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Predictors of the Intensity of Cluster Symptoms in Patients With Breast Cancer

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Abstract

Purpose—To examine the influence of selected demographic and clinical variables on the intensity of symptoms in two previously identified symptom clusters (psychoneurological and upper gastrointestinal) across the treatment trajectory for breast cancer.

Design—A secondary analysis was conducted with a sample of 282 female breast-cancer patients who were receiving chemotherapy or radiation therapy in two American cancer centers. Data were collected three times across the treatment trajectory: baseline (before chemotherapy or radiation treatment) and two follow-up times after treatment initiation.

Method—Multiple regression analyses were done at each time point to examine the influence of selected demographic and clinical variables on the intensity of symptoms in each cluster.

Findings—Baseline physical performance status was a consistent predictor of symptom intensity in the psychoneurological cluster across time whereas age and treatment modality were consistent predictors of symptom intensity in the upper gastrointestinal cluster. Poor physical performance at baseline predicted more intense psychoneurological symptoms. Young women and women undergoing chemotherapy experienced more intense gastrointestinal symptoms. In addition, at the second follow-up treatment modality also influenced intensity of symptoms in the psychoneurological cluster and race and baseline physical performance status also influenced the intensity of symptoms in the upper gastrointestinal cluster.

Conclusions—Clinicians can anticipate that young patients, patients with poor baseline physical performance status, and patients who receive chemotherapy will have more intense treatment-related gastrointestinal and psychoneurological symptoms during adjuvant breast cancer therapy. Further research is needed to determine whether collective management for symptoms in a cluster may be beneficial.

Clinical Relevance—Clinicians can use findings from the present study to identify patients who need greater attention to symptom assessment and management, including anticipatory counseling of patients and families.

Keywords

Symptom clusters; treatment; symptom management; symptom assessment; breast cancer; predictors

Symptom clusters are stable groups of simultaneously occurring interrelated symptoms (Kim, McGuire, Tulman, & Barsevick, 2005). Oncologic symptom clusters have received attention because symptoms as a group can be an efficient target for assessment and management. In order to develop symptom assessment and management strategies for clusters, identification of the predictors of symptom intensity in a cluster is necessary. The identified predictors, such as treatment modality, can then be used in assessment of, and intervention for, that symptom cluster (Cooley, Short, & Moriarty, 2003).

In the present study we build upon previous work in which two symptom clusters were identified in a sample of women undergoing treatment for breast cancer: a psychoneurological cluster and an upper gastrointestinal cluster (Kim, Barsevick, Tulman, & McDermott, 2008). The two clusters were identified by factor analysis of common oncologic treatment-related symptoms. The symptom clustering patterns were consistent at baseline (before chemotherapy or radiation treatment) and two follow-up times (after initiating such treatment). Across the treatment trajectory, nausea, vomiting, and decreased appetite formed an upper gastrointestinal cluster, and depressed mood, cognitive disturbance, fatigue, insomnia, and pain formed a psychoneurological cluster. At only one measurement time, factor analysis indicated that the symptom of hot flashes had strong correlations with other psychoneurological symptoms and was part of that cluster. The current analyses were aimed at examining the influence of the theoretically important demographic and clinical variables on the intensity of symptoms in these clusters across the treatment trajectory.

Background

The theory of unpleasant symptoms (Lenz, Pugh, Milligan, Gift, & Suppe, 1997) guided this study. The theory indicates that multiple symptoms can occur simultaneously (i.e., symptom clusters) and that various factors (situational, physiologic, and psychologic) influence symptoms. Although direct empirical data do not exist to explain influencing factors on symptom cluster intensity, researchers investigating correlates of single or multiple symptoms provide some insights.

Several demographic variables (gender, age, employment status, marital status) have been reported to influence individual symptom intensity. For example, Pater and colleagues (1997) found that women had more severe fatigue than did men, controlling for cancer site, age, metastatic and performance status. Furthermore, a significant negative association between symptom intensity and age was reported in several studies (Bower et al., 2000; Pater, Zee, Palmer, Johnston, & Osoba, 1997). In addition, employment status (Akechi, Kugaya, Okamura, Yamawaki, & Uchitomi, 1999) and marital status (Bower et al., 2000) were reported to be associated with symptom intensity. Patients who were not employed reported less fatigue than did patients who were working fulltime. Unmarried and unpartnered women were more likely to report fatigue than were those who were married or had partners.

