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Distinct Evening Fatigue Profiles in Oncology Outpatients Receiving Chemotherapy

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Abstract

Background—Fatigue is the most common and debilitating symptom experienced by oncology patients during chemotherapy (CTX). Fatigue severity demonstrates a large amount of inter-individual and diurnal variability.

Purpose—Study purposes were to evaluate for subgroups of patients with distinct evening fatigue profiles and evaluate how these subgroups differed on demographic, clinical, and symptom characteristics.

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Methods—Outpatients with breast, gastrointestinal, gynecological, or lung cancer (n=1332) completed questionnaires six times over two cycles of CTX. Lee Fatigue Scale (LFS) evaluated evening fatigue severity. Latent profile analysis was used to identify distinct evening fatigue profiles.

Results—Four distinct evening fatigue classes (i.e., Low (14.0%), Moderate (17.2%), High (36.0%), Very High (32.8%)) were identified. Compared to the Low class, patients in the Very High evening fatigue class were: younger, female, had childcare responsibilities, had more years of education, had a lower functional status, had a higher comorbidity burden, and were diagnosed with breast cancer. Patients in the Very High class reported higher levels of depressive symptoms, sleep disturbance, and evening fatigue at enrollment.

Conclusions—Findings provide new insights into modifiable risk factors for higher levels of evening fatigue. Clinicians can use this information to identify higher risk patients and plan appropriate interventions.

Keywords

evening fatigue; chemotherapy; diurnal variations; symptom profiles; latent class analysis

Introduction

Fatigue is the most common and debilitating symptom experienced by oncology patients during chemotherapy (CTX).[1] Fatigue negatively impacts patients' daily activities and their quality of life (QOL).[2] While a growing body of evidence suggests that average fatigue severity is associated with a number of demographic and clinical characteristics,[3–10] these studies did not evaluate diurnal variations in fatigue severity. Recent work by our research team [11–14] and others [15–17] found that fatigue severity is extremely variable over the course of a day and among individuals. However, the majority of the studies cited above used correlational methods of analysis, which are unable to capture patterns of within group variation.

Latent profile analysis (LPA) uses observable characteristics to group people into previously unknown classes who share similar characteristics.[18] By identifying groups of patients with distinct fatigue profiles, characteristics that are associated with these groups can be determined and a more refined understanding of fatigue severity is possible. Only three studies used LPA to identify groups of oncology patients undergoing CTX with distinct fatigue profiles.[12,19,20] In the two studies that used average fatigue scores,[19,20] Higher and Lower Fatigue classes were identified. In both studies, patients in the Higher Fatigue class were significantly younger and reported lower levels of physical activity.

In the third study of oncology patients with breast, gastrointestinal (GI), gynecological (GYN), and lung cancer (N=582),[12] we used LPA to evaluate for subgroups of patients with distinct evening fatigue severity profiles. Three subgroups (i.e., Moderate, High, Very High) were identified. Compared to the Moderate class, patients in the Very High class were more likely to be younger and female. In addition, these patients were more likely to have

childcare responsibilities and a diagnosis of breast cancer, as well as a lower functional status, and a worse comorbidity profile.

While progress is being made in understanding diurnal variations in fatigue severity, as well as distinct phenotypes, for this study, our focus was on the identification of distinct phenotypes for evening fatigue, as well as the determination of additional risk factors for this symptom. Therefore, the purposes of this study using a larger sample of patients (n=1332) was to evaluate for subgroups of patients with distinct evening fatigue profiles; evaluate how these subgroups differed by demographic, clinical, and symptom characteristics; and confirm our previous LPA findings.

Methods

Patients and Settings

The methods for this study were published previously.[12,14] In brief, eligible patients had a diagnosis of breast, GI, GYN, or lung cancer; had received CTX within the preceding four weeks; were scheduled for at least two additional CTX cycles; were 18 years of age; could read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 2,234 patients were approached and 1,343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment.

Instruments

Demographic questionnaire obtained information on age, sex, ethnicity, marital status, living arrangements, education, employment status and income. Karnofsky Performance Status (KPS) scale was used to evaluate functional status.[21] Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms).[22,23]

Self-Administered Comorbidity Questionnaire (SCQ) consists of 13 common medical conditions simplified into language that can be understood without prior medical knowledge. [24] Patients indicated if they had the condition; if they received treatment for it; and if the condition limited their activities. Total SCQ scores range from 0 to 39. The SCQ has well established validity and reliability.[25]

Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire that assesses alcohol consumption, alcohol dependence, and the consequences of alcohol abuse in the last 12 months. The total AUDIT score can range from 0 to 40. Scores of 8 are defined as hazardous use and scores of 16 are defined as use of alcohol that is likely to be harmful to health.[26] The AUDIT has well established validity and reliability.[27] In our, its Cronbach's alpha was 0.63.

Lee Fatigue Scale (LFS) consists of 18 items designed to assess physical fatigue and energy. [28] Each item was rated on a 0 to 10 numeric rating scale (NRS). Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items,

respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate LFSs, patients rated each item based on how they felt within 30 minutes of awakening (i.e., morning fatigue, morning energy) and prior to going to bed (i.e., evening fatigue, evening energy). The LFS has established cut-off scores for clinically meaningful levels of fatigue (i.e., 3.2 for morning fatigue, 5.6 for evening fatigue) [29] and energy (i.e., 6.2 for morning energy, 3.5 for evening energy).[29] It was chosen for this study because it is relatively short, easy to administer, and has well established validity and reliability.[28,30] In our study, the Cronbach's alphas were 0.96 for morning and 0.93 for evening fatigue and 0.95 for morning and 0.93 for evening energy.

Spielberger State-Trait Anxiety Inventories (STAI-S and STAI-T) each have 20 items that are rated from 1 to 4. The summed scores for each scale can range from 20 to 80. The STAI-T measures a person's predisposition to anxiety as part of one's personality. The STAI-S measures a person's temporary anxiety response to a specific situation or how anxious or tense a person is "right now" in a specific situation. Cutoff scores of 31.8 and 32.2 indicate high levels of trait and state anxiety, respectively. The STAI-T and STAI-S inventories have well established validity and reliability.[31] In our study, the Cronbach's alphas for the STAI-T and STAI-S were 0.92 and 0.96, respectively.

