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Subjective fatigue in women receiving six cycles of adjuvant chemotherpy for breast cancer

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SUBJECTIVE FATIGUE IN WOMEN RECEIVING SIX CYCLES OF ADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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They say that learning is life-long. At times it seemed as though the dissertation was going to be life-long too!

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ABSTRACT

SUBJECTIVE FATIGUE IN WOMEN RECEIVING SIX CYCLES OF ADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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Subjective fatigue is reported to be a significant and distressing problem in women receiving chemotherapy (CT) for breast cancer. Despite this fact, no previous study has attempted to characterize fatigue in these women over time. The primary purpose of this study was to determine prospectively, the incidence, timing, and intensity of subjective fatigue symptoms in women with breast cancer receiving adjuvant CT. A secondary purpose was to predict risk factors (age, stage of disease, performance status, hematocrit level, length of CT cycle [21-day vs 28-day], inclusion of Adriamycin in the regimen, mood/affective states [vigor, depression, mood disturbance] and social support) for the development of subjective fatigue over time (chronic). Selected components of an investigator-developed and published fatigue framework integrating fatigue theories guided this study. Fatigue was measured by the Profile of Mood States' Fatigue-Inertia Subscale (POMS F/I), the Piper Fatigue Scale (PFS), and the Fatigue Symptom Checklist (FSCL) during the first three consecutive and sixth and final CT cycles, including nadirs (Times 1-8). Mood states were measured by the POMS (Times 1-8); social support by the Norbeck Social Support Questionnaire (Times 1, 5 & 7). Repeated measures ANOVA, Pearson correlations, Chi Square analyses, and independent t-tests were used to determine changes over time, validity estimates and relationships between fatigue and moderator variables. Forward, stepwise multiple regression and graphic residual analyses were used to determine predictors of fatigue over time. In this sample (n=37, Stage I/II disease, predominantly CMF CT), the number and intensity of fatigue symptoms did not increase over time. No significant differences in fatigue were noted as a function of length of CT cycle or by the inclusion of Adriamycin in the treatment regimen. Significant insomnia and declines in social support were documented. Study results suggest that knowledge about depression, vigor and mood disturbance scores can enable the clinician to predict, with a 47-76% degree of accuracy, a woman's risk for developing fatigue over time while receiving adjuvant CT for breast cancer. If these risk factors can be confirmed by other studies, the timing and selection of fatigue interventions can be tailored to those at high risk.

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Ada M. Lindsey, Ph.D., R.N., F.A.A.N., Chairperson

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CHAPTER ONE

THE STUDY PROBLEM

Introduction

Breast cancer is the most frequently occurring malignancy in American women, accounting for 32% of all malignancies diagnosed in women (Boring, Squires, & Tony, 1992). One out of every nine American women will develop breast cancer during the course of her lifetime (American Cancer Society, 1992). It is the second leading cause of death from malignancy in American women; only lung cancer has a higher mortality rate (Boring et al, 1992). Death from breast cancer frequently occurs because of distant micrometastases that have disseminated months to years before the initial or primary lesion is diagnosed or treated (Osteen et al, 1990).

Adjuvant systemic chemotherapy (CT) or chemotherapy that follows local treatment with curative intent, such as modified radical mastectomy or lumpectomy followed by radiation therapy (Harris, Hillman, Canellos, & Fisher, 1985), is designed to eradicate these occult micrometastases and thus improve survival rates in these women (Goodman, 1991). Currently, the accepted standard regimen for adjuvant CT in premenupausal, node-positive women consists of six months of CMF (cyclophosphamide/ Cytoxan, methotrexate, and 5-fluorouracil/5-FU) given on a 21-day or 28-day treatment cycle. In women who are postmenupausal, node and receptor-positive, adjuvant tamoxifen for two years or longer is standard treatment. Treatment consensus for node-negative women awaits results from ongoing clinical trials (Goodman, 1991; Osteen et al, 1990).

Fatigue is reported to be a significant and distressing problem for women receiving adjuvant CT for breast cancer (Greene, Nail, & Fieler, 1992; Meyerwitz, Sparks, & Sparks, 1979; Meyerwitz, Watkins, & Sparks, 1983; Knobf, 1986). In addition, two studies suggest that more emotional distress and disruption in self-care abilities are associated with the more long term side effects of CT such as tiredness and weakness

than from the more acute side effects, such as nausea and vomiting (Nerenz, Levanthal, & Love, 1982; Rhodes, Watson, & Hanson, 1988). Despite these facts, little is known about fatigue in these women. This is surprising since a recent appraisal of the research literature indicates that 80-96% of all CT patients experience fatigue (Irvine, Vincent, Bubela, Thompson, & Graydon, 1991).

Statement of the Problem

Subjective fatigue is considered to be a universal precursor and sequela of disease progression and treatment (Piper, Lindsey, & Dodd, 1987), yet its actual incidence and prevalence in specific populations remains undocumented (Piper, et al, 1987; Piper, 1993). Fatigue is so ubiquitous in clinical practice that health care providers may not assess systematically for its presence and patients may hesitate to report such a common symptom unless it becomes unusual, excessive or constant or begins to disrupt valued activities (Hart & Freel, 1982; Morris, 1982). In addition, data about fatigue are not routinely collected or reported unless fatigue becomes a dose-limiting treatment toxicity (Piper, et al, 1989b).

Documenting the incidence, timing, and intensity of subjective fatigue over time is an essential first step to tailoring the timing of fatigue interventions to those at high risk. Documenting these subjective dimensions of fatigue: the temporal (incidence, timing and duration), intensity, and symptomatology (sensory dimension), establishes what is known about fatigue's occurrence in women with breast cancer and enables nurses to predict better the onset and duration of fatigue in these women. Since more women than ever before are receiving adjuvant CT for breast cancer (Knobf, 1991), prospective studies urgently are needed to document subjective fatigue in these women.

Significance of the Problem

Fatigue is thought to have a protective function. In extreme forms of exercise, fatigue usually occurs before adenosine triphosphate (ATP) is depleted and muscle contractures occur (Fatigue, 1988). In some metabolic myopathies this protection is

lacking and painful muscle cramps, necrosis, myoglobinuria and renal damage can result (Fatigue, 1988; Edwards & Jones, 1983).

Fatigue has been associated with decreased quality of life (Frank-Stromberg & Wright, 1984; Meyerwitz et al, 1983; Padilla & Grant, 1985) and functional health status (Davis, 1983; Mayer, Hetrick, Riggs, & Sherwin, 1984); social isolation, depression (Piper, 1988), caregiver role fatigue (Goldstein, Regnery, & Wellin, 1981), and perceived caregiver burden (Jensen & Given, 1991). Patients may be unable to participate in treatment and research protocols (Kaempfer, 1982) and may lose their desire to go on living (Piper, 1991). Maintaining hope, fighting disease, coping with side effects and participating in treatment protocols all take energy. For some people who become chronically fatigued, it simply may take too much energy to go on living.