Several researchers have found an association between individual symptom intensity and disease-related factors, such as the stage of cancer (Can, Durna, & Adydiner, 2004; Pater et al., 1997), cancer sites (Pater et al., 1997; Smets, Visser, Willems-Groot, Garssen, Oldenburger et al., 1998) and comorbidity (Mast, 1998). A few studies indicate that symptom intensity differs according to treatment type. For example, Cooley et al. (2003) reported that the most distressing symptoms at entry into the study varied according to treatment modality in patients with lung cancer: pain, fatigue, and insomnia in the surgery group; fatigue, nausea, and loss of appetite in the radiotherapy group; fatigue, insomnia, and

loss of appetite in the chemotherapy group; and fatigue, pain, and insomnia in the combined-therapy group (defined as receiving more than one type of cancer treatment).

Investigators have noted a relationship between performance status and symptom intensity (Akechi et al., 1999; Given, Given, Azzouz, & Stommel, 2001). The direction of the relationship between performance status and individual symptoms, however, remains unresolved. Several investigators assert that more severe symptoms were associated with lower functional performance level (Given, Given, Azzouz, & Stommel). However, poor functional performance could also increase the intensity of symptoms such as depression or fatigue (Smets, Visser, Willems-Groot, Garssen, Schuster-Uitterhoeve, et al., 1998).

The relationship between demographic and clinical factors and the intensity of individual symptoms, however, were not replicated in other studies (Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998; Cooley et al., 2003; Irvine, Vincent, Graydon, & Bubela, 1998; Jacobsen et al., 1999). Thus, relationships between demographic and clinical variables and the intensity of individual symptoms remain inconclusive. Nevertheless, the reviewed studies indicate the possibility that demographic and clinical variables may influence the intensity of symptoms in a cluster, and thus these variables were considered in the current study.

Methods

In this study, we used a secondary analysis of data from a randomized clinical trial for the treatment of fatigue (Barsevick et al., 2004) in which the experimental group received a cognitive-behavioral intervention for fatigue, and the control group received information about nutrition. The parent study consisted of a convenience sample ($N = 396$) from two cancer centers in United States from 1999 to 2002. All of the patients were beginning a new treatment regimen for various types of cancer and were to receive a minimum of three cycles of chemotherapy (CTX), 6 weeks of radiation treatment (RTX), or concurrent RTX and CTX. In addition, they had not had any previous treatment other than surgery for at least 1 month before enrollment in the study and were receiving treatment either for cure or local control (i.e., not palliation). Patients were excluded if they could not read and understand English; had planned to receive stem-cell transplantation, interleukins, interferon, or tumor necrosis factor; had a previous diagnosis of chronic fatigue syndrome or showed evidence of a psychiatric disorder; had been started on treatment for anemia or depression during the previous 3 weeks; or had participated in another psychoeducational intervention study. Approvals of the institutional review boards were obtained.

Data Collection

In the parent study, data were collected at baseline (Time 1) and two follow-up points (Times 2 and 3) during or after cancer therapy. The follow-up points were selected in the parent study to capture maximal level of fatigue (Irvine et al., 1998; Meek et al., 2000). For patients receiving chemotherapy, the follow-up times were 48 hours after the second and third treatments. For patients receiving radiation therapy, the follow-up times were the last week of RTX (of a total of 6 weeks of treatment) and 1 month after completion of treatment. Thus, patients within each treatment-modality group were studied at similar time points in relation to their treatment.

Measures

The General Fatigue Scale (GFS) was used to measure fatigue (Meek, Nail, & Jones, 1997; 1–10 range, *no fatigue* to *greatest possible fatigue*). The GFS consists of seven items for measuring several aspects of fatigue (i.e., intensity, distress, effect on daily activities) during

various timeframes. Only one item (fatigue in the past week), however, was used for the current study for consistency with the recalled timeframes and dimensions of the other measured symptoms. Acceptable construct validity for the GFS has been reported (Meek et al., 1997). Two subscales (depression and confusion) of the Profile of Mood States-Short Form (POMS-SF) were used to measure depressed mood and cognitive disturbance in the last 2–3 days (McNair, Lorr, & Droppleman, 1981). Each subscale is composed of five items scored on a 5-point scale ranging from 0 (*not at all*) to 4 (*extremely*) with Cronbach's alphas of .81 and .75, respectively, in this study. McNair et al. reported acceptable content and concurrent validity. The Pittsburgh Sleep Quality Inventory (PSQI) was used to measure insomnia in the past month (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Cronbach's alpha for the global score of the PSQI was .74 in the current study. Acceptable construct validity has been reported (Buysse et al., 1989).