Center for Epidemiological Studies-Depression (CES-D) scale consists of 20 items selected to represent the major symptoms in the clinical syndrome of depression. A total score can range from 0 to 60, with scores of 16 indicating the need for individuals to seek clinical evaluation for major depression. The CES-D has well established validity and reliability.[32] In our study, the Cronbach's alpha for the CES-D total score was 0.89.

General Sleep Disturbance Scale (GSDS) consists of 21 items designed to assess the quality of sleep in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. A GSDS total score of 43 indicates a significant level of sleep disturbance.[29] The GSDS has well established validity and reliability.[30,33] In our study, the Cronbach's alpha for the GSDS total score was 0.83.

Attentional Function Index (AFI) consists of 16 items designed to measure attentional function.[34] A higher total mean score on a 0 to 10 NRS indicates greater capacity to direct attention.[34] Total scores are grouped into categories of attentional function (i.e., <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function).[35] The AFI has well established validity and reliability.[34] In our study, the Cronbach's alpha for the total AFI score was 0.93.

Pain occurrence was evaluated using the Brief Pain Inventory.[36] Patients who responded yes to the question about having pain were asked to indicate if their pain was or was not related to their cancer treatment.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the infusion unit to discuss

participation in the study. Written informed consent was obtained from all patients. Depending on the length of their CTX cycles, patients completed questionnaires in their homes, a total of six times over two cycles of CTX (i.e., prior to CTX administration (i.e., recovery from previous CTX cycle, Assessments 1 and 4), approximately 1 week after CTX administration (i.e., acute symptoms, Assessments 2 and 5), approximately 2 weeks after CTX administration (i.e., potential nadir, Assessments 3 and 6)).

Data Analysis

Data were analyzed using SPSS version 22 (IBM, Armonk, NY). Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics.

Latent profile analysis (LPA) was used to identify subgroups of patients with distinct evening fatigue profiles over the six assessments. Given the complexity of the pattern of change in evening fatigue over the two cycles of CTX, means were estimated from the LFS at each of the six assessments with covariances included to incorporate the expected correlations among the repeated measures to reduce model complexity. Estimation was carried out with full information maximum likelihood with standard errors and a Chi-square test that are robust to non-normality and non-independence of observations. To determine the best fitting model to characterize the latent class structure, multiple information criteria were used. Lower values for the Akaike Information Criteria (AIC) and Bayesian Information Criterion (BIC) represent better fitting models. Entropy values classify the quality of the model, in which values close to 1 indicate good classification. When using the Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR) to compare the models, a significant p-value suggests that one estimated model fits the data better than another model with one fewer group.[37,38] Estimation of model fit was conducted with Mplus Version 7.2 [39] with 1,000 to 2,400 random starts.

Differences in demographic and clinical characteristics among the latent classes were evaluated using analyses of variance and Kruskal-Wallis or Chi-Square tests with Bonferroni corrected post hoc contrasts. All calculations used actual values. A p-value of <.05 was considered statistically significant.

Results

Latent classes for evening fatigue

As shown in Supplemental Table 1, a four-class solution was selected because the profile of the means was clinically meaningfully different and the four-class solution fit better than a one-, two- or three-class solution. In addition, a five-class did not provide a significant improvement over the four-class solution. The evening fatigue classes were labeled as Low, Moderate, High, and Very High based on the clinically meaningful LFS cut-off score of 5.6 for evening fatigue. As shown in Figure 1, the trajectories for evening fatigue differed among the latent classes. For the Low (14.0%), High (36.0%), and Very High (32.8%) classes, evening fatigue scores remained relatively stable across the six assessments. For the Moderate class (17.2%), evening fatigue scores exhibited a distinct increase at the second and fifth assessments.

Differences in demographic and clinical characteristics

As shown in Table 1, no differences were found among the latent classes for most of the demographic and clinical characteristics. However, compared to the Low class, patients in the other three evening fatigue classes were significantly younger, had lower KPS scores, were more likely to be diagnosed with breast cancer, and were less likely to have GI cancer. In terms of gender differences, compared to the Low and High classes, patients in the Moderate and Very High classes were more likely to be female. In terms of ethnic differences, compared to the Low and Moderate classes, patients in the High and Very high classes were more likely to be White. In addition, compared to the Low class, patients in the High and Very High classes were less likely to be Black. Compared to the other three classes, patients in the Very High class were less likely to be Asian or Pacific Islander. In terms of income, compared to the Moderate class, a larger percentage of patients in the Very High class reported a higher income.

In terms of comorbidities, compared to the Low class, patients in the High and Very High classes reported higher SCQ scores. In addition, compared to the Low class, a lower percentage of patients in the High class reported high blood pressure. Compared to the High class, a higher percentage of patients in the Very High class reported anemia. Compared to the Low class, a higher percentage of patients in the High and Very High classes reported depression. Finally, compared to the Moderate and High classes, a higher percentage of patients in the Very High class reported depression.

Differences in symptom characteristics

As shown in Table 2, compared to the Low class, patients in the other three evening fatigue classes had higher trait anxiety, state anxiety, depression, sleep disturbance, and morning fatigue scores and lower attentional function scores. In addition, compared to the Moderate and High classes, patients in the Very High evening fatigue class had higher trait anxiety, state anxiety, depression, sleep disturbance, and morning fatigue scores and lower attentional function scores. In terms of evening fatigue scores, the pattern was as expected (i.e., Low < Moderate < High < Very High). For morning energy, patients in the Very High evening fatigue class had lower scores than the High class. For evening energy, compared to patients in the other three classes, patients in the Very High evening fatigue class had lower scores.