Three studies suggest that the presence of fatigue at diagnosis, as measured by the Fatigue-Inertia Subscale of the Profile of Mood States (POMS F/I) (Levy, Herberman, Maluish, Schlein, & Lippman, 1985; Temoshok, 1987), or by the Symptom Distress Scale (Kukell, McCorkle, & Driever, 1986) may predict a negative outcome in breast cancer (Levy et al, 1985), lung cancer (Kukell et al, 1986) and malignant melanoma patients (Temoshok, 1987). In one of these studies, the POMS F/I scores predicted nodal status in breast cancer patients with a 71% degree of accuracy (i.e., higher POMS F/I scores predicted greater nodal involvement)(Levy et al, 1985); higher scores similarly were associated with an unfavorable outcome and shorter survival time in malignant melanoma patients (Temoshok, 1987). In lung cancer patients, increased fatigue and symptom distress were "...associated with an increased risk of death...[and] with a decreased probability of survival over time." (Kukell, et al, 1986, p. 101). In women with ovarian cancer, a positive correlation between subjective fatigue and disease activity was demonstrated (Pickard-Holley, 1991). As tumor burden declined (CA-125, a tumor marker), so did subjective fatigue. (Pickard-Holley, 1991). While prospective studies are needed to confirm these retrospective, cross-sectional

findings, research clearly is warranted to document subjective fatigue over time.

Purpose of the Study

The primary purpose of this study was to document the incidence, timing and intensity of subjective fatigue in women with breast cancer receiving six cycles of adjuvant CT. A secondary purpose was to predict risk factors (age, stage of disease, performance status, hematocrit level, length of CT cycle [21-day vs 28-day], inclusion of Adriamycin in the regimen, mood/affective states [vigor, depression, mood disturbance], and social support) for the development of subjective fatigue over time.

CHAPTER TWO

REVIEW OF THE LITERATURE

Introduction

Because fatigue is a complex, multicausal and multidimensional sensation (Piper et al, 1987), it defies easy definition, explanation and measurement. No one definition has gained universal acceptance (Eidelman, 1980). Fatigue has been defined by the investigator's interest or focus (i.e., neuromuscular versus subjective fatigue); by its proposed origin or cause (i.e., central versus peripheral, pathologic versus psychologic, or "attentional" fatigue); by the exclusion of all other diseases (i.e., Chronic Fatigue Syndrome); by its response to electrical stimulation (i.e., high-frequency versus low-frequency fatigue); and by its duration (i.e., acute versus chronic fatigue) (Piper, 1993). Subjective indicators are key to the understanding of how fatigue may vary between healthy and ill populations (Piper, 1991).

Thus, the best way to currently assess and measure fatigue in clinical populations is to determine the person's own perception of the fatigue experience (Piper et al, 1989b). It generally is accepted that subjective fatigue occurs on a continuum ranging from tiredness to exhaustion. (Grandjean, 1970) Thus, the perception of the intensity and duration of fatigue should be an essential component to any definition. (Piper, 1993).

Defining Subjective Fatigue

Subjective Tiredness

Everyone experiences tiredness; it is a universal sensation that is expected to occur normally at certain times of the day (circadian rhythmicity) or after certain types of activity or exertion. It usually has an identifiable cause; is short-lived; and is easily dissipated by a good night's sleep or rest (Piper, 1993).

Subjective Fatigue

In contrast to tiredness, subjective fatigue is perceived as unusual, abnormal or excessive whole-body tiredness, disproportionate to or unrelated to activity or exertion. It may be acute or chronic; it is not dispelled easily by sleep or rest; and it can have a profound, negative impact on the person's quality of life (Piper, 1993).

Acute and Chronic Fatigue

The literature suggests that differences exist between acute and chronic fatigue states (Bartley & Chute, 1947; Cameron, 1973; McFarland, 1971; Muncie, 1941; Piper, 1988; Poteliakhoff, 1981; Potempa, Lopez, Reid, & Lawson, 1986; Riddle, 1982; Roberts & Smith, 1989; Rockwell & Burr, 1977). Chronic fatigue is thought to last anywhere from one (Piper, 1988; Potempa et al, 1986; Kirk et al, 1990) to three (Komaroff & Goldenberg, 1989), to six months or longer (Holmes et al., 1988). In cancer patients, cumulative fatigue or fatigue that gradually increases over time, has been documented in RT patients across treatment sites (Haylock & Hart, 1979; Kobashi-Schoot, Hanewald, Van Dam, & Bruning, 1985; King, Nail, Kreamer, Strohl, & Johnson, 1985). Anecdotally, cumulative fatigue also is reported to occur over successive CT cycles. This study investigated whether fatigue increased over time during adjuvant CT.

Unfortunately, the literature makes no distinction between fatigue and tiredness states. As a consequence, what has been described in previous literature as acute fatigue, may instead be the state of tiredness. (Piper, 1993) Acute fatigue and tiredness may differ by severity and duration. As Carpenito states; "fatigue is different from tiredness...a transient, temporary state...Fatigue is a pervasive, subjective, drained feeling...not relieved by rest." (1992, pp. 362-363). Research needs to clarify whether these distinctions exist and determine if acute and chronic fatigue states can coexist simultaneously within the same individual as can acute and chronic pain states (Piper, 1991).

Fatigue in Women with Breast Cancer Receiving Chemotherapy

There are only six studies that have examined fatigue and other symptoms in women with breast cancer receiving CT; three are retrospective, one time interview studies (Bruera et al, 1989; Knobf 1986; Meyerwitz et al, 1979; 1983); three are prospective, repeated measures designs with both heterogeneous (Cimprich, 1990; Piper, Dibble, & Dodd, 1991) and homogeneous samples (Greene, Nail, & Fieler, 1992).

Meyerwitz and associates were the first to study the impact of adjuvant CT in women with breast cancer (Meyerwitz et al, 1979; 1983). Fifty women with stage II disease post mastectomy were interviewed once about perceived psychosocial effects of CT, one to 30 months into their adjuvant CT program (average length of treatment preinterview was 11.4 months). Treatment consisted of CMF with or without Bacillus Calmette-Guerin (BCG). CMF was administered on a 28-day treatment cycle for four cycles; followed by 42-day treatment cycles for 8 additional cycles. BCG was administered to 45 women weekly for 11 weeks and every other week thereafter for two years.

Every woman reported adverse changes in her life as a result of the adjuvant program (Meyerwitz et al, 1979). The most frequently reported psychosocial effect was a decrease in social and work-related activities. Forty-eight women (96%) experienced fatigue; it was the most common and disruptive symptom experienced (Meyerwitz et al, 1979, 1983). Fatigue seemed to be related directly to CT since energy levels were improved between treatment cycles. Overall distress tended to be worse in women who experienced a longer treatment break between cycles (four weeks versus two weeks) (Meyerwitz et al, 1979; 1983). Anecdotally, patients frequently state that no sooner do they begin to recover from the effects of their previous CT cycle and begin to feel "normal" again, that they have to return for their next treatment cycle. This finding suggests that longer treatment breaks between CT cycles may be more psychologically

distressing than shorter breaks.

In the second study, Knobf (1986) investigated physical and psychologic distress and life style changes in 78 women with stage II breast cancer. The majority of women were on a CMF regimen with or without vincristine and prednisone. Women were interviewed once using a semistructured interview guide developed by the investigator that included a modified Symptom Distress Scale (SDS)(McCorkle & Young, 1978) and the Psychiatric Status Schedule (PSS)(Spitzer et al, 1970). Fifty women were receiving CT at the time of their interview (average time on CT at the time of the interview was 10 months); 28 women had completed CT (range= two months to five years). Fatigue caused the greatest distress in these women, followed by insomnia. Average severity ratings for fatigue were low (below three on a 1-5 likert scale) despite the high level of distress. Fatigue correlated positively with depressed mood ($p < .01$) and difficulty concentrating.

