The Effects of Health State, Hemoglobin, Global Symptom Distress, Mood Disturbance, and Treatment Site on Fatigue Onset, Duration, and Distress in Patients Receiving Radiation Therapy

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Purpose/Objectives: To describe the fatigue experience of patients with cancer receiving radiation therapy and determine to what extent diverse correlates of fatigue affect fatigue onset, duration, and distress.

Design: Descriptive correlational study completed by secondary data analysis.

Sample/Setting: Data were obtained from 384 subjects recruited from two urban, university-affiliated, radiation oncology clinics located in a large, Midwestern city.

Methods: The effects of health indicators and treatment site on fatigue onset, duration, and distress were examined using correlational analyses and analyses of variance.

Main Research Variables: Hemoglobin, health status, global symptom distress, mood disturbance, treatment site, and fatigue onset, duration, and distress.

Findings: Fatigue started near the middle of the second week of treatment, was moderately distressing, and lasted approximately 32 days. Higher levels of health and hemoglobin at the start of therapy were associated with a delayed onset, shorter duration, and lower levels of fatigue distress. In contrast, higher pretreatment levels of global symptom distress and mood disturbance were associated with an earlier onset, longer duration, and greater severity of fatigue distress.

Conclusion: The fatigue experience in patients undergoing radiation therapy is highly individualized. Variations in the health states of patients as well as the area of the body being treated can influence fatigue onset, duration, and distress.

Implications for Nursing: Pretreatment screening for fatigue and its correlates is needed to identify patients at risk for an earlier onset, longer duration, and more distressing fatigue.

Key Points . . .

➤ Little is known about the fatigue experience of patients with cancer who are receiving radiation to different areas of the body.

➤ Knowing what factors affect fatigue onset, duration, and severity of distress can help nurses adjust the timing and content of patient teaching.

➤ Pretreatment screening is needed to identify patients who are vulnerable to early onset, longer duration, and more distressing fatigue because of poor health, low hemoglobin, mood disturbance, or symptom distress.

Fatigue is a commonly reported and distressing side effect of radiation therapy (Munro & Potter, 1996; Oberst, Hughes, Chang, & McCubbin, 1991; Portenoy, Thaler, Kornblith, Lepore, & Fiedlander-Klar, 1994). Providing care to patients experiencing fatigue requires that nurses have, at least, accurate general information about the fatigue experience, including its onset, duration, and severity of distress. This general level of knowledge can be made more specific by understanding further how factors in people and their environments affect the symptom experience. Diverse factors, such as hemoglobin, health state, global symptom distress, mood disturbance, and area of the body being treated, have been examined in relation to fatigue severity, but the effect of these correlates of fatigue on fatigue onset, duration, and distress is virtually unknown. The purposes of this study were to (a) describe the fatigue experience in terms of its onset, duration, and distress in adult patients with cancer being treated with radiation to different areas of the body, and (b) determine to what extent hemoglobin, health status, global symptom distress, mood disturbance, and area of the body being treated influence fatigue onset, duration, and severity of distress.

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Literature Review

Fatigue has been described as a subjective experience of unusual, excessive, or overwhelming tiredness that results in a decreased desire or capacity for mental or physical activity (Mock, 1997). In patients with cancer, fatigue is a pervasive, discouraging, and debilitating symptom that can adversely affect daily functioning, quality of life, health, and personal well-being (Ferrell, Grant, Dean, Funk, & Ly, 1996; Irvine, Vincent, Graydon, & Bubela, 1998; Irvine, Vincent, Graydon, Bubela, & Thompson, 1994; Kobashi-Schoot, Hanewald, van Dam, & Bruning, 1985; Longman, Braden, & Mishel, 1999; Magnan, 2001; Oberst et al., 1991; Vogelzang, Breitbart, Cella, Curt, & Groopman, 1997). The fatigue experienced by patients with cancer differs from the ordinary fatigue of day-to-day living in that it tends to be more severe, more distressing, prolonged, and unrelied by ordinary measures such as sleep and rest (Holmes, 1991; Oberst et al.; Piper, Lindsey, & Dodd, 1987; Richardson & Ream, 1997; Richardson, Ream, & Wilson-Barnett, 1998).