In terms of pain, compared to the High and Very High classes, a higher percentage of patients in the Low evening fatigue class reported not having pain. In addition, compared to the Low class, a higher percentage of patients in the Moderate, High, and Very High classes reported both cancer and non-cancer pain.

Discussion

This study extends our prior work on the identification of subgroups of patients with distinct evening fatigue profiles. While in our previous study,[12] three distinct evening fatigue profiles (i.e., Moderate, High and Very High) were identified, in this study, four profiles (i.e., Low, Moderate, High and Very High) were found. The addition of 750 patients enabled us to reliably discriminate between a three- and a four-class solution. Using the clinically

meaningful cutoff score for evening fatigue, a “Low” class was identified in this study. Compared to the Moderate class in the previous study who had an average enrollment LFS score of 2.9,[12] the average LFS score for the Low class in this study was 2.3. While in our previous study, the evening fatigue classes were named using the clinically meaningful LFS cutoff scores, with the larger sample size in the current study, we were able to further refine not only the number but the naming of the latent classes. Compared to the relatively stable trajectories of the Low, High, and Very High profiles, the Moderate profile had a distinct increase in LFS at assessments two and five (Figure 1). That said, the distinctions between the Moderate and High classes appear to be more subtle. Compared to the Moderate class, a lower percentage of female patients and a higher percentage of White patients were in the High evening fatigue class. These two distinct classes warrant confirmation in future studies.

One of our goals was to identify modifiable and non-modifiable characteristics that place patients at higher risk for more severe evening fatigue. Based on our previous [12] and current LPAs, as well as an HLM analysis,[14] the phenotypic characteristics associated with membership in the Very High evening fatigue classes, as well as higher evening fatigue scores are summarized in Table 3. The remainder of the discussion describes these characteristics within the context of the published literature on evening fatigue.

The most common demographic characteristics associated with higher levels of evening fatigue across our three analyses were: younger age, being female, having childcare responsibilities, and having a higher level of education. While age, gender, and years of education are non-modifiable demographic characteristics, they are easily identifiable risk factors. Consistent with prior reports,[8,40,41] younger age was associated with higher fatigue severity. Potential explanations for this association may include: older patients being given lower doses of CTX;[42] age-related changes that modify inflammatory responses; [43] or a “response shift” in the symptom perceptions of older patients.[44]

While the findings on gender differences in fatigue severity are inconsistent,[45] in all our analyses with the current sample, it is difficult to determine the relative contribution of gender versus cancer diagnoses to evening fatigue severity, because the majority of the patients were female with breast cancer. It is interesting to note that patients diagnosed with GI cancer, which occurs relatively equally in both genders, were more likely to be in the Low evening fatigue class. Additional studies of patients with cancers that occur across both genders (e.g., GI, lung) will allow for an evaluation of the independent contributions of gender and cancer diagnosis to evening fatigue severity. In prior reports,[5,9,46] the association between years of education and higher mean fatigue scores is inconsistent. Whether education is a proxy for some other demographic characteristic (e.g., socioeconomic status) warrants investigation in further studies.

In terms of modifiable demographic characteristics, the need to care for children was consistently associated with a higher evening fatigue profile. Again, this characteristic may be associated with female gender. Clinicians should assess for this risk factor and provide social and structural supports that help to decrease evening fatigue severity.

Consistent with prior reports,[47,48] lower functional status was one of the clinical characteristics associated with higher levels of evening fatigue. In the current study, compared to the Low, Moderate, and High classes, patients in the Very High class had not only statistically significant but clinically meaningful decrements in KPS scores (i.e., $d=0.78$, $d=0.35$, $d=0.35$, respectively).[49] As a modifiable risk factor, exercise may be an effective intervention to improve patients' functional status and decrease evening fatigue. [50]

A higher comorbidity burden was another clinical characteristic associated with membership in the Very High evening fatigue class. On average, patients in our sample had a comorbidity burden (i.e., SCQ score of 5.48 ± 3.2) that was comparable to hospitalized medical-surgical patients (i.e., SCQ score of 5.61 ± 4.1).[24] Compared to the Low class, patients in the High and Very High classes had clinically meaningful differences in SCQ scores (i.e., $d=0.29$, $d=0.43$, respectively). In previous studies of oncology patients, a higher comorbidity burden was associated with increased symptom occurrence rates and severity scores,[51] as well as decreased coping and functional abilities.[52] Future studies need to determine if specific comorbid conditions are associated with higher levels of evening fatigue and whether optimal management of comorbid conditions reduces fatigue severity.

Consistent with prior reports of associations between depressive symptoms [53,54] and sleep disturbance [4,55,56] and higher levels of mean fatigue severity, these two symptoms were associated with more severe evening fatigue. Compared to the Low, Moderate, and High classes, patients in the Very High class had CES-D scores (16.5 ± 11.2) that were higher than the clinically meaningful cutoff score of 16. In addition, statistically significant and clinically meaningful differences in CES-D scores were found between the Low, Moderate, and High classes compared to the Very High evening fatigue class (i.e., $d=1.43$, $d=0.53$, $d=0.53$, respectively). While collinearity between depressive symptoms and fatigue is possible, the items of the LFS assess physical fatigue rather than somatic symptoms. As with exercise, treatment of depressive symptoms may help to alleviate evening fatigue severity.

In terms of sleep disturbance, the Moderate, High, and Very High evening fatigue classes had GSDS scores above the clinically meaningful cut-off score of 43 (i.e., GSDS scores of 50.1, 51.8, 61.2, respectively). Findings from previous studies suggest that sleep disturbance occurs in 30% to 75% of oncology patients [57] and is associated with higher fatigue severity.[58] In addition, oncology patients with different morning-evening chronotypes have varying levels of sleep disturbance and fatigue.[59] Future studies are needed that examine the relationships between different chronotypes and evening fatigue scores. Of note, fatigue, depressive symptoms, and sleep disturbances share common underlying mechanisms.[53] Additional studies that examine the shared and unique mechanisms among these symptoms may increase our understanding of these co-occurring symptoms and inform the development of interventions.

