL and PT

	CBT (BL)(%)	CBT (PT)(%)	TAU (BL)(%)	TAU (PT)(%)
Insomnia				
Absent	0	52	0	17.5
Present	100	48	100	82.5
Fatigue				
Absent	9.6	20.5	10	7.5
Present	90.4	79.5	90	92.5
Anxiety				
Absent	79.5	79.5	77.5	72.5
Present	20.5	20.5	22.5	27.5
Depression				
Absent	90.4	95.9	92.5	87.5
Present	9.6	4.1	7.5	12.5
Symptom free	0	9.6	0	0

BL, baseline; PT, post-treatment; CBT, cognitive behaviour therapy; TAU, treatment as usual.

Anxiety

Anxiety remission at post-treatment was noted in 5.8% (CBT) and 5.6% (TAU) of the cases, respectively. The majority of both groups maintained their baseline anxiety scores at post-treatment (94.2% CBT and 94.4% TAU). No significant associations were found between treatment allocation and anxiety symptom change [$\chi^2(1,\ N=105)=0.003$, $p=1.00$] (using Fisher's exact test).

Depression

About 8.5% of the CBT group showed depression remission at post-treatment, compared with 0% of the TAU group. As with anxiety, the majority of those in the CBT group (91.5%) maintained their baseline depression scores at post-treatment (compared with 100% of the TAU group). No significant associations were found between treatment allocation and depression symptom change [$\chi^2(1, N=109)=3.398, p=0.09$] (using Fisher's exact test).

Overall, we can conclude that there is a significant relationship between group allocation (i.e. CBT or TAU) and changes in clinical levels of insomnia and fatigue. No such relationship was found between group allocation and mood variables.

Worsening of symptoms

Whilst calculating change score data from the CBT group, we discovered that in a small number of cases, symptoms seemed to worsen at post-treatment (characterised by post-treatment data exceeding clinical levels when baseline data had not). Given that this finding was not isolated to the TAU group, we decided to analyse data from these individuals separately. Given that all participants had baseline insomnia scores that exceeded clinical cut-offs, it was not possible for insomnia to worsen at post-treatment (according to our criteria). Also, it is not surprising that insomnia-related symptoms would worsen in the TAU group over time. Therefore, only those people with worsening symptoms of fatigue, anxiety and depression following CBT are examined. Of the eight people, four reported worsening fatigue, two reported worsening anxiety and two reported worsening anxiety + depression.

Discussion

All participants in our original trial of CBT versus TAU met the criteria for clinical insomnia [16]. However, less than a quarter of them ($n=37$) were troubled by sleep problems alone, with the majority ($N=113$) experiencing other co-morbid symptoms such as fatigue, anxiety and

DOI: 10.1002/pon

depression. Further analysis of this symptom cluster revealed that clinical fatigue was the most common co-morbid symptom, experienced by the majority of participants at baseline. Almost a third of participants in this study presented with three or more coexisting symptoms that exceeded clinical cut-offs. These findings are consistent with previous evidence of the high prevalence of symptom clusters in cancer patients [5–9].

At baseline, anxiety was more prevalent than depression across both groups, although the number of participants experiencing clinical levels of either symptom was small. Findings from a large prospective study examining symptoms in early breast cancer patients over 5 years also reported higher levels of clinically significant anxiety than depression (14.4% vs. 3.1%) [29,30]. Our data indicate a relatively small association between clinical insomnia and mood disturbance, which is in contrast to numerous studies reporting high rates of co-morbidity between insomnia and depression and insomnia and anxiety in cancer patients [8,9,11,15]. However, the current study applied strict clinical cut-offs for identifying those with depression and anxiety, which may explain this reduced prevalence. Low levels of clinically meaningful anxiety and depression in this sample may also be due to the time since diagnosis in our sample (median of approximately 2 years), as initially high levels of distress after diagnosis and during treatment would be expected to decrease over time. Insomnia is commonly viewed as an expected consequence of depression or anxiety, but this low insomnia–mood association indicates that the majority of participants (67%) in this study experienced chronic insomnia without any significant clinical mood disturbance. It is therefore important that mood and sleep symptoms are recognised as distinct disorders and measured and treated in their own right.