The etiologic mechanisms of cancer fatigue have not been fully elucidated, but it appears to be caused both by the disease and its treatment (Portenoy et al., 1994). Although reports of an association between radiation exposure and fatigue appeared in the literature as early as the late 19th century (Walsh, 1897), the systematic study of fatigue in patients with cancer receiving radiation therapy is still in its infancy. During the last two decades, estimates of fatigue prevalence in this population have ranged from 65%–100% (Graydon, Bubela, Irvine, & Vincent, 1995; Greenberg, Sawicka, Eisenthal, & Ross, 1992; Haylock & Hart, 1979; Hickok, Morrow, McDonald, & Bellg, 1996; Irvine et al., 1998; King, Nail, Kreamer, Strohl, & Johnson, 1985; Kubrictch, 1984).

The onset of fatigue in relation to the start of radiation therapy is not clearly delineated (Glaus, 1993; Irvine et al., 1994; King et al., 1985). Research suggests an early onset, with fatigue starting near the end of the first week or the beginning of the second week of treatment (Greenberg, Gray, Mannix, Eisenthal, & Carey, 1993; Greenberg et al., 1992; Haylock & Hart, 1979; Irvine et al., 1998). The proximity of a recent surgical intervention to the start of radiation therapy has been associated with an earlier onset of fatigue in patients treated for lung cancer (Hickok et al., 1996), but this finding has not been corroborated by studies involving patients undergoing radiotherapy treatment to different areas of the body (breast, cervical, or endometrial) (Irvine et al., 1994).

The fatigue experienced by patients undergoing radiation therapy often extends beyond the treatment period. How far it extends beyond treatment is difficult to say. Evidence from the literature suggests that the area of the body being treated, as well as the size of the treatment field, influence fatigue duration (Devlen, Maguire, Phillips, Crowther, & Chambers, 1987; Fobair et al., 1986; King et al., 1985). Patients with non-Hodgkin’s lymphoma, for example, treated by whole body radiation have reported fatigue lasting as long as one year beyond the end of treatment (Devlen et al.; Fobair et al.). Among women irradiated for breast cancer, two studies have reported a return to baseline levels of fatigue by three months post-treatment (Greenberg et al., 1992; Irvine et al., 1994). On the other hand, patients receiving treatment to different areas of the body, such as the pelvis and thorax, have continued to report fatigue as long as six months post-treatment (King et al.). Also, the literature suggests that patients treated for lung cancer and those irradiated to the head and neck area have a higher incidence and longer duration of fatigue than individuals receiving therapy to other areas of the body (King et al.; Piper et al., 1989). However, the prospective data needed to accurately estimate the duration of fatigue in these seemingly more vulnerable groups have yet to be produced.

Significant relationships between global symptom distress and fatigue, as well as mood disturbance and fatigue, have been reported across a number of studies involving patients with cancer receiving radiation (Blesch et al., 1991; Greenberg et al., 1992; Holmes, 1991; Irvine et al., 1998, 1994; Jamar, 1989; McCorkle & Young, 1987; Mock et al., 1997; Pickard-Holley, 1991; Piper et al., 1989; Visser & Smets, 1998). Also, a relationship between anemia and fatigue has been proposed for patients undergoing different kinds of cancer treatment (Maxwell, 1984), but research to date has failed to demonstrate a significant relationship between these variables when studied in patients with cancer receiving radiation (Blesch et al.; Glaus, 1993; Greenberg et al., 1992; Irvine et al., 1994).

Few studies have examined the effect of treatment site on the fatigue experience. As noted earlier, several studies have linked fatigue duration to the area of the body treated. In addition, Piper et al. (1989) reported that fatigue was more severe for patients with lung cancer than those with breast cancer. However, the effects of treatment site on fatigue onset and distress are virtually unknown.

Methods

Sample and Setting

The research questions for this corollary study were answered by secondary data analysis. The data source, referred to as the parent study, was a longitudinal, controlled clinical trial of nursing interventions designed to enhance self-care knowledge and performance in patients receiving radiation. Data for the parent study were obtained from two university-affiliated, outpatient radiation oncology clinics located in a large Midwestern city. Participants in the parent study were 18 years of age or older, English-speaking, and scheduled to receive a minimum of 20 treatments. Subjects were excluded from the parent study if irradiated to an extremity only or irradiated to the brain with anticipated cognitive compromise. The inclusion/exclusion criteria of the parent study applied to this corollary study, with the added stipulation that subjects reported whether fatigue started or got worse during treatment.