While in the current study a number of other symptoms were associated with membership in the Very High evening fatigue class (i.e., anxiety, attentional function, decrements in morning and evening energy, pain) these findings warrant confirmation in future studies. Of note, most of the clinical characteristics (i.e., BMI, number and type of prior treatments,

CTX cycle length, metastatic involvement, hemoglobin and hematocrit levels, exercise frequency) were not associated with higher levels of evening fatigue. These findings warrant additional confirmation.

Several limitations must be acknowledged. Because patients were recruited at various time points in their CTX treatment, fatigue profiles from the initiation of CTX through the completion of treatment were not evaluated. The findings related to ethnicity need to be interpreted with caution given the relatively small sample sizes for the different ethnic groups. However, this large representative sample of oncology patients, assessments of evening fatigue over two cycles of CTX, and comparisons of modifiable and non-modifiable risk factors across three studies using two different statistical approaches are major strengths of this study.

Conclusions

This study improves our understanding of the risk factors associated with distinct evening fatigue profiles. Using this information, clinicians can identify patients who are at higher risk for more severe evening fatigue during CTX. Additional research is warranted, using objective measures of physical function, on the impact of evening fatigue on oncology patients' physical function. Future studies need to evaluate for differences among these evening fatigue profiles in terms of a variety of psychosocial adjustment characteristics (e.g., resilience, coping stress) and genomic markers (e.g., candidate genes, gene expression).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, Schnipper HH, Lacchetti C, Ligibel JA, Lyman GH, Ogaily MS, Pirl WF, Jacobsen PB. American Society of Clinical Oncology. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation. *J Clin Oncol*. 2014; 32:1840–50. [PubMed: 24733803]
2. Berger AM, Mooney K, Alvarez-Perez A, Breitbart WS, Carpenter KM, Cella D, Cleeland C, Dotan E, Eisenberger MA, Escalante CP, Jacobsen PB, Jankowski C, LeBlanc T, Ligibel JA, Loggers ET, Mandrell B, Murphy BA, Palesh O, Pirl WF, Plaxe SC, Riba MB, Rugo HS, Salvador C, Wagner LI, Wagner-Johnston ND, Zachariah FJ, Bergman MA, Smith C. National Comprehensive Cancer Network. Cancer-Related Fatigue, Version 2.2015. *JNCCN*. 2015; 13:1012–39. [PubMed: 26285247]
3. Bischel LE, Ritchie C, Kober KM, Paul SM, Cooper BA, Chen LM, Levine JD, Hammer M, Wright F, Miaskowski C. Age differences in fatigue, decrements in energy, and sleep disturbance in oncology patients receiving chemotherapy. *Eur J Oncol Nurs*. 2016; 23:115–23. [PubMed: 27456383]

4. Ancoli-Israel S, Liu L, Rissling M, Natarajan L, Neikrug AB, Palmer BW, Mills PJ, Parker BA, Sadler GR, Maglione J. Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. *Support Care Cancer*. 2014; 22:2535–45. [PubMed: 24733634]
5. Andrykowski MA, Donovan KA, Jacobsen PB. Magnitude and correlates of response shift in fatigue ratings in women undergoing adjuvant therapy for breast cancer. *J Pain Symptom Manage*. 2009; 37:341–51. [PubMed: 18757176]
6. Berger AM, Lockhart K, Agrawal S. Variability of patterns of fatigue and quality of life over time based on different breast cancer adjuvant chemotherapy regimens. *Oncol Nurs Forum*. 2009; 36:563–70. [PubMed: 19726396]
7. Brown LF, Rand KL, Bigatti SM, Stewart JC, Theobald DE, Wu J, Kroenke K. Longitudinal relationships between fatigue and depression in cancer patients with depression and/or pain. *Health Psychol*. 2013; 32:1199–208. [PubMed: 22924447]
8. Butt Z, Rao AV, Lai JS, Abernethy AP, Rosenbloom SK, Cella D. Age-associated differences in fatigue among patients with cancer. *J Pain Symptom Manage*. 2010; 40:217–23. [PubMed: 20541901]
9. Huang HP, Chen ML, Liang J, Miaskowski C. Changes in and predictors of severity of fatigue in women with breast cancer: A longitudinal study. *Int J Nurs Stud*. 2014; 51:582–92. [PubMed: 24094610]
10. Wang XS, Zhao F, Fisch MJ, O'Mara AM, Cella D, Mendoza TR, Cleeland CS. Prevalence and characteristics of moderate to severe fatigue: a multicenter study in cancer patients and survivors. *Cancer*. 2014; 120:425–32. [PubMed: 24436136]
11. Dhruva A, Aouizerat BE, Cooper B, Paul SM, Dodd M, West C, Wara W, Lee K, Dunn LB, Langford DJ, Merriman JD, Baggott C, Cataldo J, Ritchie C, Kober K, Leutwyler H, Miaskowski C. Differences in morning and evening fatigue in oncology patients and their family caregivers. *Eur J Oncol Nurs*. 2013; 17:841–8. [PubMed: 24012189]
12. Kober KM, Cooper BA, Paul SM, Dunn LB, Levine JD, Wright F, Hammer MJ, Mastick J, Venook A, Aouizerat BE, Miaskowski C. Subgroups of chemotherapy patients with distinct morning and evening fatigue trajectories. *Support Care Cancer*. 2016; 24:1473–85. [PubMed: 26361758]
13. Wright F, D'Eramo Melkus G, Hammer M, Schmidt BL, Knobf MT, Paul SM, Cartwright F, Mastick J, Cooper BA, Chen LM, Melisko M, Levine JD, Kober K, Aouizerat BE, Miaskowski C. Predictors and trajectories of morning fatigue are distinct from evening fatigue. *J Pain Symptom Manage*. 2015; 50:176–89. [PubMed: 25828559]
14. Wright F, D'Eramo Melkus G, Hammer M, Schmidt BL, Knobf MT, Paul SM, Cartwright F, Mastick J, Cooper BA, Chen LM, Melisko M, Levine JD, Kober K, Aouizerat BE, Miaskowski C. Trajectories of evening fatigue in oncology outpatients receiving chemotherapy. *J Pain Symptom Manage*. 2015; 50:163–75. [PubMed: 25828560]
15. Molassiotis A, Chan CW. Fatigue patterns in Chinese patients receiving radiotherapy. *Eur J Oncol Nurs*. 2004; 8:334–40. [PubMed: 15550363]
16. Jim HS, Small B, Faul LA, Franzen J, Apte S, Jacobsen PB. Fatigue, depression, sleep, and activity during chemotherapy: daily and intraday variation and relationships among symptom changes. *Annals Behav Med*. 2011; 42:321–33.
17. Dimsdale JE, Ancoli-Israel S, Ayalon L, Elsmore TF, Gruen W. Taking fatigue seriously, II: variability in fatigue levels in cancer patients. *Psychosomatics*. 2007; 48:247–52. [PubMed: 17478594]
18. Jung T, Wickrama K. An introduction to latent class growth analysis and growth mixture modeling. *Social Person Psychol Compass*. 2008; 2:302–17.
19. Kober KM, Smoot B, Paul SM, Cooper BA, Levine JD, Miaskowski C. Polymorphisms in cytokine genes are associated with higher levels of fatigue and lower levels of energy in women after breast cancer surgery. *J Pain Symptom Manage*. 2016; 52:695–708. [PubMed: 27664835]
20. Bødcher H, Bidstrup PE, Andersen I, Christensen J, Mertz BG, Johansen C, Dalton SO. Fatigue trajectories during the first 8 months after breast cancer diagnosis. *Qual Life Res*. 2015; 24:2671–9. [PubMed: 25972303]

