ONLINE EXCLUSIVE

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Pain, Sleep Disturbance, and Fatigue in Patients With Cancer: Using a Mediation Model to Test a Symptom Cluster

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Purpose/Objectives: To test whether sleep disturbance mediates the effect of pain on fatigue.

Design: Cross-sectional.

Setting: Radiation therapy clinic, oncology ambulatory clinic, and inpatient oncology unit in an urban teaching hospital.

Sample: 84 patients with cancer with multiple primary diagnoses who were experiencing pain. Fifty-three percent were female and 92% were Caucasian, with a mean age of 54 years.

Methods: All participants completed a symptom questionnaire that included the Brief Pain Inventory–Short Form, the Pittsburgh Sleep Quality Index, and the fatigue subscale of the Profile of Mood States questionnaire. Multistage linear regression was used to test a mediation model.

Main Research Variables: Fatigue, pain, and sleep disturbance.

Findings: Mediation analyses indicate that pain influences fatigue directly as well as indirectly by its effect on sleep. About 20% (adjusted $R^2 = 0.20$) of the variation in fatigue is explained by pain. Thirty-five percent of the variance in fatigue explained by pain was accounted for by the mediation pathway.

Conclusions: Some of the effect of pain on fatigue is mediated by sleep disturbance, but pain has a direct effect on fatigue as well.

Implications for Nursing: Although the relationship can be explained only partially by the commonsense point of view that people who are in pain lose sleep and naturally report more fatigue, this finding is important and leads to a potential intervention opportunity. Strategies to improve sleep by better pain management may contribute to decreased fatigue.

Key Points . . .

- ➤ Pain is related significantly to fatigue in individuals experiencing cancer pain.
- ➤ Although some of the effect of pain on fatigue is mediated by sleep disturbance, pain has a direct effect on fatigue as well.
- ➤ Strategies to improve sleep by effectively managing pain may decrease fatigue.

Unrelieved symptoms significantly affect quality of life for individuals with cancer. Much of the research to date has focused on single symptoms, yet most patients with cancer experience more than one symptom at a time. Pain, sleep disturbance, and fatigue are three of the most common symptoms; however, the relationship among these variables has not been studied fully. Two models regarding the association among these three constructs could be proposed. First, individuals who are in pain sleep less and show greater fatigue. Second, pain and fatigue are related but independent of sleeplessness. In this second model, pain has a role in fatigue that is above and beyond the relationship between sleeplessness and fatigue. This article examines the symptom cluster of pain, sleep disturbance, and fatigue in a sample of 84 patients with cancer-related pain who participated in a study to examine the symptom experience.

Background

In oncology, the study of symptoms has focused primarily on single symptoms, overall symptom burden, and, more recently, symptom pairs. Yet, experienced oncology specialists know that individuals undergoing cancer therapy often experience multiple symptoms of different origin, pattern, and duration. Recent work (Dodd, Miaskowski, & Lee, 2004; Dodd, Miaskowski, & Paul, 2001) has helped to refocus the study of cancer symptoms on "symptom clusters." However, although patients with cancer seem to experience clusters of symptoms, the research into cancer symptoms has not

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progressed to a point where healthcare providers know why cancer symptoms form aggregates or clusters or what underlying processes cause symptoms to coexist.

In other healthcare arenas, the examination of symptom clusters has been useful in the diagnosis and treatment of syndromes. For example, premenstrual symptoms have been shown to form clusters that vary across the menstrual cycle, distinguishing among women with and without premenstrual problems (Woods, Mitchell, & Lentz, 1999). With regard to chronic pain, individuals with varying symptom patterns have been shown to benefit from different approaches to therapy (Geisser, Perna, Kirsch, & Bachman, 1998).

In oncology, the study of multiple symptoms is complicated by differences in the origin of specific symptoms. Some symptoms are disease related, whereas others are related specifically to treatment. For example, nausea and vomiting might be caused by a bowel obstruction or chemotherapy. Other symptoms may be related to disease and treatment (e.g., fatigue), whereas still others result from noncancer comorbidity (e.g., pain caused by arthritis). Finally, the possibility exists that one or more symptoms could cause another symptom (e.g., sleep disturbance could cause fatigue).