Pain and hot flashes were measured by use of a single item from the side-effect checklist, which was derived from a self-care diary (Nail, Jones, Greene, Schipper, & Jensen, 1991). A 4-point scale of 1 (*not at all severe*) to 4 (*quite a bit severe*) was used to measure the intensity of pain and of hot flashes for the past week. Absence of a symptom was recorded as zero. Performance status was measured before therapy was initiated (baseline) using the Eastern Cooperative Oncology Group Performance Status (ECOG), a widely used reliable measure (Conill, Verger, & Salamero, 1990). The ECOG is composed of a single item, 5-point scale for measuring activity (0 = *normal activity without symptoms* to 4 = *unable to get out of bed*). Acceptable validity for self-evaluation has been reported (Conill et al., 1990).

Sample for the Present Study

Data from only patients with breast cancer in the parent study ($N = 282$) were used for the current analyses with no additional exclusion criteria applied. The same data set was previously used to identify the two symptom clusters: psychoneurological and gastrointestinal (Kim et al., 2008). Table 1 shows the demographic and clinical characteristics of the study sample. Patients from the experimental ($n = 141$) and control ($n = 141$) groups were combined for the current analyses because of the absence of clinical differences in the fatigue level between the two groups in the parent study: $M = 3.3$ ($SD = 1.8$) vs. 3.3 (1.8) at Time 1 (baseline); 4.6 (± 2.2) vs. 4.6 (± 2.0) at Time 2; and 4.1 (± 2.2) vs. 4.7 (± 2.1) at Time 3. The 0.6 difference at Time 3 was statistically significant but not clinically meaningful, given the range of the scores (10 points). The two groups also did not differ ($p > .05$) in cancer stage, type of cancer treatment, or mean symptom severity of 16 other treatment-related symptoms.

Data Analysis

At each time point, multiple regression analyses were conducted with a factor-based score for each symptom cluster (psychoneurological and upper gastrointestinal) as the dependent variable. These symptom clusters are reported elsewhere (Kim et al., 2008). To obtain factor-based scores, all symptoms in a cluster were standardized and then summed to compute a combination score. The combination score was converted to a percentile, and finally the percentile scores were standardized into a T-score with a mean of 50 and standard deviation of 10. This procedure was used to compute normally distributed standardized scores.

Independent variables were demographic (age, race, marital status, employment status) and clinical (baseline physical performance status, comorbid conditions, treatment modality, disease stage). Variables were selected from previous studies indicating influencing factors of single symptoms (e.g., fatigue) in cancer patients. Independent variables were entered simultaneously into regression analyses. Comorbid conditions were entered as a continuous

variable (total number of comorbid conditions) and also as a dichotomous variable (presence of at least one comorbid condition vs. absence of a comorbid condition) in separate regressions. The independent variables for the regression model at Time 1 did not include treatment modality because patients had not begun CTX or RTX. Instead, disease stage was entered at this time point only. Furthermore, disease stage was closely related to the treatment modality ($r = -.57, p < .0001$) and therefore treatment modality rather than disease stage was included in the regression analyses at Times 2 and 3.

The sample size for the analyses varied across time and was smaller than 282 because of missing data (see Table 2). No imputations were done for missing data; information about patients missing one or more time points was included in the analyses to salvage data and increase the variance. Multivariate outliers with high influence were detected by studentized residual, leverage, and Cook's distance (UCLA Academic Technology Service, 2005). Influential outliers were deleted only when the deletion substantially changed a model: The number of deleted outliers was less than or equal to five cases in each regression model.

Results

Predictors of Symptom Intensity in the Psychoneurological Cluster

Seven demographic and clinical variables explained 25% of the variance in the intensity of symptoms in the psychoneurological cluster at Time 1 (Table 2). Only the variables of age and baseline physical performance status were significant independent predictors, with symptom intensity declining with increasing age and with better baseline physical performance status.

At Time 2, demographic and clinical variables explained 22% of the variance in symptom intensity (Table 2). Again, age and baseline physical performance status were significant independent predictors with lower intensity associated with increasing age and better baseline physical performance status.