21. Karnofsky D, Abelmann WH, Craver LV, Burchenal JH. The use of nitrogen mustards in the palliative treatment of carcinoma. *Cancer*. 1948; 1:634–56.
22. Ando M, Ando Y, Hasegawa Y, Shimokata K, Minami H, Wakai K, Ohno Y, Sakai S. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. *Br J Cancer*. 2001; 85:1634–9. [PubMed: 11742480]
23. Schnadig ID, Fromme EK, Loprinzi CL, Sloan JA, Mori M, Li H, Beer TM. Patient- physician disagreement regarding performance status is associated with worse survivorship in patients with advanced cancer. *Cancer*. 2008; 113:2205–14. [PubMed: 18780322]
24. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum*. 2003; 49:156–63. [PubMed: 12687505]
25. Brunner F, Bachmann LM, Weber U, Kessels AG, Perez RS, Marinus J, Kissling R. Complex regional pain syndrome 1--the Swiss cohort study. *BMC Musculoskelet Disord*. 2008; 9:92. [PubMed: 18573212]
26. Babor, TF., Higgins-Biddle, JC., Saunders, JB., Monteiro, MG. AUDIT: The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care. Geneva, Switzerland: World Health Organization; 2001.
27. Berner MM, Kriston L, Bentele M, Harter M. The alcohol use disorders identification test for detecting at-risk drinking: a systematic review and meta-analysis. *J Stud Alcohol Drugs*. 2007; 68:461–73. [PubMed: 17446987]
28. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. *Psychiatry Res*. 1991; 36:291–8. [PubMed: 2062970]
29. Fletcher BS, Paul SM, Dodd MJ, Schumacher K, West C, Cooper B, Lee K, Aouizerat B, Swift P, Wara W, Miasowski CA. Prevalence, severity, and impact of symptoms on female family caregivers of patients at the initiation of radiation therapy for prostate cancer. *J Clin Oncol*. 2008; 26:599–605. [PubMed: 18235118]
30. Miasowski C, Lee KA. Pain, fatigue, and sleep disturbances in oncology outpatients receiving radiation therapy for bone metastasis: a pilot study. *J Pain Symptom Manage*. 1999; 17:320–32. [PubMed: 10355211]
31. Spielberger, CG., Gorsuch, RL., Suchene, R., Vagg, PR., Jacobs, GA. Manual for the State-Anxiety (Form Y): Self Evaluation Questionnaire. Palo Alto, CA: Consulting Psychologists Press; 1983.
32. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychol Measure*. 1977; 1:385–401.
33. Lee KA. Self-reported sleep disturbances in employed women. *Sleep*. 1992; 15:493–8. [PubMed: 1475563]
34. Cimprich B, Visovatti M, Ronis DL. The Attentional Function Index--a self-report cognitive measure. *Psychooncology*. 2011; 20:194–202. [PubMed: 20213858]
35. Cimprich B, So H, Ronis DL, Trask C. Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psychooncology*. 2005; 14:70–8. [PubMed: 15386786]
36. Daut RL, Cleeland CS, Flanery RC. Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. *Pain*. 1983; 17:197–210. [PubMed: 6646795]
37. Muthen, BO. Latent variable analysis: Growth mixture modeling and related techniques for longitudinal data. In: Kaplan, DW., editor. *Handbook of Quantitative Methodology for the Social Sciences*. Newbury Park, CA: Sage Publications; 2004. p. 345-68.
38. Nylund KL, Asparoutiov T, Muthen BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Struct Equ Modeling*. 2007; 14:535–69.
39. Muthen, LK., Muthen, BO. *Mplus User's Guide*. 7. Los Angeles, CA: Muthen & Muthen; 1998–2012.
40. Soltow D, Given BA, Given CW. Relationship between age and symptoms of pain and fatigue in adults undergoing treatment for cancer. *Cancer Nurs*. 2010; 33:296–303. [PubMed: 20467311]