Our CBT-I intervention, delivered primarily to treat sleep disturbance, resulted in a significant reduction in insomnia prevalence at post-treatment compared with TAU. However, further exploration of the data reveals that treating insomnia with CBT offers additional benefits to the symptom cluster as a whole. Participants receiving CBT-I also experienced significant reductions in fatigue, and 10% of the CBT-I group no longer met the clinical criteria for any symptoms post-treatment. None of the participants in the TAU group were symptom free at post-treatment, indeed symptoms often worsened in this group at post-treatment assessment. This suggests that improvements in the CBT-I group did not occur simply as an artefact of natural symptom reduction over time but as a direct result of the intervention.

The most notable symptom reduction within the CBT-I group was for sleep and fatigue symptoms. The CBT-I treatment clearly improved sleep symptoms and had some effect on fatigue. It appears that participants were more able to manage their fatigue symptoms after receiving the intervention, reducing the impact of fatigue on their quality of life. Researchers have begun to investigate the interactional relationship between disturbed sleep and fatigue in cancer patients [5], and further exploration of the shared and individual mechanisms of these symptoms for this group would be beneficial. There is currently no accepted gold standard treatment for cancer-related fatigue, although psychological and exercise interventions have shown promise [33,34]. It would be useful to further explore the role of CBT interventions in the treatment of this sleep + fatigue symptom cluster.

Although these findings were derived from a relatively large sample of cancer patients, we cannot assume that our sample is representative of the cancer population as a whole. The majority of our patients were female, and breast/prostate cancer was the most common tumour type. It is therefore difficult to generalise these findings to patients with different tumour types, as it is possible that the prevalence of the symptom cluster may differ between cancer types. However, these results do provide further evidence of the development of and associations between common symptom clusters in this patient group and indicate the usefulness of CBT for reducing clinical levels of insomnia and fatigue in cancer patients.

Acknowledgements

The authors gratefully acknowledge funding support from the Cancer Research UK (ref. C8265/A3036) and the Dr Mortimer and Theresa Sackler Foundation.

Conflict of interest

The authors have declared no conflicts of interest.

Note

1. In order to enhance the validity of our results, we opted to use a cut-off of 11 on the HADS. We acknowledge that this potentially reduces the possibility of identifying clinical cases of depression and anxiety and therefore higher rates of co-morbidity. However, we feel that the integrity of our results is enhanced by applying more rigorous criteria to the diagnosis of clinical mood symptoms.

References

1. Munro AJ, Potter S. A quantitative approach to the distress caused by symptoms in patients treated with radical radiotherapy. *Br J Cancer* 1996;**74**:640–647.
2. Davidson JR, MacLean AW, Brundage MD, Schulze K. Sleep disturbance in cancer patients. *Social Sci Med* 2002;**54**:1309–1321.
3. Sateia MJ, Nowell PD. Insomnia. *The Lancet* 2004;**364**:1959–1973.
4. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. *J Clin Oncol* 2001;**19**:895–908.

5. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *Eur J Cancer Care* 2001;**10**:245–255.
6. Ancoli-Israel S, Liu L, Marler M, *et al*. Fatigue, sleep and circadian rhythms prior to chemotherapy for breast cancer. *Support Care Cancer* 2006;**14**:201–209.
7. Carpenter JS, Elam JL, Ridner SH, Carney PH, Cherry GJ, Cucullu HL. Sleep, fatigue and depressive symptoms in breast cancer survivors and matched healthy women experiencing hot flashes. *Oncol Nurs Forum* 2004;**31**:591–598.
8. Payne JK, Piper B, Rabinowitz I, Zimmerman B. Biomarkers, fatigue, sleep, and depressive symptoms in women with breast cancer: a pilot study. *Oncol Nurs Forum* 2006;**33**:775–783.
9. Reyes-Gibby CC, Aday LA, Anderson KO, Mendoza TR, Cleeland CS. Pain, depression and fatigue in community-dwelling adults with and without a history of cancer. *J Pain Symptom Manage* 2006;**32**:118–128.
10. Portenoy RK, Thaler HT, Kornblith AB, *et al*. Symptom prevalence, characteristics and distress in a cancer population. *Qual Life Res* 1994;**3**:183–189.
11. Liu L, Fiorentino L, Natarajan L, *et al*. Pretreatment symptom cluster in breast cancer patients is associated with worse sleep, fatigue and depression during chemotherapy. *Psycho-Oncology* 2008;**18**(2):187–94.
12. Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? *J Affect Disord*2003;**76**:255–259.
13. Malone M, Harris AL, Luscombe DK. Assessment of the impact of cancer on work, recreation, home, management, and sleep using a general health status measure. *J Res Soc Medicine* 1994;**87**:386–389.
14. Redd WH, Andersen BL, Bovbjerg DH, *et al*. Physiologic and psychobehavioural research in oncology. *Cancer* 1991;**67**:813–822.
15. Sharma N, Hansen CH, O'Connor M, *et al*. Sleep problems in cancer outpatients: prevalence and associations. *Psycho-Oncology* 2012;**21**(9): 1003–1009.
16. Espie CA, Fleming L, Cassidy J, *et al*. Randomized controlled clinical effectiveness trial of cognitive behavior therapy versus treatment as usual for persistent insomnia in cancer patients. *J Clin Oncol* 2008;**26**(28):4651–4658.
17. Savard J, Simard S, Ivers H, Morin CM. A randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer: part 1—sleep and psychological effects. *J Clin Oncol* 2005;**23**:6083–6096.
18. Miaskowski C, Dodd M, Lee K. Symptom clusters: the new frontier in symptom management research. *J Natl Cancer Inst Monogr* **2004**;2004:17–21.
19. Lee BN, Dantzer R, Langley KE, *et al.* A cytokine-based neuroimmunologic mechanism of cancer-related symptoms. *Neuroimmunomodulation* 2004;**11**:279–292.
20. American Sleep Disorders Association. *International Classification of Sleep Disorders: Diagnostic and Coding Manual (Revised)*. ASDA: Rochester, MA, 1997.
21. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*. APA: Washington, DC, 1994.
22. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989;**28**:193–213.
23. Beck SL, Schwartz AL, Towsley G, Dudley W. Psychometric evaluation of the Pittsburgh Sleep Quality Index in cancer patients. *J Pain Symptom Manage* 2004;**27**:140–148.
24. National Institute for Clinical Excellence. Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia. Technology Appraisal Guidance 77, 2004.
25. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandanavica* 1983;**67**:361–370.
26. Hann DM, Jacobsen PB, Azzarello LM, *et al*. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. *Qual Life Res* 1998;**7**: 301–310.
27. Morin CM, Culbert JP, Schwartz MS. Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *Am J Psychiatry* 1994;**151**:1172–80.
28. Davidson JR, Waisberg JL, Brundage MD, MacLean AW. Nonpharmacologic group treatment of insomnia: a preliminary study with cancer survivors. *Psycho-Oncology* 2001;**10**:389–397.
29. Ibbotson T, Maguire P, Selby P, *et al*. Screening for anxiety and depression in cancer patients: the effects of disease and treatment. *Eur J Cancer* 1994;**30**(A):37–40.
30. Razavi D, Delvaux N, *et al*. Screening for adjustment disorders and major depressive disorders in cancer in-patients. *Br J Psychiatry* 1990;**156**:79–83.
31. Webster K, Odom L, Peterman A, Lent L, Cella D. The Functional Assessment of Chronic Illness Therapy (FACIT) measurement system: validation of version 4 of the core questionnaire. *Qual Life Res* 1999;**8**(7):604.
32. Donovan KA, Jacobsen PB, Small BJ, Munster PN, Andrykowski MA. Identifying clinically meaningful fatigue with the Fatigue Symptom Inventory. *J Pain Symptom Manage* 2008;**36**(5):480–487.
33. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: a systematic and meta-analytic review of non-pharmacological therapies for cancer patients. *Psychol Bull* 2008;**134**(5):700–741.
34. Goedendorp MM, Peters MEWJ, Gielissen MFM, Witjes JA, Leer JW, Verhagen GB. Is increasing physical activity necessary to diminish fatigue during cancer treatment? Comparing cognitive behaviour therapy and a brief nursing intervention with usual care in a multicenter randomized controlled trial. *Oncologist* 2010;**15**(10):1122–1132.