Given the complexity of cancer symptoms, bivariate correlational models alone are unlikely to adequately describe the nature of the relationships among them or lead to an understanding of which processes lead to the clustering of symptoms. Others have used multiple regression and factor analysis as approaches to exploring the complexity of these relationships (Dodd et al., 2001; Gift, Jablonski, Stommel, & Given, 2004). An alternate approach is to use more complex path analysis models such as "mediation" (Baron & Kenny, 1986) modeling, in which one symptom is proposed to influence another symptom through its relationship to a third symptom or factor. A move from bivariate descriptive models to more complex explanatory models could yield important information about the nature of the relationships among symptoms and suggest new avenues for symptom management (Beck, 2004).

Fatigue

Fatigue has been described as the most frequent problem related to cancer and its treatment (Lawrence, Kupelnick, Miller, Devine, & Lau, 2004). Fatigue is distressing and interferes with quality of life regardless of diagnosis, treatment, or prognosis (Nail, 2002). Cancer-related fatigue has profound effects on patients' ability to function in usual roles and activities, causes delays in treatment, can linger for months or years, and may be predictive of shorter survival in certain cancer populations (Patrick et al., 2003; Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003).

Insomnia and Sleep Disturbance

Insomnia is defined as difficulty initiating or maintaining sleep or as nonrestorative sleep causing clinically significant distress or impairment of social, occupational, or other areas of functioning. Insomnia may include increased sleep latency (defined as time to fall asleep), reduced sleep efficiency (defined as time asleep or total time in bed), or increased number and duration of awakenings (American Sleep Disorders Association, 1990; Morin, 1993). Sleep disturbance indicates the degree to which sleep may be disrupted by environmental and personal factors. The prevalence rates for nocturnal sleep-wake disturbances range from 31%–75% among people with cancer (Clark, Cunningham, McMillan, Vena, & Parker, 2004). In a telephone survey of 150 outpatients with cancer, 44% reported insomnia in the prior month (Engstrom, Strohl, Rose, Lewandowski, & Stefanek, 1999). The most common problem was awakening during the night (90%) or sleep disturbance. Sleeping fewer hours (85%) and difficulty returning to sleep (75%) also were prevalent. Differences in prevalence may be related to type of cancer and, for a significant proportion of patients, may exist prior to diagnosis (Clark et al., 2004).

Pain

Pain is experienced by patients undergoing cancer treatment as well as those with advanced disease. Approximately 33%–50% of patients with cancer experience pain at some time during the course of their illness; rates are higher in the palliative care setting (McGuire, 2004). A majority (62%) of people receiving treatment for bone metastases reported going to sleep at night with moderate to severe pain (Miaskowski & Lee, 1999). The prevalence of pain in specific populations includes 10%–12% of older adults with cancer during a one-year period (Given, Given, Azzouz, Kozachik, & Stommel, 2001), 29% of women with lung cancer (Sarna, 1993), and 54% of a mixed cancer population (Glover, Dibble, Dodd, & Miaskowski, 1995). Average ratings of pain were moderate (Gaston-Johansson, Fall-Dickson, Bakos, & Kennedy, 1999; Glover et al.; Miaskowski & Lee; Sarna).

Fatigue and Insomnia

Several studies have documented a correlation between fatigue and insomnia in patients with cancer (Broeckel, Jacobsen, Horton, Balducci, & Lyman, 1998; Carpenter et al., 2004; Hann et al., 1997; Jacobsen et al., 1999; Longman, Braden, & Mishel, 1999). In people treated with radiation therapy for bone metastases, Miaskowski and Lee (1999) found that improvement in fatigue from evening to morning was associated with higher total sleep time, decreased nighttime awakening, and better sleep efficiency. Berger and Farr (1999) found that less active women with breast cancer who took more naps and had more nighttime awakenings had higher levels of fatigue. These findings suggest that insomnia, and sleep disturbance in particular, could be a cause of fatigue in patients with cancer.

Fatigue and Pain

Evidence also is accumulating of an association between fatigue and pain. A weak to moderate correlation between fatigue and pain has been demonstrated (Dodd et al., 2001; Glover et al., 1995). Given et al. (2001) found that pain and fatigue were independent and additive predictors of symptom burden. Patients who had fatigue and pain reported a greater number of symptoms than those who had fatigue or pain alone or those reporting neither symptom.

Insomnia and Pain

Only one study examined insomnia and pain in patients with cancer. Miaskowski and Lee (1999) reported that 62% of their sample indicated having moderate or severe pain; 75% had decreased sleep efficiency (using a wrist actigraph measure). However, the relationship between these two symptoms was not reported.