Data Collection

Data collection for the parent study started in April 1995 and ended in December 1999. Data collectors trained in conducting semistructured interviews obtained information on major study variables at five points in time: pretreatment (T1), at the second (T2) and final weeks (T3) of treatment, and again at one month (T4) and three months (T5) post-treatment. Data pertinent to this corollary study were retrieved from the computerized databases of the parent study.

Measurement

Variables in this corollary study included hemoglobin, health state, global symptom distress, mood disturbance, and fatigue.
onset, duration, and distress. Hemoglobin, measured at the start of therapy, ranged from 8.10–17.00 (X = 13.09, SD = 1.59). The mean level for men was about 1 g higher (X = 13.66, SD = 1.62) than the mean level for women (X = 12.64, SD = 1.44), but the means for both men and women were at levels recognized as normal for their gender. Five areas classified the treatment site: head and neck, lung, breast, prostate, and female pelvic area.

Global symptom distress was the level of anguish experienced from a set of commonly reported health complaints. It was assessed using a modified, pretreatment administration of Mood’s Symptoms Scale (Mood, 1994). This instrument uses a 0–2 response format to obtain self-assessments of how bothersome symptoms are across 13 commonly reported health complaints. The three response choices are worded to fit each specific item and correspond essentially to no trouble, some, or a lot. To ensure independence in the measurement of the variables (independent and dependent), this instrument was modified for this study by removing one item that assesses energy. The theoretical range for the modified version was 0–24, with higher scores indicating higher levels of global symptom distress. Scores for the current study ranged from 0–20 (X = 4.53, SD = 3.28). The total score provided an internally consistent measure of global symptom distress with a Cronbach’s alpha of 0.72.

Mood disturbance was measured pretreatment using a shortened version of the Profile of Mood States (POMS) (Mood, 1994). This 14-item instrument was adapted from the 64-item version (McNair, Lorr, & Droppleman, 1971) by the second author to reduce the burden that patients with cancer experienced by answering the longer version. The shortened POMS contains at least one item from each of the original subscales, except vigor and fatigue. The design of the shortened version follows that of the longer one. A 0–4 response format on 14 paired items is used to generate a total score measuring the affective state. The theoretical range is 0–56, with higher scores indicating higher levels of mood disturbance. In the current study, scores ranged from 0–56, with a mean of 7.96 (SD = 9.65). The instrument was internally consistent with a Cronbach’s alpha of 0.95.

Health state was assessed using a pretreatment administration of the Functional Assessment of Cancer Therapy (Cella, Tulsky, Gray, Sarfflan, & Linn, 1993). This quality-of-life measure was used as a proxy to determine health state because it separates aspects of general health unrelated to the cancer experience from dimensions of functioning pertinent to cancer and its treatment. The instrument consists of 27 core items rated on a five-point scale, with lower scores indicating lower levels of functional quality of life. Four dimensions of quality of life are assessed: physical (7 items), social (7 items), emotional (6 items), and functional (7 items). The instrument was modified by removing one item from the physical subscale that measures energy. The theoretical range for the modified version was 0–104. Subjects’ scores ranged from 5–104, with a mean of 79.29 (SD = 15.17). The internal consistency reliability of the modified instrument was 0.87.

Attributes of fatigue—its presence, date of onset, and severity of distress—were measured at the second (T2) and final weeks (T3) of treatment and again at one month (T4) and three months (T5) post-treatment. Fatigue onset was determined by patients’ self-reports and quantified as the number of calendar days from the start of therapy to the first reported day of fatigue. Fatigue duration was calculated based on patients’ self-reports of fatigue onset and cessation and quantified as the actual number of calendar days. Fatigue distress was the level of anguish experienced from fatigue. It was measured by self-report using a five-point Likert-type scale (5 = severe).