Bruera and associates studied "aesthenia: the combination of physical and mental fatigue" in 64 Canadian women with locally recurrent or metastatic disease (1989). The majority of women (76%) were treated with CT (CMF with or without vincristine and prednisone or adriamycin-velban combinations). The remainder were being treated with hormonal therapy (Tamoxifen or Depo-Provera)(Bruera et al, 1989). An age-matched control group also was used. Subjects rated their energy levels and ability to perform specific activities of daily living on visual analogue scales. A questionnaire was used to assess specific physical tasks. Additional data were collected on nutritional and psychological status.

Significantly more patients than controls reported substantial increases in their physical fatigue during the past year. Forty-one percent were considered aesthenic. Aesthenia correlated with depression and psychological status but not with nutritional status, tumor mass, anemia or type of treatment (Bruera et al, 1989).

In the first prospective study, Cimprich studied "attentional fatigue" which she

defined as "a state of reduced effectiveness and discomfort that follows intense mental efforts or excessive use of directed attention" in 32 women with early stage breast cancer (1990, p.8). Subjects were studied over four time periods during the first three months following surgery; on the day before discharge from the hospital; prior to the initiation of subsequent treatment; at the end of radiation therapy or two cycles of CT and at three months. A battery of neurocognitive tests such as reciting numbers and letters, were used to measure attentional capacity. No subjective measure of whole body, generalized fatigue was used in this study. Subjects were randomized to a control or experimental group that tested the effects of a self-selected restorative activity program carried out three times per week for 30 minutes designed to conserve or restore attentional capacity over time. All subjects had significant losses in attentional capacity at time one and continued to have some loss in attentional capacity up to 60 days postoperatively. The intervention group however, showed more consistent improvement over time in their attentional capacity.

Dodd and associates (Piper, et al, 1991) were the first to document generalized, whole body fatigue prospectively in CT patients and family members. In this study, 100 CT patients (48% had breast cancer) and 126 family members were studied over a 6-month period (Times 1-5) as they underwent treatment for newly diagnosed or recurrent disease. There were no significant differences in patient fatigue scores over time as measured by the POMS F/I. Only at Time 5 was there a significant difference between groups; newly diagnosed patients ($n=64$) had more fatigue ($p<.05$) than did the recurrent disease group ($n=34$). Fatigue incidence, measured by the Chemotherapy Knowledge Questionnaire (Dodd & Mood, 1981), revealed that fatigue was the most commonly experienced side effect across all time periods. Fatigue incidence increased over time indicating that cumulative fatigue also may be present in CT patients.

Patients were very concerned about their fatigue as measured by the Inventory of Current Concerns (Weisman, Worden, & Sobel, 1980). "Feeling tired" was the

second most frequently cited concern second only to concern about the future, Times 1 and 4. By Time 5 however, fatigue had become the most common concern cited.

Family members of newly diagnosed patients experienced significantly greater fatigue Times 1 and 4 than family members experiencing recurrent disease. Fatigue was the second most frequent concern family members had about themselves, second only to their concern about the future. Over 80% were concerned about the patient's fatigue. It was the number one family member concern about the patient over time (Piper et al, 1991).

As part of a larger, prospective study, Greene and associates (1992) studied side effects associated with three different CT regimens in a subset of 85 women with breast cancer. Regimens consisted of CMF (n=36), FAC (n=29; 5-FU, Adriamycin and Cytoxan) and CNF (n=20; Cytoxan, Mitoxantrone and 5-FU). Subjects completed a self-care diary documenting the incidence and severity (1-5 scale) of various side effects, days two and five after the first and second treatment cycles.

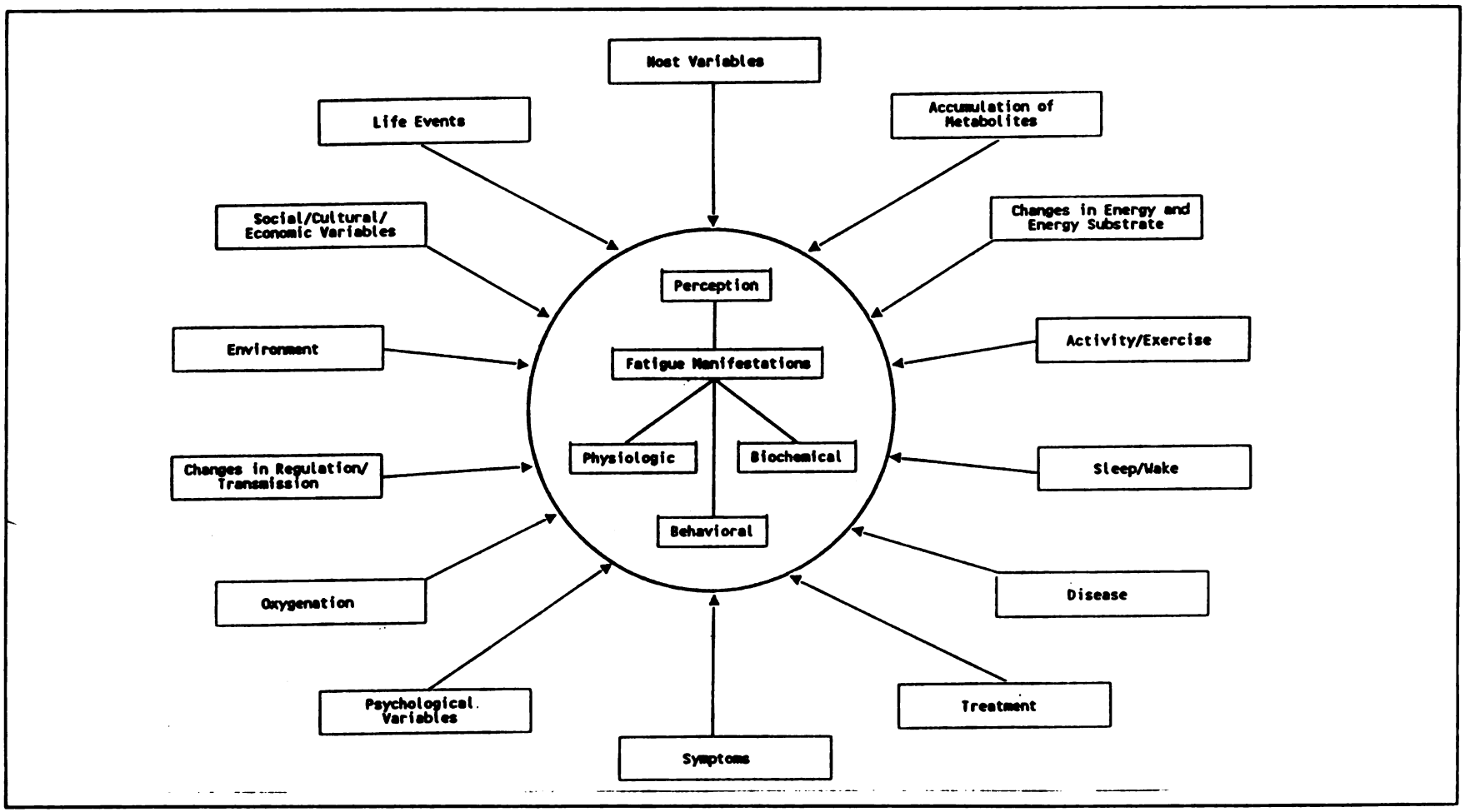
Fatigue, nausea and anorexia were the most frequently reported side effects across all treatment regimens. Fatigue was the only side effect experienced by at least 50% of the subjects across all groups and time periods. The FAC group had the highest fatigue and nausea scores on day two after the first treatment cycle (Greene et al, 1992). Clearly fatigue is a significant problem for women with breast cancer receiving CT.