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Pain, Fatigue, and Sleep Insufficiency

Dodd et al. (2001) studied the symptom cluster of pain, fatigue, and sleep insufficiency in 93 patients with cancer. They used a hierarchical multiple regression approach and found that age, pain, and fatigue explained 48% of the variance in functional status. Sleep insufficiency was not a significant factor. A limitation of the study was that symptom measures were restricted to individual items on a quality-of-life instrument. Gift et al. (2004) used a factor analytic approach in patients with lung cancer; the symptom cluster of pain, sleep disturbance, and fatigue did not emerge as a factor.

Summary

Together, these studies demonstrate the authors' initial understanding of the problem of symptom clusters in a mixed group of patients with varying diagnoses, treatment regimens, and stages of disease. All provided some evidence to support the association among two or more symptoms. However, previous research has not addressed a most crucial question: What is the nature of the relationship among a group of commonly experienced symptoms? This limitation also is reflected in the current stage of existing conceptual models. The Symptoms Experience Model (Armstrong, 2003), the Theory of Unpleasant Symptoms (Lenz & Pugh, 2003), and the Explanatory Model of Fatigue (Berger & Walker, 2001) provide a framework for the study of multiple symptoms. Within these models, an individual may experience multiple symptoms at one time, each with varying levels of severity. Symptoms may be multiplicative in nature and may act as catalysts for the occurrence of other symptoms. These mid-range theories propose that symptoms are related but generic; they do not specify any symptoms or any order to their relationship. The current study thus builds on mid-level theory but adds the specificity of systematically examining the pattern of relationships among three commonly reported symptoms in patients with cancer: pain, sleep disturbance, and fatigue. Fatigue is known to be the most prevalent symptom, yet pain, sleep disturbance, or both could cause fatigue. This information would be useful in targeting an intervention appropriately to the root cause. An additional possibility is that one symptom could affect another symptom indirectly through the mediating effect of a third symptom. In this article, the authors will examine the proposition that pain increases fatigue severity by causing sleep disturbance. In this case, resolving or reducing fatigue and sleep disturbance would require improved pain management.

Purpose

The aims of this study were to (a) examine the relationships among three symptoms—pain, sleep disturbance, and fatigue, (b) determine to what extent pain intensity affects sleep disturbance and fatigue, and (c) test whether sleep disturbance mediates the effect of pain on fatigue.

Methods

Design

This cross-sectional study was designed to evaluate the relationships among common symptoms experienced by individuals with cancer and used a prospective, consecutive sampling approach. The study was approved by an institutional review board. Completion of a symptom questionnaire implied voluntary consent to participate.

Sample and Setting

All patients who were receiving care in three settings (outpatient oncology, radiation therapy, and inpatient oncology) at the University of Utah during a designated time period were screened for study eligibility and invited to complete a questionnaire designed to assess their symptom experience.

Measures

A symptom questionnaire was comprised of several tools with established psychometric properties. All tools were framed within the context of "the past week."

Pain: The symptom questionnaire included the **Brief Pain Inventory–Short Form (BPI)**, a self-report tool that is used widely to measure pain (Daut, Cleeland, & Flanery, 1983). The BPI is brief and easy to complete (Serlin, Mendoza, Nakamura, Edwards, & Cleeland, 1995). The World Health Organization adopted the BPI to evaluate the effectiveness of national cancer pain relief programs. The intensity subscale of the BPI consists of four items that ask patients to rate their pain intensity as worst pain, least pain, and average pain in the past week, as well as pain now. Each item is rated on a scale from 0 (no pain) to 10 (the worst pain imaginable).

Evidence exists to support the reliability and validity of the BPI. Test-retest reliability of the worst pain scale was 0.93 over a two-day period in a sample of 20 hospitalized patients with cancer. Internal consistency for the intensity scale was an alpha of 0.87 (Lin & Ward, 1995; Serlin et al., 1995). In the current study's sample, the Cronbach's alpha for the BPI was 0.875.

Sleep: The **Pittsburgh Sleep Quality Index (PSQI)**, a self-report questionnaire that assesses sleep quality and quantity, was used to measure sleep. The original version was designed to measure sleep reports during a one-month interval (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The 19-item self-report questionnaire yields seven component scores: subjective sleep quality, sleep latency, duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. A sleep disturbance score is computed by taking the sum of 10 items that assess the degree to which a variety of factors have interfered with sleep.