41. Wada S, Shimizu K, Inoguchi H, Shimoda H, Yoshiuchi K, Akechi T, Uchida M, Ogawa A, Fujisawa D, Inoue S, Uchitomi Y, Matsushima E. The association between depressive symptoms and age in cancer patients: A multicenter cross-sectional study. *J Pain Symptom Manage*. 2015; 50:768–77. [PubMed: 26300022]
42. Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, Falandry C, Artz A, Brain E, Colloca G, Flamaing J, Karnakis T, Kenis C, Audisio RA, Mohile S, Repetto L, Van Leeuwen B, Milisen K, Hurria A. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol*. 2014; 32:2595–603. [PubMed: 25071125]
43. Bower JE. Cancer-related fatigue--mechanisms, risk factors, and treatments. *Nat Rev Clin Oncol*. 2014; 11:597–609. [PubMed: 25113839]
44. Schwartz CE, Sprangers MA. Methodological approaches for assessing response shift in longitudinal health-related quality-of-life research. *Soc Sci Med*. 1999; 48:1531–48. [PubMed: 10400255]
45. Miaskowski C. Gender differences in pain, fatigue, and depression in patients with cancer. *J Natl Cancer Inst*. 2004; 32:139–43.
46. Peoples AR, Roscoe JA, Block RC, Heckler CE, Ryan JL, Mustian KM, Janelins MC, Peppone LJ, Moore DF Jr, Coles C, Hoelzer KL, Morrow GR, Dozier AM. Nausea and disturbed sleep as predictors of cancer-related fatigue in breast cancer patients: a multicenter NCORP study. *Support Care Cancer*. 2017; 25:1271–78. [PubMed: 27995318]
47. Minton O, Berger A, Barsevick A, Cramp F, Goedendorp M, Mitchell SA, Stone PC. Cancer-related fatigue and its impact on functioning. *Cancer*. 2013; 119(Suppl 11):2124–30. [PubMed: 23695924]
48. Mallinson T, Cella D, Cashy J, Holzner B. Giving meaning to measure: linking self-reported fatigue and function to performance of everyday activities. *J Pain Symptom Manage*. 2006; 31:229–41. [PubMed: 16563317]
49. Osoba D. Interpreting the meaningfulness of changes in health-related quality of life scores: lessons from studies in adults. *Int J Cancer Suppl*. 1999; 12:132–7. [PubMed: 10679884]
50. Meneses-Echavez JF, Gonzalez-Jimenez E, Ramirez-Velez R. Effects of supervised multimodal exercise interventions on cancer-related fatigue: Systematic review and meta-analysis of randomized controlled trials. *Biomed Res Int*. 2015; 2015:328636. [PubMed: 26167483]
51. Wright F, Hammer MJ, D'Eramo Melkus G. Associations between multiple chronic conditions and cancer-related fatigue: an integrative review. *Oncol Nurs Forum*. 2014; 41:399–410. [PubMed: 24849813]
52. Bayliss EA, Ellis JL, Steiner JF. Barriers to self-management and quality-of-life outcomes in seniors with multimorbidities. 2007:395–402.
53. Bortolato B, Hyphantis TN, Valpione S, Perini G, Maes M, Morris G, Kubera M, Kohler CA, Fernandes BS, Stubbs B, Pavlidis N, Carvalho AF. Depression in cancer: The many biobehavioral pathways driving tumor progression. *Cancer Treat Rev*. 2017; 52:58–70. [PubMed: 27894012]
54. Brown LF, Kroenke K. Cancer-related fatigue and its associations with depression and anxiety: a systematic review. *Psychosomatics*. 2009; 50:440–7. [PubMed: 19855028]
55. Garrett K, Dhruva A, Koettters T, West C, Paul SM, Dunn LB, Aouizerat BE, Cooper BA, Dodd M, Lee K, Wara W, Swift P, Miaskowski C. Differences in sleep disturbance and fatigue between patients with breast and prostate cancer at the initiation of radiation therapy. *J Pain Symptom Manage*. 2011; 42:239–50. [PubMed: 21454042]
56. Van Onselen C, Cooper BA, Lee K, Dunn L, Aouizerat BE, West C, Dodd M, Paul S, Miaskowski C. Identification of distinct subgroups of breast cancer patients based on self-reported changes in sleep disturbance. *Support Care Cancer*. 2012; 20:2611–9. [PubMed: 22290719]
57. Ancoli-Israel S. Sleep Disturbances in Cancer: A Review. *Sleep Medicine Research*. 2015; 6:45–9.
58. Palesh OG, Roscoe JA, Mustian KM, Roth T, Savard J, Ancoli-Israel S, Heckler C, Purnell JQ, Janelins MC, Morrow GR. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. *J Clin Oncol*. 2010; 28:292–8. [PubMed: 19933917]

59. Palesh O, Bjarnason GA, Ulusakarya A, Spiegel D, Levi F. Symptoms associated with circadian rest-activity rhythm disruption in 237 patients with metastatic colorectal cancer. *J Clin Oncol*. 2015; 33:1. [PubMed: 25332246]

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Figure 1.
Trajectories of evening fatigue for the latent classes.

Table 1
Differences in demographic and clinical characteristics among the evening fatigue latent classes