Integrated Fatigue Framework

Various theories have been proposed to explain how fatigue occurs. These theories have been integrated into a previously published fatigue framework developed by the investigator and associates (Piper et al, 1987; Piper, 1991)(Figure 1).

In the center of the framework are the subjective (perceptual) and objective (physiological, biochemical/metabolic and behavioral) indicators of fatigue reported in the literature (Piper, et al, 1987). Surrounding the center of the framework are the

Figure 1: Integrated Fatigue Framework*



* Adapted with permission from Piper, B.F. (1991), Alterations in Energy: The sensation of fatigue. In S.B. Baird, R. McCorkle, & M. Grant (Eds.). Cancer Nursing: A Comprehensive Textbook (figure 58.2, p. 897), Phila: WB Saunders.

metabolic, neurophysiological, situational, and developmental stressors that may cause and/or modulate the signs and symptoms of fatigue. These include such stressors as the accumulation of various metabolites, changes in regulation/transmission, environmental factors or the common transitional events associated with growth and development or maturation such as pregnancy, parenting, or divorce (life events).

Since a variety of factors may influence the expression of subjective fatigue, only selected components of this integrated framework were used to guide data collection and test relationships among the variables in this study. For this study, data were collected on the subjective indicators of fatigue: fatigue symptoms and intensities (perception); and selected variables reflecting changes in energy substrate and sleep/wake cycles.

Changes in Energy and Energy Substrate

Changes in energy production and substrate can profoundly influence human performance and the development of fatigue. In cancer patients, changes in energy patterns are common and may result from abnormalities in energy expenditure, cancer cachexia, anorexia, infection, fever, and imbalances in thyroid hormones (Piper et al, 1987). For these reasons, data were collected in this study on baseline weight, height, and quality of appetite (i.e., poor, fair, good, excellent), and changes in weight and appetite over time.

Sleep/Wake Variables

Alterations in the sleep/wake cycle can lead to fatigue. Lack of restful sleep at night can lead to increased sleepiness and fatigue during the day. This "daytime" fatigue increases the need for daytime napping and sleep at night (Hart, 1978; Jamar, 1989). In general, the amount of sleep needed declines between 20 and 50 years of age; thereafter increases occur in the amount of sleep needed including the need for daytime napping (Hayter, 1983; Tune, 1969).

Only four studies have investigated sleeping disorders in cancer patients; none

have addressed fatigue as an outcome variable (Beszterczey & Lipowski, 1977; Hauri, Silverfarb, Oxman, & O'Leary, 1985; Lamb, 1982; Cannici, 1980). In one study, difficulty falling asleep and staying asleep were the most frequent complaints in RT patients. Insomnia correlated positively with anxiety and depression in these patients (Beszerterczey & Lipowski, 1977). In another study, subjects experienced sleep onset insomnia, defined by self-report as the inability to fall asleep within 30 minutes, for a mean of 3.5 years. Subjects required an average of 1.5 hours to fall asleep (Cannici, 1980). These subjects benefited from a muscle relaxation training group. A third study examined the presence of sleep disorders, anxiety, and depression in 15 cancer patients and 15 matched controls (Lamb, 1982). No differences were found in sleeping patterns between the groups, however, depression was significantly higher in cancer patients. In the fourth study, 13 lung and breast cancer patients, who were receiving RT, were age and sex-matched to normal sleepers (Hauri, et al, 1985). All subjects slept three consecutive nights in a sleep laboratory. Cancer patients slept worse than controls and under-reported their sleep problems even to people who were interested in their sleep patterns. For this current study, data were collected on the perceived quality of sleep and naps, the amount of time spent sleeping and napping, and changes in these patterns over time.