The PSQI has reliability and validity when used in older adults (Buysse et al., 1991; Gentili, Weiner, Kuchibhatla, & Edinger, 1995), bereaved spouses (Reynolds et al., 1993), patients with panic disorder (Stein, Chartier, & Walker, 1993), and patients with phobias (Stein, Kroft, & Walker, 1993). A Cronbach's alpha of 0.83 was reported for the Global Sleep Quality Scale. Psychometric evaluation of the PSQI in this sample and another sample of patients with cancer undergoing treatment supported its internal consistency reliability and construct validity (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004). In this sample, Cronbach's alpha was 0.81 for the Global Sleep Quality Scale and 0.69 for the Sleep Disturbance Scale.

Fatigue: The **Profile of Mood States (POMS)** (McNair, Lorr, & Droppleman, 1992) is a 30-item adjective checklist with subscales that measure six dimensions of mood: tension-anxiety, depression-dejection, anger-hostility, vigor, fatigue-inertia, and confusion-bewilderment. Each item is rated from 1–5. In this research, the five items on the fatigue scale were used as a measure of fatigue. Six independent-factor analytic studies have been conducted in the development and validation of the POMS (McNair et al.). Meek et al.'s (2000) findings for the fatigue subscale with patients with cancer showed

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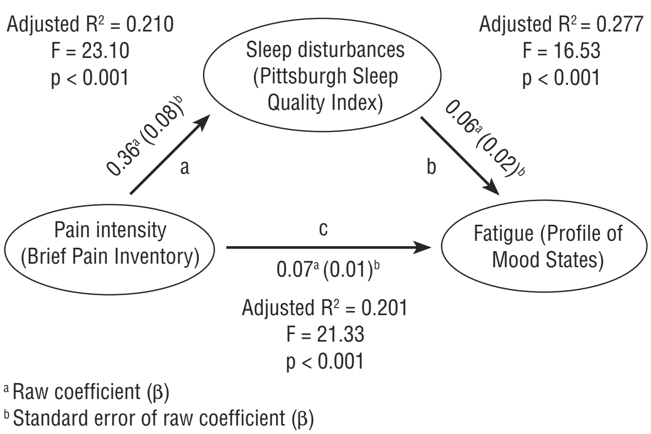

Figure 1. Test of the Mediation Model

a Cronbach's alpha of 0.91. In the current study's sample, the Cronbach's alpha was 0.925.

Analysis

Data were analyzed with SPSS® version 11.0 (SPSS Inc., Chicago, IL). Analysis included summary statistics to examine the range, distribution, mean, and standard deviation for each subscale. Relations among symptoms were evaluated with bivariate correlations. To evaluate the effect of pain on fatigue and sleep with analysis of variance (ANOVA), the mean pain intensity score was recoded using the following categories: 1–4 = mild pain (1), 5–6 = moderate pain (2), and 7–10 = severe pain (3).

The mediation pathway from pain to fatigue through sleep disturbance was tested as recommended by MacKinnon (1994). MacKinnon's model is an extension of the three-step model proposed by Baron and Kenny (1986) and Judd and Kenny (1981). This multistage linear regression model of testing mediation (see Figure 1) includes four tests.

1. Pain is associated with fatigue (path c).
2. Pain is associated with sleep disturbance (path a).
3. When controlling for pain, sleep disturbance is associated with fatigue (path b), and the association between pain and fatigue (path c) is either no longer statistically significant (full mediation) or reduced significantly (partial mediation).
4. A statistically significant indirect path exists between pain and fatigue through sleep disturbance.

In practice, healthcare providers typically find evidence of partial mediation—that is to say, that in step 3 above, the association between pain and fatigue remains statistically significant but is reduced by a statistically significant amount. MacKinnon's (1994) expanded model allowed the authors to test the mediation effect in the face of partial mediation.

$$t_{a*b} = \frac{a*b}{se_{ab}}$$

Where

$$se_{a*b} = \sqrt{(a^2*seb^2) + (b^2*sea^2)}$$

Figure 2. Sobel Test Equation

The fourth step provides a statistical test that the indirect path is greater than zero. It sometimes is referred to as the "Sobel Test" and is computed as a t test (see Figure 2).