The regression model explained 33% of the variance in the psychoneurological cluster at Time 3 (Table 2). As in the Time 1 and 2 regression models, baseline physical performance status was the strongest predictor for the psychoneurological cluster. Although age was not a significant predictor at this time, treatment modality was significant with women receiving chemotherapy experiencing more intense symptoms in this cluster.

Predictors of Symptom Intensity in the Upper Gastrointestinal Symptom Clusters

Note that in previous work, the upper gastrointestinal symptom cluster was not found at Time 1 (Kim et al., 2008). At Time 2, seven demographic/clinical variables explained 48% of the variance in the intensity of symptoms in the upper gastrointestinal cluster (Table 3). Only age and treatment modality were significant independent predictors. As with the psychoneurological cluster, increasing age was associated with lower symptom intensity. Patients receiving chemotherapy had a higher level of symptom intensity than did patients receiving radiation therapy.

At Time 3, the seven selected variables explained 51% of the variance (Table 3). Age and treatment modality continued to be significant predictors and, in addition, race and baseline physical performance status were statistically significant, with Caucasians reporting more intense symptoms than did non-Caucasians. Women with poorer baseline physical performance status reported more intense symptoms. As in Time 2, treatment modality was the strongest independent predictor of the upper gastrointestinal cluster at Time 3.

Discussion

An interesting similarity was found in the predictors of the intensity of symptoms in a cluster across time points (Table 4). Across time points, age and treatment modality were consistent significant predictors for the upper gastrointestinal cluster, and baseline physical performance status was a consistent significant predictor for the psychoneurological cluster.

Age was a significant predictor of the intensity of symptoms in both the psychoneurological cluster and the upper gastrointestinal clusters. Although some controversy exists regarding the association between symptom intensity (such as fatigue intensity) and age (Cooley et al., 2003), the present study indicated a relatively consistent negative association between age and the intensity of symptoms in a cluster across time points. The effect of age on symptom intensity could be attributed to several age-related characteristics which were not directly examined in this study. First, younger patients, in general, are more likely to be well educated and may be more active in symptom self-assessment. Second, it may be possible that younger women have had greater physical and psychological burdens from household, family, and career responsibilities as well as their jobs, and thus they might not get enough rest (Woo, Dibble, Piper, Keating, & Weiss, 1998). Younger patients might have had more aggressive treatment (e.g., chemotherapy regimens) than did older patients with the same disease stage. This interpretation was not directly tested because the information regarding chemotherapy regimens and dosage was not available from the parent study. However, younger women in this study were more likely to receive chemotherapy than radiation treatment ($p < .0001$).

Baseline physical performance status was the strongest consistent predictor of the intensity of symptoms in the psychoneurological cluster with better baseline performance associated with less intensity. The relationship between individual symptom intensity and physical performance status has been reported in many studies (Akechi et al., 1999; Jacobsen et al., 1999; Pater et al., 1997). The present study, however, found that the intensity of collective symptoms in a cluster was associated with performance status. The direction of the relationship between symptom intensity and physical performance status has been unclear. However, because physical performance status was measured at baseline in this study, one could conclude that physical performance status predicted symptom intensity and not the reverse. Similarly, Smets et al. (1998a; 1998b) reported that the level of baseline functioning (physical, mental, and social) was an important predictor of the level of fatigue 2 weeks and 9 months following radiotherapy.

We recommend that clinicians assess baseline physical performance or functional status and use this information both for anticipatory counseling of their patients and for evaluating interventions to control symptoms. Also, the strong association between physical performance status and the intensity of symptoms in a psychoneurological cluster may indicate the possibility that all symptoms in this cluster during cancer treatment can be better managed by improving the level of physical functioning. The effect of exercise has been focused on fatigue, but its effect on the other symptoms in the psychoneurological cluster has not been thoroughly examined. This type of collective intervention for a symptom cluster should be further investigated so that multiple symptoms can be managed more efficiently.

Treatment modality was the strongest and most consistent predictor of upper gastrointestinal symptom intensity, with patients receiving chemotherapy having more intense symptoms than did those receiving radiation. The influence of this variable on gastrointestinal symptoms is understandable because patients receiving chemotherapy experience more serious gastrointestinal symptoms (Shapiro & Recht, 2001).