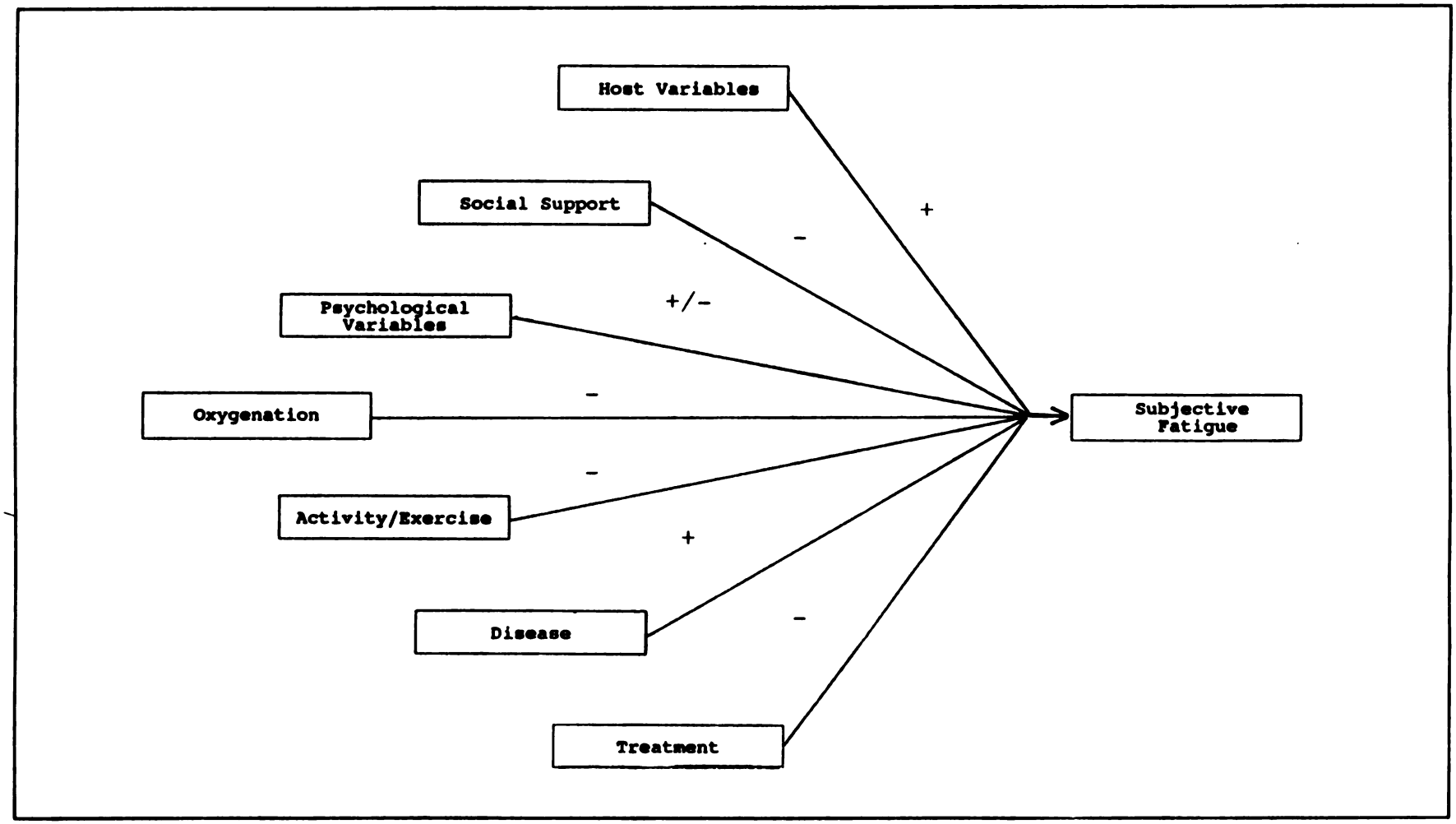
Hypothesized Model for Fatigue

Seven of the 14 components of the integrated fatigue framework (Figure 1) were tested for their ability to predict fatigue in this study. These components are shown in Figure 2.

Host Variables

Innate host factors such as age, gender, genetic makeup, race, and unique circadian rhythms may influence fatigue (Piper et al, 1987). Since data are limited and often conflicting about the relationships between these factors and fatigue (i.e., no relationship thus far has been documented between age and fatigue in cancer patients

Figure 2: Hypothesized Model for Fatigue



NOTE: Directions of hypothesized relationships indicated by "+" (positive relationship) and "-" (negative relationship).

[Haylock & Hart, 1978; Pickard-Holley, 1991]), more prospective, comparative studies are needed to better define these relationships (Piper, 1993). In this study, it was anticipated that a positive relationship existed between age and fatigue; the older the woman, the more the fatigue. Gender was controlled for by having only women with breast cancer participate in this study. Circadian rhythmicity was addressed by asking subjects to complete all instruments at the same time of day when they were the most fatigued, over the course of the study. If this was not possible for them to do (i.e., because they were too tired), they were asked to pick a convenient and consistent time of day to complete the forms over the course of the study.

Social Support

Social support may have an effect on fatigue. Studies have explored the relationship between social support and a variety of health outcomes (Bloom, 1982; Bruhn & Phillips, 1984; Cobb, 1976; Kesselring, Lindsey, Dodd, & Lovejoy, 1986; Lindsey, Ahmed, & Dodd, 1985; Lindsey, Chen, & Dodd, 1985; Lindsey, Norbeck, Carrieri, & Perry, 1981; Norbeck, Lindsey, & Carrieri, 1981, Norbeck, Lindsey, & Carrieri, 1983; Rock, Green, Wise, & Rock, 1984).

Interviews with patients receiving RT and CT suggest that having someone available to provide emotional and physical support during the diagnostic and treatment phases, often dissipates much of the stress-induced fatigue responses seen with cancer. Common sense suggests that patients who have other family members or friends available to them to assist with the everyday responsibilities of shopping, cleaning and cooking often can delegate these responsibilities to others and "rest more" when they are tired or are experiencing other side effects of treatment. Whether this ability to "rest more" results in less fatigue and the capability to recuperate faster from the demands of treatment is unknown. It is believed that patients who have an available and supportive social support network, will experience less fatigue than patients who do not have such a supportive network.

Social support, like fatigue, is a multidimensional construct that requires more precision in its conceptualization (Bloom, 1982). While numerous definitions and theories about social support exist in the literature (Lindsey et al, 1981), it commonly is accepted that both function and network properties are essential to measuring social support (Lindsey, 1984). Network properties include interpersonal relationships such as the number of people in the network, the duration of relationship, the frequency of contact (size, stability and availability) and recent losses; functional properties describe the function or purpose served by the relationship such as affect, affirmation and aid (Kahn, 1979; Norbeck et al, 1981).

While the availability and quality of social support may have an important moderating effect upon subjective fatigue in cancer patients, its effect has not been well studied. There are only two studies that have examined the effects of social support on fatigue in cancer patients, and the results are conflicting (Jamar, 1989; Lindsey, Dodd, Dibble, & Brecht, 1992).

Jamar conducted a one-time semi-structured interview with 16 women with ovarian cancer (Stages I-IV) at various points in their CT regimens. Data collection instruments included the Pearson-Byars Fatigue Feeling Tone Checklist (Pearson & Byars, 1956), the Symptom Distress Scale (McCorkle & Young, 1978), and the POMS short form (Shachem, 1983). Degree of social support was determined by selected demographic variables (i.e., single versus married; living alone versus living with someone else); no formal measure of social support was used. Single parents and women without assistance in the home were found to have higher fatigue levels than married counterparts ($p < .01$) (Jamar, 1989).

Dodd and associates (Lindsey, Dodd, Dibble, & Brecht, 1992), studied subjective fatigue, social support and coping strategies prospectively in 100 cancer patients (48% breast cancer) receiving CT and 126 family members (1990). Data collection instruments included the POMS F/I, the NSSQ (Norbeck et al, 1981; 1982),

and the Omega Coping Strategies Scale (Weisman & Worden, 1976-1977). Fatigue was measured five times during the study (Times 1-5); social support at time 1 (within 3 weeks of beginning CT) and Time 5 (six months later); and coping, Times 1, 4, and 5. In this study, social support (network and functional) was unrelated to patients' fatigue and coping strategies over time. Only in family members was a significant correlation found. The total number of people in the family's social network at Time 1 was related significantly to fatigue at Time 4 ($r=.28$, $p<.01$). For family members, fatigue predicted coping at Times 1 & 5 (Lindsey et al, 1992). The NSSQ was used in this current study to measure social support.

Psychological Variables

Psychological factors such as usual response to stressors, degree of motivation, distraction, boredom, and beliefs and attitudes may influence fatigue (Piper et al, 1987). Positive beliefs and attitudes have been associated with decreased levels of fatigue in one study (Cotanch, Sturm, & Hood, 1984). Cotanch and associates found that patients with colon cancer who held more positive pretreatment expectations about the efficacy of interferon alpha (IFN), were significantly less likely than others to experience fatigue and other symptoms (1984).

Both positive and negative moods or affective states may influence fatigue. Affective states are psychological states that are short-lived (minutes to days) whereas mood states are psychological traits that may last longer (days, weeks, months, or years) (Gottschalk, 1984). Vigor, a "positive" mood state considered to be reflective of a "high energy" state, has been negatively associated with fatigue, depression and other mood states (McNair et al, 1971).

In contrast to these positive beliefs and mood states, tiredness, fatigue and sleep disturbances are common symptoms of depression (Wittenborn & Buhler, 1979). Depression is thought to be a principal cause of fatigue in patients who report being tired upon rising (Cardenas Kutner, 1982). In hospitalized cancer patients, depression

may range from 17-42% (Petty & Noyes, 1981; Bukberg, Penman, & Holland, 1984).

Mood or affective states in normal, nonpsychiatric and psychiatric populations have been measured extensively by the Profile of Mood States (POMS) (McNair et al, 1971). The POMS measures six mood states: tension/anxiety, depression/dejection, anger/hostility, fatigue/inertia, confusion/bewilderment, and fatigue/inertia.