This four-step process was conducted using SPSS programming developed by Dudley, Benuzillo, and Carrico (2004). This programming tests the mediation effect and the proportion of variance that can be attributed to the mediation effect.

Findings

Sample

Of those who were eligible, 214 patients in the following areas consented to participate: radiation therapy (n = 81), outpatient oncology clinic (n = 86), and inpatient oncology

Table 1. Demographic Characteristics of the Sample and Subgroup With Pain

	Total Sample (N = 214)		Patients With Pain (N = 84)	
Characteristic	**n**	**%**	**n**	**%**
Gender				
Male	107	51	39	47
Female	103	49	44	53
Missing	4	–	1	–
Race or ethnicity				
African American	1	1	1	1
Asian/Pacific Islander	3	1	–	–
Native American	5	2	2	2
Hispanic	7	3	4	5
Caucasian	193	92	76	92
Missing	5	–	1	–
Marital status				
Single	28	13	11	13
Married or living with a partner	142	68	55	67
Separated or divorced	21	10	10	12
Widowed	18	9	6	7
Missing	5	–	2	–
Education				
0–11 years	19	9	9	11
High school graduate	57	27	23	28
Some college or technical school	72	35	30	37
College graduate	28	14	7	9
Postgraduate	32	15	13	16
Missing	6	–	2	–
Employment status				
Full-time	53	25	16	20
Part-time	11	5	4	5
On sick leave or disability	36	17	21	26
Retired	70	33	26	32
Not employed outside the home	40	19	15	18
Missing	4	–	2	–
Net family income ($)				
Less than 14,999	42	23	21	28
15,000–34,999	46	25	20	27
35,000–69,999	59	32	22	29
More than 70,000	36	20	12	16
Missing	31	–	9	–
Age (years)				
$\bar{X}$	53.15		54.49	
SD	16.57		15.48	

Note. Because of rounding, not all percentages total 100.

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Table 2. Clinical Characteristics of the Sample and Subgroup With Pain

	Total Sample (N = 214)		Patients With Pain (N = 84)	
Characteristic	**n**	**%**	**n**	**%**
Type of cancer				
Breast	41	19	13	16
Lymphoma or leukemia	41	19	12	14
Prostate, testicular, or bladder	28	13	6	6
Lung	14	7	5	6
Gastrointestinal (colorectal, esophagus, pancreas)	14	7	5	6
Head and neck	10	5	7	8
Melanoma	11	5	6	7
Cervical or ovarian	9	4	7	8
Other	46	22	23	27
Extent of disease				
Local	27	14	10	13
Regional	72	39	23	30
Advanced	88	47	44	57
Missing	27	–	7	–

Note. Because of rounding, not all percentages total 100.

unit (n = 47). The study demographic characteristics are summarized in Table 1. Participants were 49% female with ages ranging from 14–88 years and a mean age of 53. Racial and ethnic diversity was limited; 92% were Caucasian, which was reflective of the state's population at that time. All were English speaking. Of these 214 participants, 84 (39%) were experiencing pain and completed the pain instrument included in the questionnaire. The sample of patients with pain was 53% female and 92% Caucasian and ranged in age from 17–82 with a mean of 54. The patients had multiple types of cancer primary diagnosis (see Table 2). Of the patients with pain, 57% had advanced disease as compared to 40% of those without pain. A chi-square test of association indicated that this was borderline significant ($p = 0.07$). No significant differences existed between the patients with pain and the remaining sample on any demographic characteristics.

Summary statistics for the three symptom measures are included in Table 3. The range of scores was acceptable, and adequate variance existed in the responses.

Relationship Among Pain, Sleep Disturbance, and Fatigue

Bivariate Pearson correlations were used to evaluate relationships among symptom variables. A positive correlation existed among pain and fatigue, pain and sleep disturbance, and fatigue and sleep disturbance. The correlations all were statistically significant and moderate in strength, ranging from 0.46–0.47 (see Table 4).

Pain Intensity Effects on Sleep and Fatigue

Two separate one-way ANOVA were performed with categorized pain (mild, moderate, or severe) as the independent variable and fatigue and sleep disturbance as dependent variables (see Figures 3 and 4 and Table 5). Pain level had a significant effect on fatigue ($F[2, 79] = 6.17$, $p < 0.001$) and on sleep ($F[2, 81] = 9.72$, $p < 0.001$). Scheffé tests ($p = 0.05$) showed that those with severe pain had significantly higher fatigue and sleep disturbances than those with mild pain.