As shown in Table 4, Time 3 findings differed from those at Times 1 and 2. The difference may be because patients receiving radiation at Time 3 had completed their treatment 1 month earlier whereas patients receiving chemotherapy were still receiving treatment. Treatment modality was a significant predictor for the psychoneurological cluster only at Time 3 and patients receiving chemotherapy experienced more intense symptoms in the psychoneurological cluster. Because the time lapse after treatment in patients receiving radiation was much longer than for those receiving chemotherapy, treatment modality might explain symptom intensity at this time point. In other words, this variable might not allow measurement of treatment modality per se at this point; instead, it might allow measurement of the time lapse since treatment completion or whether patients are currently receiving treatment. This finding might indicate that the psychoneurological cluster in this sample was treatment-related and was alleviated some time after treatment completion.

Race was a predictor for the upper gastrointestinal cluster only at Time 3, with Caucasians having more intense symptoms than did non-Caucasians. A similar finding was reported by Cooley et al. (2003), who also found that demographic variables, including race, were associated with individual symptom distress at some time points but were not consistent predictors. As indicated by their findings and those in the present study, other variables might differentiate Caucasians and non-Caucasians, and these variables may be responsible for the difference in symptom intensity. In the current study, Caucasians and non-Caucasians did not differ in educational level ($p = .15$) or disease stage ($p = .13$). Other variables differentiating the two groups, however, should be further examined, including attitudes toward symptoms, access to care for treatment of symptoms, and likeliness to report symptoms, particularly those of low intensity. In addition, the present study included only a small number of non-Caucasians ($n = 24$) and thus findings must be interpreted with caution.

Comorbid conditions were not associated with the intensity of symptoms in a cluster after controlling for other predictors, although some investigators have found relationships between symptoms and comorbid conditions (Gift, Jablonski, Stommel, & Given, 2004; Given, Given, Azzouz, Kozachik, & Stommel, 2001; Mast, 1998). The lack of association between comorbid conditions and symptom-cluster intensity in this study indicates support for the conclusion that the symptom cluster was induced by cancer or its treatment, not by comorbid conditions. This can be further supported by more than half (56%) of the patients in this sample having comorbid conditions, but the types of comorbid conditions were diverse. Furthermore, hypertension, the most prevalent comorbid condition ($n = 74$), is not usually accompanied by any specific symptoms, unless the disease damages organs. In designing symptom-cluster research, the effect of comorbid conditions should be carefully considered.

Also, the selected demographic and clinical variables explained a smaller amount of variance of the psychoneurological symptom cluster (25% at Time 1, 22% at Time 2, 33% at Time 3) than the variance of the gastrointestinal symptom cluster (48% at Time 2, 51% at Time 3). The lack of psychological factors (such as social support, coping, or illness uncertainty) or biological factors (such as hemoglobin or cytokine levels), as predictors of psychoneurological symptom clusters in the regression model, could be factors. The effects of psychological and biological variables on the intensity of symptom clusters should be further investigated. Identifying additional predictors of clusters could further elucidate the mechanisms underlying symptom clusters and could provide a basis for developing effective management strategies.

Conclusions

Previous research (Kim et al., 2008) indicates that psychoneurological and gastrointestinal symptoms formed two unique symptom clusters across the treatment trajectory in patients with breast cancer. The analyses reported here were that several demographic and clinical variables were predictive of greater intensity of symptoms for each cluster during treatment. Although these analyses need replication, clinicians can tentatively use the predictive variables of the intensity of the symptom clusters to identify those patients most at risk for experiencing intense symptom clusters during treatment. Researchers should examine other possible predictors and use of predictors for clinical practice and research. The possibility of collective interventions for certain clusters should also be examined.

Clinical Resources

- American Cancer Society: <http://www.cancer.org/>
- National Cancer Institute: <http://www.cancer.gov/>
- Oncology Nursing Society: <http://www.ons.org/>

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Table 1Demographic and Clinical Characteristics of the Sample ($N = 282$)

Variables	Number of patients (%)
Age (mean years $\pm$ SD)	55.21 ($\pm$ 12.1)
Race	
White	258 (91.5)
Non-white	24 (8.5)
Marital status	
Married	198 (70.2)
Not married	79 (28.0)
Missing	5 (1.8)
Employment status	
Employed	138(48.94)
Not employed	144(51.06)
Treatment modality during the study	
Chemotherapy	125 (44.3)
Radiation therapy	157 (55.7)
Disease stage	
Stage 0	25 (8.9)
Stage 1	114 (40.4)
Stage 2	106 (37.6)
Stage 3	27 (9.6)
Stage 4	4 (1.4)
Missing	6 (2.1)
Comorbid condition	
One or more	157 (55.7)
None	124 (44.0)
Missing	1 (0.3)