There are a number of studies that have used the POMS to measure mood states in cancer patients (Cassileth, Lusk, Brown, & Cross, 1985; Cella et al, 1989; Jamar, 1989; MacVicar & Winningham, 1986; Pickard-Holley, 1991; Piper et al, 1989a; Shacham, 1983; Shachem, Reinhardt, Raubertas, & Cleeland, 1983; Silberfarb, et al, 1983; Spiegel, Bloom, & Yalom, 1981; Spiegel & Bloom, 1983). Six studies provide data on individual subscale scores such as depression-dejection and fatigue-inertia subscales (Cella et al, 1989; MacVicar & Winningham, 1986; Shachem, 1983; Shachem et al, 1983); two provide normative and psychometric data (Cassileth et al, 1985; Shachem, 1983); two document significant correlations between depression and fatigue (Jamar, 1989; Piper et al, 1989a); one does not (Pickard-Holley, 1991).

Shacham and associates (1983) found that mean fatigue scores were the highest of all the mood states over time in a group of patients with pain from metastatic tumor involvement. As pain control was achieved, negative mood states including depression and fatigue declined, while vigor scores improved. However, the association between pain, fatigue and depression was not as consistent as was the relationship between pain and vigor scores.

Spiegel and colleagues (1981; 1983) investigated the relationship between pain and mood states and group support in women with metastatic breast cancer. Pain duration was correlated significantly with fatigue and depression (1983); less fatigue and depression were reported by women who participated in a support group for one year (1981).

Silberfarb and colleagues (1983) found that fatigue scores in patients with small

cell lung cancer receiving CT increased significantly over time; depression scores were worse in patients receiving vincristine therapy, but not significantly so. Piper and associates found a positive correlation ($r=.46$, $p<.01$) between fatigue, as measured by the PFS and POMS depression scores in patients receiving RT for lung and breast cancer (1989a). Jamar (1989) also demonstrated significant correlations between fatigue scores as measured by the Pearson-Byars Scale and POMS depression scores ($r=.94$, $p<.001$) in women with ovarian cancer receiving CT. While some studies have demonstrated a correlation between depression and fatigue in cancer patients (Jamar, 1989; Bruera et al, 1989; Piper et al, 1989a); others have not (Pickard-Holley, 1991). In this study, vigor, depression, and mood disturbance were analyzed for their ability to predict fatigue. Vigor was anticipated to have a negative relationship to fatigue; depression and mood disturbance, a positive one.

Oxygenation Variables

Any factor that alters or interferes with the ability to obtain or maintain adequate oxygenation levels in the lungs or blood can influence fatigue (Piper et al, 1987). Easy fatigibility, reduced stamina, and endurance are associated with patients who are anemic. In cancer patients, anemia defined as "...the number of erythrocytes, quantity of hemoglobin, and volume of packed erythrocytes (RBCs) per 100 ml of blood [which is] less than normal." (Maxwell, 1984, p. 321), is a common finding (Leite & Hoogstraten, 1977). Bleeding, bone marrow invasion by tumor, hemolysis and anemia of chronic disease are contributing factors (Leite & Hoogstraten, 1977; Maxwell, 1984).

Anemia less commonly is associated with CT administration, since these agents act primarily on rapidly dividing cells and RBCs have a long life span in the peripheral blood (120 days), and a slow rate of replication (Maxwell, 1984). Notable exceptions to this rule include alkylating agents such as cytoxan which can produce anemia 10-21 days into treatment and the nitrosoureas (Leite & Hoogstraten, 1977).

Correlating measures of subjective fatigue with objective indicators such as decreased hematocrit or hemoglobin values is difficult (Piper, 1993). A number of factors, including hydration status can affect hematocrit values (Fishbach, 1980). In evaluating the signs and symptoms of anemia, the total amount of circulating hemoglobin may be of greater physiologic importance than the number of circulating erythrocytes (Fishbach, 1980).

Only one study thus far has documented a relationship between fatigue and anemia in cancer patients (Jamar, 1989). In this cross-sectional study of 16 women with ovarian cancer treated with CT, negative correlations were documented between subjective fatigue and hematocrit levels when readings were taken from the most recent blood work available.

Ideally, specimens for laboratory analyses should be drawn concurrently or within a few hours of subjective measurements if at all possible (Piper, 1993). In the office practice settings where this study was conducted, specimens were drawn immediately before or on day one of each treatment cycle. Nadir blood values were drawn during the first cycle only unless there were complications. Thus, the hematocrit values in this study were recorded and analyzed from the nadir of the first treatment cycle only.

Activity/Exercise Variables

Alterations in activity or exercise can play significant roles in the prevention, cause, and alleviation of fatigue. Unnecessary sedentarism, prolonged bedrest and immobility contribute to weakness and fatigue. Skeletal muscle that is not exercised loses its oxidative capacity. In this circumstance, more oxygen is required for the performance of comparable work than for conditioned muscle. This factor alone can contribute significantly to the development of fatigue (Astrand & Rodahl, 1986; Ingersoll, 1989; Wegner & Hellerstein, 1984) and is one of the reasons why aerobic endurance exercise often is prescribed (Piper, 1993). Exercise also may cause or

intensify fatigue (St. Pierre, Kasper, & Lindsey, 1992; Winningham & MacVicar, 1988; Winningham, MacVicar, Bondoc, Anderson, & Minton, 1989).

For this study, data about hours per week worked, shift worked, type and frequency of exercise and changes in these activity/exercise variables over time were collected for demographic purposes. Since functional performance status frequently is used as an indicator of activity status, women were asked to rate their perceived functional status over time using the Karnofsky Performance Status Scale (KPS). This scale was used in this study because it is the most widely used measure by physicians to rate functional performance status in cancer patients (Karnofsky & Burchenal, 1949; Schag, Heinrich, & Ganz, 1984). It is unusual, however, to have patients rate themselves on the KPS, as was done in this study. Performance status was anticipated to have a negative relationship to fatigue in this study.

Disease Variables

While fatigue may precede, accompany or follow many adult and pediatric malignancies (Waskerwitz & Leonard, 1986), fatigue patterns by disease site have not been identified prospectively. In one retrospective study with Hodgkin's disease patients, energy levels were reported to take one to five years following treatment to return to normal (Fobair et al, 1986). Rapidity of energy return was "...inversely related to age, stage of disease and intensity of treatment." (Fobair, et al, 1986, p. 812). To control for disease factors that may affect fatigue, only women who were newly diagnosed with breast cancer were eligible for this study. Stage of disease was analyzed for its contribution to fatigue. It was anticipated that a positive relationship existed between stage of disease and fatigue; the more extensive the disease, the more the subjective fatigue.