Sleep Disturbance Mediation of the Effect of Pain on Fatigue

The results are provided in Figure 1. The results indicate that in step 1, pain was significantly associated with fatigue (path c): $F(1, 80) = 21.33$, $p < 0.001$. About 20% (adjusted $R^2 = 0.201$) of the variation in fatigue is explained by pain.

In step 2, pain was significantly associated with sleep disturbance (path a): $F(1, 82) = 23.10$, ($R^2 = 0.210$), $p < 0.001$. In step 3, when controlling for pain, sleep disturbance was significantly associated with fatigue (path b): $F(2, 79) = 16.53$, ($R^2 = 0.277$), $p < 0.001$. Finally, step 4, the Sobel test, was significant ($p = 0.011$), indicating that sleep disturbances partially mediated the relationship between pain and fatigue. Thirty-five percent of the variance in fatigue explained by pain was accounted for by the mediation pathway. This role of sleep disturbance as a mediator between pain and fatigue indicates that one reason pain is related to fatigue is because sleep disturbance partially mediates the relationship between pain and fatigue. In other words, patients who experience pain also experience fatigue; however, this relationship between pain and fatigue was because, at least partially, pain led to sleep disturbances that, in turn, led to fatigue.

Discussion

Three symptoms that are reported commonly during the cancer experience were selected for this analysis: pain, sleep disturbance, and fatigue. The first aim was to examine the bivariate relationships among the three symptoms. These relationships were positive, statistically significant, and moderate in strength. Thus, an increase in any one symptom was associated with an increase in the others. These results add evidence to the positive relationships reported by others (Broeckel et al., 1998; Dodd et al., 2001; Glover et al., 1995; Hann et al., 1997; Jacobsen et al., 1999; Longman et al., 1999).

The second aim was to determine to what extent pain intensity affects sleep disturbance and fatigue. Using a model in which pain was viewed as an independent variable, significant increases existed in fatigue and sleep disturbance as pain intensity categorically increased from mild to moderate to severe. This specific approach to conceptualizing and analyzing the effect of pain is new and the linear relationship is impressive. The

Table 3. Symptom Scale Scores

Scale	N	Minimum	Maximum	Possible Range	$\bar{X}$	SD
Sum of Brief Pain Inventory pain intensity	84	1	33	0–40	16.23	7.17
Sum of fatigue (Profile of Mood States)	82	5	25	5–25	16.50	5.45
Sum of the Pittsburgh Sleep Quality Index sleep disturbances	84	0	23	0–30	13.07	5.57

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Table 4. Bivariate Relationships Among Pain, Fatigue, and Sleep Disturbance

Scale	Pearson Correlation	p (Two-Tailed)	N
Sum of Brief Pain Inventory (BPI) pain with sum fatigue (Profile of Mood States [POMS])	0.459	0.000	82
Sum of BPI pain with sum sleep disturbances	0.469	0.000	84
Sum fatigue POMS with sum sleep disturbances	0.474	0.000	82

mechanism by which pain contributes to fatigue is not known, but the influence of pain on sleep is much more explainable given that it would serve as a counter-stimulus and significant discomfort might keep someone from falling asleep or wake them from their sleep. The clinical significance of these findings is that relieving pain is an important strategy to improving sleep and reducing fatigue. These findings lead directly to the third aim of the study—to examine whether the effect of pain on fatigue is mediated through its effect on sleep.

The results of the mediation analysis indicate that pain directly influences fatigue and indirectly influences fatigue by its effect on sleep. In a full mediation model, the direct effect of pain on fatigue would have become insignificant when the role of sleep was added to the model. The model demonstrates only partial mediation because the path between pain and fatigue (path c) stays significant in the full model. Thus, although some of the effect of pain on fatigue clearly passes through sleep, pain has a direct effect on fatigue as well. Although the relationship can be explained only partially by the commonsense point of view that people who are in pain lose sleep and naturally report more fatigue, this finding is important and leads to a potential intervention opportunity. Strategies to improve sleep by improved pain management may contribute to decreased fatigue. Research to test such intervention strategies in a prospective way is recommended. In addition, research to evaluate the alternative mechanisms by which pain directly causes fatigue is needed. Finally, considerable variance in fatigue exists that is not explained in a three-symptom cluster model. Testing of alternative models and more complex approaches that include additional variables will increase future knowledge of the complex human experience of multiple symptoms associated with cancer and its treatment.