Data Analysis

Data were analyzed using SPSS® PC 9 (SPSS, Inc., Chicago, IL). Both descriptive and inferential statistics were used to analyze the data. Inferential statistics included correlational analyses, paired sample t tests, and analyses of variance (ANOVA). In the parent study, subjects were randomly assigned to one of three experimental conditions: a control group, an educational intervention, or an intervention that included education plus contingency contracting. Preliminary ANOVA showed no significant between-group differences in pretreatment hemoglobin, health state, global symptom distress, or mood disturbance or in the level of fatigue distress experienced by subjects randomized to different experimental conditions in the parent study. Therefore, subjects from these different groups were pooled for analysis. Fatigue distress was expected to be at its worst during the final week of treatment; therefore, these final week (T3) measures of fatigue distress were used for correlational analyses and ANOVA. The alpha for statistical significance was set at 0.05.

Results

Sample Characteristics

The 384 subjects in this corollary study included 175 (46%) men and 209 (54%) women ranging in age from 24–87 years (X = 58.94, SD = 11.73). Subjects in the sample were ethnically, educationally, socially, and economically diverse, treated to different areas of the body, and heterogeneous on cancer stage (see Table 1). The greatest number of subjects was treated for breast cancer (n = 143, 37%), followed by prostate cancer (n = 122, 32%). Subjects receiving treatment to one of these two sites comprised 69% of the sample. The remaining 31% of the sample included subjects receiving treatment to the head and neck region (n = 55, 14%), lung (n = 41, 11%), or female pelvic region for cervical or endometrial cancers (n = 23, 6%). Treatment was predominantly for localized cancers (stages 0, I, II), but 68 (18%) of the subjects had regional extension (stage III), and another 48 (12%) of the subjects had distant metastasis (stage IV). Data on cancer staging were not reported for three subjects.

Fatigue Onset, Duration, and Distress

Fatigue onset varied widely. When determined by the number of actual treatment days, using a five-day treatment week, patients reported fatigue onset as early as the first and as late as the 38th day of treatment. The average onset (X = 7.69 treatment days, SD = 6.89) was approximately halfway through the second week of treatment.

Figure 1 shows the daily distribution of fatigue onset during treatment weeks one and two. Reports of onset were greatest on the first treatment day of each week, then peaked on the third and fifth treatment days of each week. Although the average onset of fatigue was near the middle of the second week of treatment, 168 subjects (44%) reported fatigue onset during the first week of treatment, with another 124 (32%) reporting onset by the end of the second week. Thus, three-
quarters (n = 292, 76%) of the subjects reported fatigue onset by the end of the second week of treatment. Notably, 80 (20%) of the subjects reported that fatigue started or got worse by the end of the second week of treatment. Notably, 80 quarters (n = 292, 76%) of the subjects reported fatigue onset by the end of the second week of treatment. On the other hand, two correlates that were negative health indicators were associated with an earlier onset of fatigue, more severe fatigue distress, and a longer duration of fatigue. Global symptom distress was positively and significantly related to fatigue distress (r = 0.20, p < 0.001) and duration (r = 0.11, p = 0.037) but negatively and significantly related to fatigue onset (r = 0.07, p = 0.002). Mood disturbance, like symptom distress, was positively and significantly related to fatigue distress (r = 0.06, p = 0.002) and fatigue duration (r = 0.12, p = 0.014) but negatively and significantly related to fatigue onset (r = 0.02, p = 0.016).

The last correlate to be examined was treatment site. The effect of treatment site on fatigue distress, onset, and duration was evaluated using one-way ANOVAs to compare means on fatigue onset, duration, and severity of distress. The results of this analysis showed that the mean level of fatigue onset did not differ by treatment site (see Table 2). However, the main effect of treatment site was significant for both fatigue duration, F(4, 379) = 3.01, p = 0.018, and fatigue distress, F(4, 379) = 3.01, p = 0.018. Post hoc analyses using a Bonferroni correction (alpha = 0.05) showed that the only significant difference in mean duration was between patients with prostate cancer and those treated for gynecologic cancer (mean differ-
ence = –9.22, p = 0.017), indicating that fatigue duration in patients with gynecologic cancer was longer than fatigue duration in patients with prostate cancer. With respect to fatigue distress, the only significant mean difference (mean difference = –0.63, p = 0.034) was between subjects treated for prostate cancer or lung cancer, indicating that fatigue distress was greater in subjects treated for lung cancer than it was in subjects treated for prostate cancer.