Treatment Variables

In cancer patients in general, subjective fatigue is reported to be a major clinical problem (Blesch et al, 1991; Irvine et al, 1991; Piper, 1991). It has been associated

with surgery (Piper, West, Halliburton, & Shiraishi, 1982), radiation therapy (Dodd, 1984; Haylock & Hart, 1979; Irvine et al, 1991; Kobashi-Schoot et al, 1985; King et al, 1985; Lee, 1991; Piper et al, 1989a), biological response modifier therapy (Davis, 1983; Rieger, 1986; Piper et al, 1989b), chemotherapy (Greene, et al, 1992; Jamar, 1989; Knobf, 1986; Meyerwitz, et al, 1979; 1983; Nerenz et al, 1982; Osteen et al, 1990; Pickard-Holley, 1991; Piper et al, 1991; Rhodes et al, 1988), and combination therapies (Fobair et al, 1986). In women with breast cancer, additional medical therapies such as those used to control certain symptoms such as nausea and vomiting (steroids), hypertension (beta blockers), radiation therapy and chemotherapy factors such as duration of treatment and types of agents used (Piper et al, 1987; Greene et al, 1992) may contribute to fatigue.

Steroids. The immunosuppressive and lympholytic action of glucocorticosteroids such as prednisone and dexamethasone make these agents valuable adjuncts to many CT regimens (Post-White, 1986). However, these drugs are not without their associated side effects such as euphoria, depression, insomnia and fatigue (Post-White, 1986). Because these side effects may confound CT-associated fatigue and mood patterns, subjects receiving long term steroid treatment were excluded from this study. Two steroids, Decadron and Hydrocortisone are used frequently as antiemetic adjuncts to CT. These drugs are administered intravenously, one time only, immediately preceding CT. Since these drugs have a relatively short half-life (8-12 hours)(Haynes & Murad, 1985), women receiving a one-time steriod dose for antiemetic effects, day one of each cycle were eligible for this study.

Beta Blockers. Feelings of lethargy, malaise, and fatigue are common side effects reported by hypertensive patients treated with beta adrenergic blocking drugs or "beta blockers" such as propranolol or Inderal, atenolol, metoprolol, or captopril (Fellenius, 1984; Hall, Kendall, & Smith, 1984; Levine, Croog, Sudilovsky, & Testa, 1987; Potempa et al, 1986). Since beta blockers are used widely in clinical practice to

treat hypertension and other conditions (Hall, et al., 1984), their side effects may confound the measurement of CT-associated fatigue in this study. For this reason, women receiving beta blocking agents were ineligible for this study.

Radiation Therapy. Cumulative fatigue occurs in the majority of radiation therapy patients regardless of treatment site (Haylock & Hart, 1979; Irvine, et al., 1991; King et al, 1985). Studies have documented a fatigue incidence rate between 60-93% during treatment; and in these patients, 32-46% may continue to experience moderate to severe fatigue three months following treatment completion (Irvine, et al, 1991; King, et al., 1985). For this reason, women who had received RT within the past year prior to beginning CT were ineligible for this study. Women who began the study but who subsequently required "sandwich" RT between the third and sixth CT cycles were permitted to continue on the study.

Chemotherapy Treatment Cycles. Retrospective and cross-sectional studies indicate that fatigue patterns seem to reflect treatment cycles (Jamar, 1989; Knobf, 1986; Meyerwitz et al 1979; 1983; Pickard-Holley, 1991; Rhodes et al, 1988). In women with ovarian cancer, fatigue is reported to be worse during the first week following chemotherapy (Jamar, 1989). Fatigue peaks on day seven (Pickard-Holley, 1991); and gradually subsides during the remainder of the cycle only to recur during the first week of each subsequent cycle (Jamar, 1989). Anecdotally, CT patients may report a "biphasic" fatigue pattern (Spross, 1987, p. 76). In these patients, fatigue occurs on day one of each treatment cycle, may last one to four days (corresponding to stress, antiemetic, and CT effects), and recurs during the nadir of each cycle (when bone marrow suppression is anticipated to be the greatest) (Spross, 1987). Research and anecdotal evidence suggests that cumulative fatigue, previously associated only with radiation therapy, can occur in CT patients (Piper et al, 1991). Anecdotally, women with breast cancer receiving CMF CT report more fatigue when taking oral cytoxan daily for 14 days as part of a 28 day treatment cycle, than women who receive cytoxan

intravenously Days 1 and 8 on a 21 day treatment cycle.

For these reasons, fatigue was measured over time during the first three consecutive cycles (Times 1-6) and during the sixth and final cycle of CT (Times 7-8); on day 1 of each cycle (Times 1, 3, 5, & 7), before CT was administered (when fatigue incidence and intensity were anticipated to be the lowest), and again at the midpoint or nadir of each cycle (Times 2, 4, 6, & 8), when fatigue incidence and intensity was anticipated to be the greatest. The incidence, timing, intensity and symptomatology were analyzed in relationship to cycle phase (day one versus day 10/14), length (21-day versus 28-day), and treatment duration (one to six cycles). In this study, it was anticipated that women on the 28-day cycle would have more fatigue.

Types of Drugs. Because fatigue can be caused by disorders in neuro-transmission, it is hypothesized that drugs that cross the blood-brain barrier or have neurotoxicities may be more likely to produce fatigue than other agents (Piper et al, 1987). Anecdotally, patients receiving vinca alkaloid CT report peripheral fatigue symptoms, such as leg and knee tiredness, and central symptoms, such as an inability to concentrate or to think clearly. Neurotoxicity is dose-limiting for vincristine and is found at high doses for vinblastine. When these drugs have been used in combination, signs of neurotoxicity, insomnia, and weakness are reported (Stewart, Maroun, Lefebvre, & Heringer, 1986). In another study, patients receiving vincristine as part of their CT regimen for small cell lung cancer showed significantly more fatigue and a trend toward increased depression, as measured by the Profile of Mood States (POMS) (McNair, Lorr, & Droppelman, 1971), than patients treated without vinca alkaloids in their regimen (Silberfarb et al, 1983).

Whether this class of agent is associated with a higher incidence of fatigue than other drug classifications is unknown. Because many agents may be used in combination drug protocols, it may be difficult to isolate the fatigue produced by one drug from that produced by another (Piper et al, 1987). However, patients receiving

vinca alkaloid CT were excluded from this current study. Since the study by Greene and associates (1992) suggested that subjects who received adriamycin-containing regimens were more fatigued than other subjects, adriamycin-containing regimens were included and analyzed for their effect on fatigue.

Assumptions

Several assumptions underlie this study. One assumption was that subjective fatigue can effectively be captured and measured by self-report scales. Another assumption was that subjective fatigue can be influenced by various independent or moderator variables such as age, stage of disease, type and duration of treatment, hematocrit levels, and perceptions about mood, social support and performance status.

Research Questions

The following research questions were posed for this descriptive and correlational study.

1. Does subjective fatigue increase in frequency and intensity over time in women receiving adjuvant CT for breast cancer?

2. Do women receiving CT on a 28-Day treatment cycle experience more fatigue than women receiving CT on a 21-Day cycle?

3. Do women receiving Adriamycin-containing regimens experience more fatigue?

4. Do women experience more fatigue when they have less vigor, are more depressed, have more mood disturbance, less social support, are older, have more extensive disease, are anemic, have a poorer perceived Karnofsky Performance Status (KPS), a longer CT cycle or the inclusion of adriamycin in the treatment regimen?

Operational Definitions

For purposes of this study, the following operational definitions were used.

Adjuvant CMF CT. Adjuvant CMF CT was defined as treatment with CMF that follows optimal local treatment with curative intent (Harris et al, 1985). The aim is to

eradicate or arrest occult micrometastatic disease (Goodman, 1991). Treatment may be given on a 21-day treatment cycle with CMF given intravenously (IV) Day one and repeated every 21 days; or on a 28-day treatment cycle (oral Cytoxan, Days 1-14, and IV methotrexate and 5-FU, Days 1 and 8 and repeated every 28 days).