Characteristic	Low (0) 186 (14.0%) Mean (SD)	Moderate (1) 230 (17.2%) Mean (SD)	High (2) 479 (36.0%) Mean (SD)	Very High (3) 437 (32.8%) Mean (SD)	Statistics
Age (years)	61.4 (11.6)	57.0 (12.5)	57.4 (12.5)	55.0 (11.9)	F=12.29, p<.001 0 > 1, 2, and 3 2 > 3
Education (years)	15.9 (3.3)	15.8 (2.9)	16.2 (3.0)	16.5 (3.0)	F=3.81, p=.01 1 < 3
Body mass index (kg/m ²)	25.7 (5.3)	26.4 (5.2)	26.3 (5.8)	26.1 (5.9)	F=0.71, p=.545
Karnofsky Performance Status score	85.7 (11.9)	80.8 (12.7)	80.7 (12.0)	76.4 (12.1)	F=26.28, p<.001 0 > 1, 2, and 3 1 and 2 > 3
Number of comorbidities	2.3 (1.4)	2.3 (1.5)	2.4 (1.4)	2.5 (1.5)	F=0.64, p=.592
SCQ score	4.7 (2.8)	5.3 (3.1)	5.5 (3.0)	5.9 (3.5)	F=5.58, p=.001 0 < 2 and 3
AUDIT score	2.7 (2.3)	2.8 (2.3)	3.1 (2.6)	3.0 (2.5)	F=1.15, p=.328
Time since cancer diagnosis (years)	1.8 (3.4)	2.0 (4.8)	2.2 (4.0)	1.8 (3.4)	KW, p=.652
Time since cancer diagnosis (median)	0.48	0.40	0.42	0.42	
Number of prior cancer treatments	1.5 (1.5)	1.5 (1.5)	1.7 (1.6)	1.6 (1.4)	F=2.26, p=.080
Number of metastatic sites including lymph node involvement	1.4 (1.2)	1.2 (1.2)	1.3 (1.2)	1.2 (1.2)	F=2.07, p=.102
Number of metastatic sites excluding lymph node involvement	1.0 (1.1)	0.7 (1.0)	0.8 (1.0)	0.7 (1.0)	F=2.39, p=.067
Hemoglobin (gm/dL)	11.6 (1.5)	11.4 (1.4)	11.7 (1.5)	11.5 (1.4)	F=2.23, p=.083
Hematocrit (%)	34.8 (4.1)	34.3 (4.0)	34.8 (4.3)	34.3 (4.0)	F=1.60, p=.187
Gender	% (n)	% (n)	% (n)	% (n)	X ² =33.14, p<.001
Female ⁺	68.3 (127)	82.6 (190)	72.9 (349)	84.9 (371)	0 and 2 < 1 and 3
Male	31.7 (59)	17.4 (40)	27.1 (130)	14.9 (65)	
Transgender [*]	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)	
Ethnicity					
White	59.0 (108)	59.6 (134)	71.3 (338)	77.1 (334)	X ² =42.70, p<.001 0 and 1 < 2 and 3 0 > 2 and 3; 1 > 2
Black	12.0 (22)	11.6 (26)	4.9 (23)	5.5 (24)	0, 1 and 2 > 3
Asian or Pacific Islander	16.9 (31)	16.0 (36)	13.7 (65)	7.6 (33)	No significant post-hoc contrasts

Characteristic	Low (0) 186 (14.0%) Mean (SD)	Moderate (1) 230 (17.2%) Mean (SD)	High (2) 479 (36.0%) Mean (SD)	Very High (3) 437 (32.8%) Mean (SD)	Statistics
Hispanic Mixed or Other	12.0 (22)	12.9 (29)	10.1 (48)	9.7 (42)	
Married or partnered (% yes)	68.6 (127)	61.7 (140)	63.1 (296)	65.7 (284)	$\chi^2=2.87$, $p=.413$
Lives alone (% yes)	15.8 (29)	24.2 (55)	23.0 (108)	21.0 (91)	$\chi^2=5.25$, $p=.154$
Child care responsibilities (% yes)	14.6 (27)	19.4 (43)	20.8 (97)	28.4 (122)	$\chi^2=17.46$, $p=.001$ $0 < 3$
Care of adult responsibilities (% yes)	7.0 (12)	7.4 (15)	7.9 (34)	8.7 (35)	$\chi^2=0.64$, $p=.888$
Currently employed (% yes)	36.6 (67)	33.3 (76)	34.2 (162)	36.5 (158)	$\chi^2=1.04$, $p=.792$
Income					
< \$30,000 ⁺	19.4 (31)	19.5 (41)	18.0 (76)	17.8 (71)	
\$30,000 to < \$70,000	23.8 (38)	25.7 (54)	22.0 (93)	16.8 (67)	
\$70,000 to < \$100,000	18.8 (30)	20.0 (42)	14.5 (61)	17.3 (69)	KW, $p=.025$ $1 > 3$
\$100,000	38.1 (61)	34.8 (73)	45.5 (192)	48.3 (193)	
Specific comorbidities (% yes)					
Heart disease	8.1 (15)	6.1 (14)	4.8 (23)	5.3 (23)	$\chi^2=2.89$, $p=.408$
High blood pressure	37.1 (69)	25.2 (58)	33.6 (161)	25.9 (113)	$\chi^2=13.48$, $p=.004$ $0 > 3$
Lung disease	10.8 (20)	9.6 (22)	11.9 (57)	11.9 (52)	$\chi^2=1.07$, $p=.784$
Diabetes	10.8 (20)	9.1 (21)	9.2 (44)	7.8 (34)	$\chi^2=1.52$, $p=.678$
Ulcer or stomach disease	3.8 (7)	5.2 (12)	4.8 (23)	5.3 (23)	$\chi^2=0.70$, $p=.873$
Kidney disease	1.6 (3)	0.9 (2)	0.8 (4)	2.3 (10)	$\chi^2=4.05$, $p=.256$
Liver disease	5.9 (11)	5.7 (13)	7.7 (37)	5.7 (25)	$\chi^2=2.00$, $p=.572$
Anemia or blood disease	9.7 (18)	13.9 (32)	9.6 (46)	15.6 (68)	$\chi^2=9.27$, $p=.026$ $2 < 3$
Depression	7.5 (14)	16.1 (37)	18.8 (90)	26.5 (116)	$\chi^2=32.89$, $p<.001$ $0 < 2$ and $3; 1$ and $2 < 3$
Osteoarthritis	10.2 (19)	12.6 (29)	11.5 (55)	13.0 (57)	$\chi^2=1.21$, $p=.750$
Back pain	24.2 (45)	27.0 (62)	25.5 (122)	26.1 (114)	$\chi^2=0.46$, $p=.928$
Rheumatoid arthritis	2.7 (5)	4.3 (10)	3.3 (16)	2.3 (10)	$\chi^2=2.36$, $p=.501$
Exercise on a regular basis (% yes)	74.7 (139)	72.5 (161)	70.6 (333)	68.5 (289)	$\chi^2=2.82$, $p=.420$
Smoking, current or history of (% yes)	28.8 (53)	34.8 (78)	36.6 (172)	36.8 (159)	$\chi^2=4.20$, $p=.241$
Cancer diagnosis					$\chi^2=36.75$, $p<.001$