In summary, an examination of the relationship of diverse correlates of fatigue to fatigue onset, duration, and distress demonstrated that correlates indicative of positive health, such as a higher health state and hemoglobin, were associated with a later onset of fatigue, lower levels of fatigue distress, and a shorter duration of fatigue. In contrast, correlates indicative of negative health, such as global symptom distress and mood disturbance, were associated with an earlier onset of fatigue, a longer duration of fatigue, and higher levels of fatigue distress. Also, fatigue distress was more severe in patients treated for lung cancer compared to patients treated for prostate cancer, whereas fatigue duration was greater for women treated for gynecologic cancers compared to men treated for prostate cancer.

### Discussion

Results of this study placed the average onset of fatigue near the middle of the second week of treatment, but a breakdown of onset by treatment week showed that 43% of the subjects actually reported fatigue onset during the first week of treatment. Thus, for a percentage of patients, fatigue started earlier in the treatment trajectory than what might be expected based on the aggregate findings and reports from the literature. This early onset for fatigue may have been a function of the timing of measurement. In the parent study, the first symptom interview occurred between the 8th and 12th day of treatment. Consequently, errors of recall regarding the onset of fatigue were likely to be less in the parent study than in studies using assessment points further removed from the start of treatment. On the other hand, the fact that 80 subjects (20% of the sample) reported that fatigue started or got worse on the very first day of treatment raises questions about the etiologic mechanisms of fatigue in patients with cancer receiving radiation.

The physiologic mechanisms of a so-called “radiation-induced fatigue” have not been fully elucidated. Therefore, it is difficult to know whether patients reporting fatigue on the very first day of treatment started therapy with a baseline fatigue as a result of other causes or were especially vulnerable to the “fatigue-inducing” effects of radiation, or both. Although it seems clear that a search for the etiologic mechanisms underlying this more immediate experience of fatigue is warranted, it seems equally clear that clinicians and researchers need be alerted to the fact that a substantial percentage (20%) of patients in this sample experienced fatigue on the very first day of treatment.

An exploration of the influential effects of symptom distress and mood disturbance on fatigue demonstrated that higher levels of the former correlated with higher levels of the latter. The magnitudes of these correlations were small (0.10–0.20), which is consistent with reports from the literature regarding the relationship between global symptom distress and fatigue severity (Irvine et al., 1998, 1994) and mood disturbance and fatigue severity (Irvine et al., 1998, 1994; McCorkle & Young, 1987; Mock et al., 1997).

Results of the current study demonstrated that both symptom distress and mood disturbance had a small but significant negative relationship with fatigue onset. This suggested that higher pretreatment levels of symptom distress and mood disturbance were risk factors for an earlier onset of fatigue.

Findings of the current study demonstrated that hemoglobin correlated negatively with fatigue distress and positively with fatigue onset. These findings suggested that lower levels of hemoglobin were consistent with higher levels of fatigue distress and an earlier onset of fatigue. Differences in the findings of this study compared to the findings of others (Blesch et al., 1991; Glaus, 1993; Greenberg et al., 1992; Irvine et al., 1994) and may be accounted for, in part, by the fact that different dimensions of fatigue (distress versus severity) were being examined. Also, in the studies previously mentioned, power to detect an effect may have been limited because of small sample sizes (N < 110). In the current study, intercorrelations between hemoglobin and attributes of fatigue were examined among 303 subjects, a sample size large enough to detect a small to medium effect with power of 0.97 (p = 0.05).

An exploration of the influence of initial health status on fatigue demonstrated that it correlated positively with fatigue onset but negatively with fatigue distress. This suggested that starting radiation therapy in a better state of health was associated with a delayed onset of fatigue and lower levels of fatigue distress.