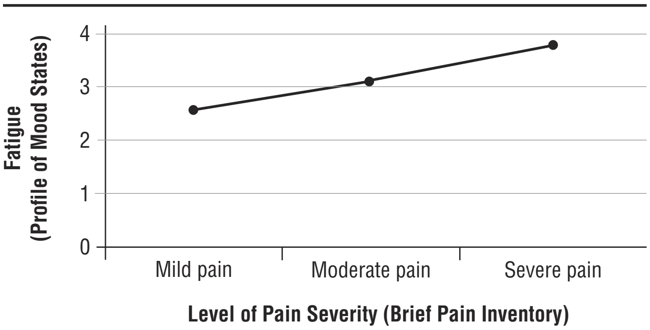

Figure 3. Plot of Means: Effect of Pain on Fatigue

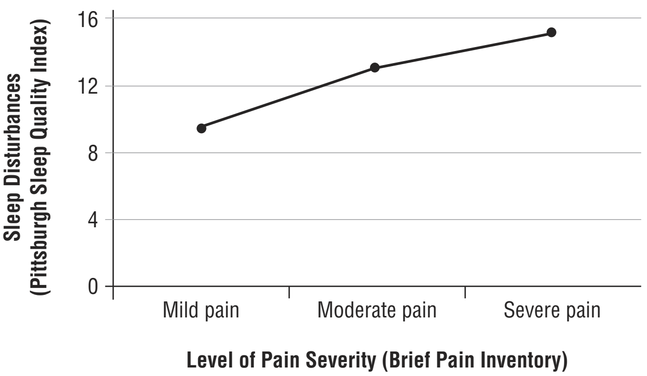

Figure 4. Plot of Means: Effect of Pain on Sleep Disturbance

The study is limited by the cross-sectional nature of its design. Future research that is longitudinal with attention to understanding the temporal relationships among these symptoms is indicated. For example, the effect of pain on sleep disturbance may be fairly immediate, whereas the effect on fatigue may be concurrent or may lag. Research that includes frequent measures of each symptom is recommended. The study sample was very heterogeneous, including many diagnoses, three settings, and patients at varying stages in the treatment trajectory. Subgroup samples were too small to include in the analysis. This analysis should be repeated in samples that are more homogeneous in regard to diagnosis and treatments because symptom profiles may be quite different based on these variables. Self-report measures that are specific to each symptom were used. The use of measures more specific to cancer populations, such as the Schwartz Cancer Fatigue Scale, and other types of sleep measures such as actigraphy are recommended.

Another limitation of this three-symptom model is that it did not use other variables that may account for fatigue, such as the effects of chemotherapy, which might jointly affect pain and fatigue. Other models could be proposed that include variables such as the contribution of age, comorbidities, or length of hospital stay as well.

Summary

Symptoms in individuals with cancer may have complex relationships with one another that need to be considered in symptom management research and practice. The findings from this study provide additional support for the concept

Table 5. Results of Analysis of Variance of Effect of Pain (Recoded) on Fatigue and Sleep Disturbance*

Groups' Pain Intensity Recoded	$\bar{X}$ Fatigue (POMS 1 = Low to 5 = High)	$\bar{X}$ Sleep Disturbances (PSQI 0 = Low to 30 = High)
Mild pain	2.44	9.34
Moderate pain	3.08	12.81
Severe pain	3.80	15.06

* $p < 0.001$

POMS—Profile of Mood States; PSQI—Pittsburgh Sleep Quality Index

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of a symptom cluster in which three symptoms—pain, sleep disturbance, and fatigue—are interrelated (Dodd et al., 2001). The study also provides an example for how to examine a symptom cluster using mediation analysis. This conceptual and analytic approach can serve to evaluate other symptom clusters in which one symptom may mediate the relationship between two other symptoms. Such studies can contribute to the development of more specific, microlevel theories related to symptom clusters.

If an initial symptom is directly or indirectly related to other symptoms, all need to be accounted for to conduct effective symptom management. In this case, evidence supports the direct and indirect (via sleep) effect of pain on fatigue. All three symptoms need to be addressed in the symptom management plan. If attention is given to fatigue and pain without addressing sleep disturbance, symptom management will be less optimal. Multifocused symptom management likely will have the greatest beneficial effect.

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