Characteristic	Low (0) 186 (14.0%) Mean (SD)	Moderate (1) 230 (17.2%) Mean (SD)	High (2) 479 (36.0%) Mean (SD)	Very High (3) 437 (32.8%) Mean (SD)	Statistics
Breast	26.3 (49)	43.0 (99)	39.5 (189)	46.0 (201)	0 < 1, 2, and 3 0 > 1, 2, and 3 No significant post-hoc contrasts No significant post-hoc contrasts
Gastrointestinal	46.8 (87)	26.1 (60)	30.5 (146)	25.6 (112)	
Gynecological	15.1 (28)	18.3 (42)	17.1 (82)	18.3 (80)	
Lung	11.8 (22)	12.6 (29)	12.9 (62)	10.1 (44)	
Type of prior cancer treatment					KW, p=.101
No prior treatment	33.5 (60)	27.1 (61)	22.5 (105)	23.0 (98)	
Only surgery, CTX, or RT	30.7 (55)	44.4 (100)	41.5 (194)	45.8 (195)	
Surgery & CTX, or surgery & RT, or CTX & RT	27.9 (50)	14.7 (33)	20.1 (94)	19.0(81)	
Surgery & CTX & RT	7.8 (14)	13.8 (31)	15.8 (74)	12.2 (52)	KW, p=.494
CTX cycle length					
14 days	47.8 (89)	40.6 (93)	41.4 (198)	40.4 (176)	
21 days	44.6 (83)	53.3 (122)	50.4 (241)	53.0 (231)	
28 days	7.5 (14)	6.1 (14)	8.2 (39)	6.7 (29)	

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, CTX = chemotherapy, gm/dL = grams per deciliter, kg = kilograms, KW = Kruskal Wallis; m^2 = meter squared, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation

* Chi Square analysis and post hoc contrasts done without the transgender patient include in the analyses

† Reference group for the post hoc comparisons

Table 2

Differences in symptom characteristics among the evening fatigue latent classes

Symptom	Low (0) 186 (14.0%) Mean (SD)	Moderate (1) 230 (17.2%) Mean (SD)	High (2) 479 (36.0%) Mean (SD)	Very High (3) 437 (32.8%) Mean (SD)	Statistics
Trait anxiety	29.6 (8.4)	33.8 (10.0)	35.0 (9.7)	38.4 (11.2)	F=33.42, p<.001 0 < 1, 2, and 3; 1 and 2 < 3
State anxiety	27.7 (9.1)	32.2 (12.0)	33.7 (10.9)	37.7 (13.9)	F=32.57, p<.001 0 < 1, 2, and 3; 1 and 2 < 3
Depressive symptoms	7.5 (6.3)	11.8 (9.1)	12.1 (8.3)	16.5 (11.2)	F=44.19, p<.001 0 < 1, 2, and 3; 1 and 2 < 3
Attentional function	7.6 (1.6)	6.6 (1.9)	6.5 (1.5)	5.7 (1.8)	F=48.78, p<.001 0 > 1, 2, and 3; 1 and 2 > 3
Sleep disturbance	37.1 (15.1)	50.1 (20.5)	51.8 (18.1)	61.2 (19.7)	F=71.31, p<.001 0 < 1, 2, and 3; 1 and 2 < 3
Morning fatigue	1.3 (1.3)	3.0 (2.3)	3.0 (1.9)	4.1 (2.4)	F=81.99, p<.001 0 < 1, 2, and 3; 1 and 2 < 3
Evening fatigue	2.4 (1.4)	4.7 (2.3)	5.1 (1.2)	7.2 (1.3)	F=466.12, p<.001 0 < 1 < 2 < 3
Morning energy	4.6 (2.7)	4.4 (2.4)	4.6 (2.0)	4.1 (2.2)	F=3.30, p=.020 2 > 3
Evening energy	4.0 (2.3)	3.9 (2.2)	4.0 (1.6)	2.7 (2.0)	F=38.77, p<.001 0, 1, and 2 > 3
Pain					
No pain	41.2 (75)	28.8 (65)	27.4 (128)	20.9 (90)	X ² =47.62, p<.001 0 > 2 and 3 0 < 3 No significant post-hoc contrasts 0 < 1, 2, and 3
Only cancer pain	18.1 (33)	24.3 (55)	25.2 (118)	32.0 (138)	
Only non-cancer pain	22.0 (40)	13.3 (30)	16.9 (79)	13.5 (58)	
Both cancer and non-cancer pain	18.7 (34)	33.6 (76)	30.6 (143)	33.6 (145)	

Abbreviations: SD = standard deviation

Table 3

Phenotypic characteristics associated with higher levels of evening fatigue

Characteristics	Very High 4 class solution	Very High 3 class solution [19]	HLM Analysis [22]
Demographic Characteristics			
Younger age	◆	◆	
Higher education	◆		◆
Being female	◆	◆	
Being Non-White		◆	◆
Being White	◆		
Having child care responsibilities	◆	◆	◆
Higher income	◆		
Clinical Characteristics			
Lower functional status	◆	◆	◆
Higher SCQ score	◆	◆	
Having a diagnosis of anemia or blood disease	◆	NT	
Having a diagnosis of depression	◆	NT	
Having a breast cancer diagnosis	◆	◆	◆
Symptom Characteristics			
Higher trait anxiety	◆	NT	
Higher state anxiety	◆	NT	
Higher depressive symptoms	◆	NT	◆
Lower attentional function	◆	NT	NT
Higher sleep disturbance	◆	NT	◆
Higher morning fatigue	◆	NT	
Higher evening fatigue	◆	NT	◆
Lower morning energy	◆	NT	
Lower evening energy	◆	NT	
Having cancer and/or non-cancer pain	◆	NT	

Abbreviations: u = association identified; NT = not tested; SCQ = Self-Administered Comorbidity Questionnaire