Few studies have examined the relationship between the area of the body being treated and fatigue onset, duration, or distress. Results of this study demonstrated that both fatigue distress and fatigue duration varied according to the area of the body being treated. In particular, fatigue distress was

### Table 2. Analyses of Variance Comparisons of Fatigue Onset, Duration, and Distress by Treatment Site

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>Head/Neck</th>
<th>Lung</th>
<th>Breast</th>
<th>Prostate</th>
<th>Gynecologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>X</td>
<td>SD</td>
<td>X</td>
<td>SD</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>7.24</td>
<td>6.45</td>
<td>6.22</td>
<td>6.60</td>
<td>7.64</td>
</tr>
<tr>
<td>Duration</td>
<td>32.93</td>
<td>12.73</td>
<td>34.87</td>
<td>14.76</td>
<td>31.69</td>
</tr>
<tr>
<td>Distress</td>
<td>2.56</td>
<td>1.45</td>
<td>2.78b</td>
<td>1.26</td>
<td>2.43</td>
</tr>
</tbody>
</table>

*Note. In post hoc analyses using a Bonferroni correction (alpha = 0.05), “a” was significantly greater than “b.”

*Equal variances could not be assumed, Levene’s F (4,379) = 3.029, p = 0.018, therefore, a more conservative value (alpha = 0.025) was used to test the significance of the omnibus F.*
worse for patients with lung cancer than it was for patients with prostate cancer, but the fatigue distress experienced by patients with lung cancer was not significantly different than the distress experienced by patients treated to other areas of the body (e.g., breast, head/neck, female pelvis). Piper et al. (1989) reported that fatigue was more severe for patients with lung cancer compared to patients with breast cancer. However, in the current study, no differences were noted in the levels of fatigue distress experienced between these two groups. Still, findings from the current study in conjunction with findings reported by other researchers (Piper et al., 1989) suggest that the fatigue experience is more severe and more distressing for patients with lung cancer than it is for patients treated for breast or prostate cancer.

Implications for Nursing Practice

Clinically, knowing when fatigue is likely to start can help nurses adjust both the timing and content of preparatory information. Because the average onset of fatigue was near the middle of the second week of treatment, one might conclude that patient counseling on symptom occurrence and management should be accomplished no later than the end of the first week of treatment. However, findings of this study suggest that assistance is needed sooner.

Given the substantial percentage of patients reporting fatigue on the first day of treatment, pretreatment screening seems warranted. This screening assessment could be performed either during the initial consultation with the radiologist or at the time of simulation. Because patients with lower levels of hemoglobin, poorer health, and higher levels of global symptom distress and mood disturbance seem especially vulnerable to an early onset of fatigue, pretreatment screening should include an assessment of these parameters.

If pretreatment screening demonstrates that the patient is positive for fatigue, an evaluation of the patient’s fatigue-related self-care system should be undertaken to detect and rectify any existing limitations in its content or use. Also, it should be recognized that the complexity of the nursing plan of care increases when patients receiving radiotherapy start treatment with lower levels of hemoglobin, in poorer states of health, or with higher levels of global symptom distress or mood disturbance. Consequently, to optimize patient outcomes, the nursing plan of care needs to address these other areas of concern as well.

Findings of this study suggest that fatigue is a highly individualized experience. Both positive and negative indicators of health, as well as the area of the body being treated, affected the fatigue experience. Therefore, it seems prudent to advise patients to avoid the trap of comparing their fatigue experience to the experiences of others.

Limitations

Fatigue, a key construct in this study, was not a key construct in the parent study and was not measured using a psychometrically sound instrument. Consequently, the psychometric properties of the fatigue measure, its reliability and validity, could not be subjected to rigorous evaluation. Using less than optimal operations of constructs is a recognized limitation of secondary data analysis (McCall & Appelbaum, 1991). A replication study using a psychometrically sound measure of fatigue is needed to determine whether the observed relationships are repeatable across studies.

Future Research

The fact that 20% of the subjects in this study reported fatigue on the very first day of treatment raises important questions for future research. Investigating in what ways these subjects differ from other subjects on characteristics such as age, extent of disease, and prior or concurrent treatment might help expand the understanding of the mechanisms contributing to fatigue in this population. In addition, how this more immediate experience of fatigue affects the fatigue trajectory, the requirement for fatigue-related self-care, the ability to engage in self-care, the achievement of fatigue control, and the quality of health-related outcomes are questions that need to be researched.

Conclusion

General knowledge of fatigue onset, duration, and severity of distress is needed to plan nursing care for patients with cancer receiving radiation. The nursing plan of care can be tailored to the patient’s situation when this general knowledge of the fatigue experience is made more specific by understanding the effects of diverse correlates of fatigue on fatigue onset, duration, and distress.

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References