Summary of Multiple Regression Analyses for Variables Predicting the Intensity of Symptoms in a Psychoneurological Cluster Across Time

Table 2

Variable	Time 1 (N=181)				Time 2 (N=158)				Time 3 (N=139)			
	B	SE B	β	p	B	SE B	β	p	B	SE B	β	p
Intercept	55.79	6.13	0	<.0001	51.54	7.17	0	<.0001	44.57	6.52	0	<.0001
Age	-.20	0.07	-.24	<.01	-.18	.08	-.21	.03	-.09	.08	-.11	.26
Race	4.07	3.50	.08	.25	4.49	3.25	.10	.17	3.10	2.67	.09	.25
Marital status	-1.79	1.56	-.08	.25	.87	1.74	.04	.62	-2.31	1.62	-.11	.16
Employment status	-.81	1.44	-.04	.57	-.40	1.64	-.02	.81	1.22	1.59	.06	.45
Physical performance	5.29	.83	.43	<.0001	5.38	.96	.41	<.0001	5.38	.89	.44	<.0001
Comorbid conditions (total number)	1.37	.80	.12	.09	.99	.90	.09	.27	1.36	.91	.12	.14
Treatment modality ^a	-1.77	1.32	-.08	.18	.10	1.58	.01	.95	7.13	1.57	.35	<.0001
R ²	.25				.22				.33			
Adjusted R ²	.22				.19				.29			
F	8.38 <.0001				6.21 <.0001				9.23 <.0001			

Note.

^a disease stage, instead of treatment modality, was used at Time 1. Coding system for the binary variables: Race: White=1, Non-white=0; Marital status: married=1, not married=0; Employment status: employed=1, not employed=0; Treatment modality: chemotherapy=1, radiation therapy=0.

Summary of Multiple Regression Analyses for Variables Predicting the Intensity of Symptoms in an Upper Gastrointestinal Cluster Across Time

Table 3

Variable	Time 2 (N=157)				Time 3 (N=140)			
	B	SE	B	p	B	SE	B	p
Intercept	47.57	5.12	0	<.0001	49.25	4.98	0	<.0001
Age	-.13	.06	-.17	.03	-.13	.05	-.18	.02
Race	1.77	2.50	.04	.48	4.65	1.92	.15	.02
Marital status	1.27	1.32	.06	.34	-1.08	1.22	-.06	.38
Employment status	-.08	1.21	-.004	.95	-1.92	1.17	-.11	.10
Physical performance	1.25	.73	.10	.09	2.02	.66	.19	<.01
Comorbid conditions ^a	.10	.68	.01	.88	-.52	1.15	-.03	.65
Treatment modality	11.62	1.19	.61	<.0001	11.86	1.15	.66	<.0001
R ²	48				51			
Adjusted R ²	46				48			
F	19.62				19.67			

Note. Coding system for the binary variables: Race: White=1, Non-white=0; Marital status: married=1, not married=0; Employment status: employed=1, not employed=0; Treatment modality: chemotherapy=1, radiation therapy=0;

^a Comorbid condition in the Time 2 regression models was entered as continuous variables (the total number of comorbid conditions). However, at Time 3, the regression model was best when a comorbid condition was entered as a binary variable (comorbid vs. non-comorbid).

Table 4**Symptom Clusters and Their Significant Independent Predictors Across Time**

	Time 1	Time 2	Time 3
Psycho-neurological Cluster	Depressed mood Cognitive disturbance Fatigue Insomnia Pain	Depressed mood Cognitive disturbance Fatigue Insomnia Pain Hot flashes	Depressed Cognitive disturbance Fatigue Insomnia Pain
Significant Predictors	-Age -Baseline physical performance	-Age -Baseline physical performance status	-Baseline physical performance status -Treatment modality
Upper gastrointestinal Cluster		Nausea Vomiting Decreased appetite	Nausea Vomiting Decreased appetite
Significant Predictors		-Age -Treatment modality	-Age -Treatment modality -Race -Baseline physical performance status