Chronic Fatigue. Chronic fatigue was defined as the subjective sensation of whole-body tiredness that becomes unusual or persistent over time (one month or longer). It was measured by the POMS F/I, the Piper Fatigue Scale, Baseline and Current forms (PRS-BD and PFS-CD), and the Fatigue Symptom Checklist (FSCL).

Mood State. Mood state was defined as the subject's perception of various feelings and affect and was measured by the Profile of Mood States (POMS) (Kukell et al, 1986; McNair et al, 1971).

Nadir. Nadir was defined as the period of time in a patient's CT cycle when myelosuppression can be anticipated to be the greatest. For this study, nadirs were defined as Day 10 on the 21-day CMF cycle, and day 14 on the 28-day treatment cycle.

Social Support. Social support was defined as a multidimensional construct of interpersonal transactions that include both functional (affect, affirmation and aid) and network properties (number, duration, and frequency of contact). It was measured by the Norbeck Social Support Scale (NSSQ).

CHAPTER THREE

METHODOLOGY

Design

This study used a prospective, descriptive repeated measures design to document subjective fatigue over time in women with breast cancer receiving six cycles of adjuvant CT.

Sample/Setting

Subjects were eligible to participate in the study if they were being treated at one of five Northern California oncology office practice settings; were beginning their initial CT cycle; had not received radiation therapy (RT) within the past year; and were not receiving concurrent steroid, beta blocker or vinca alkaloid therapies. "Sandwich" RT, between cycles three and six, and a one-time, prechemotherapy intravenous administration of decadron or hydrocortisone on day one of each cycle was permitted.

There were 74 women who consented to participate in this study; 37 women had complete data on the dependent measures of interest for all 8 data collection points (see validity of fatigue measures discussion below) and thus constituted the final sample for this study. Sixteen refusals were documented. Table 1 summarizes the reasons given for refusing to participate in the study.

Confidentiality was maintained by assigning numeric codes to each subject. All participating subjects gave informed consent (Appendix A). Consent forms with subjects' names were kept in secured files. The study received approval by the University of California, San Francisco Committee on Human Research (H452-01384-01A).

Procedures

Data were collected by 11 oncology nurses (RNs) between April, 1987 and February, 1990. While many of these RNs had previous experience collecting data for medical and pharmaceutical research protocols, none had participated previously in a

Table 1: Reasons Given for Refusing to Participate in the Study

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Overwhelmed: "I feel that I can't do it; too much going on right now to keep track of; too much paper work in my life already to take on something else; I'm just too nervous and upset; I feel I just can't handle one more thing" (n=8).

Too time-consuming: (n=2).

Physical disabilities: "I have vision problems that make it difficult for me to read the forms. I have severe Parkinson's Disease and it's uncomfortable and difficult for me to write" (n=2).

Disinterest or no reason given: (n=2).

Doesn't want to think about disease/treatment: (n=1).

Uncertainty: "I'm from out of the country and I'm not sure how long I'll remain here. I'm not sure how valid my responses will be to the social support form since my family and friends live in another county" (n=1).

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nursing research protocol.

All RNs were trained by the investigator in data collection procedures by role-playing as nurse-patient dyads at the beginning of the study. Training was repeated periodically throughout the study at one to two month intervals to insure standardization of patient explanations and data collection procedures; to problem-solve mutually about the conduct of the study; and to enhance patient accrual.

Research packets were precoded and collated ahead of time by the investigator to facilitate data collection in busy practice settings. Flow sheets were used at each site to track patients over time. The RNs were responsible for identifying eligible patients; reviewing the purposes of the study with patients; obtaining consent; and ensuring that data collection forms were completed accurately and according to the protocol schema (See Table 2). Self-report measures were completed on the night before or on Day One of each treatment cycle, before CT was administered and at anticipated nadirs, days 10 (21-day cycle) or 14 (28-day cycle) for the first three consecutive and sixth and final CT cycles (Times 1-8). The oncology nurses called subjects ahead of time to remind them to complete their forms at nadirs and/or wrote directly on the forms the actual date on which the forms needed to be completed by the subject.

Packets for data collection for the nadir period and subsequent Day one of the next CT cycle were given to patients in advance after they had completed Day one of the current treatment cycle. RNs called the subjects at the cycle's midpoint or nadir periods (Days 10 or 14) to remind them to complete and mail the nadir forms back to the office. Stamped, self-addressed envelopes were provided for this purpose. Subjects brought their completed Day one forms back to the office when they came in for their next treatment.

At the beginning of the study, patients were asked to complete their packets when they were the most fatigued during the day. If this was impossible for them to do because of fatigue, they were asked to pick a convenient time during the day when they

Table 2: Data Collection Schema

	CYCLE ONE		CYCLE TWO		CYCLE THREE		CYCLE FOUR	
Instruments	Time 1	Time 2	Time 3	Time 4	Time 5	Time 6	Time 7	Time 8
Demographic Profile (Baseline)	X							
Demographic Profile (Current)			X		X		X	
Piper Fatigue Scale (PFS) (Baseline)	X							
Piper Fatigue Scale (PFS) (Current)		X	X	X	X	X	X	X
Fatigue Symptom Checklist	X	X	X	X	X	X	X	X
Profile of Mood States (POMS)	X	X	X	X	X	X	X	X
Norbeck Social Support Questionnaire (NSSQ)	X				X		X	
Medical Record Form	X	X	X	X	X	X	X	X

could complete the forms consistently at the same approximate time throughout the study period.

Instruments

Demographics

Data about demographic and selected activity/exercise variables (work, exercise and self-perceived Karnofsky Performance Status [Karnofsky & Burchenal, 1949]); sleep/wake and nutritional variables (weight and appetite changes) were captured by Baseline and Current Demographic Profiles developed by the investigator. Each patient completed the Baseline Demographic Profile Time 1 (Day one of the first CT cycle)(Appendix B); the Current Profile was completed Times 3, 5 and 7 (Day one of each subsequent CT cycle) to capture any changes in these variables over time (Appendix C).

Piper Fatigue Scale

Subjective fatigue was measured by three self-report measures, two multidimensional scales: the Piper Fatigue Scale (PFS) and the Fatigue Symptom Checklist (FSCL); and one unidimensional scale: the POMS F/I. The PFS consists of two forms, a baseline form that measures baseline/usual patterns of fatigue (PFS-B) administered at Time 1; and a current form (PFS-C) administered at Times 2-8. The PFS-B contains 76 items and took an average of 17 minutes to complete (Appendix D); the PFS-C contains 73 items and took an average of 10-12 minutes to complete (Appendix E). Items on both scales measure four dimensions of subjective fatigue: temporal (relating to the timing, pattern, onset and duration), severity (relating to intensity, degree of distress and interference in activities of daily living [ADL]), affective (relating to the subject's emotional meaning or significance of the fatigue), and sensory (relating to physical, emotional, cognitive/mental sensations attributable to fatigue).

Mean subscale scores were summed to calculate a total fatigue score. If there

were missing data and subjects answered 75% or more of the items on a given subscale, the mean of the answered items was substituted for the missing subscale items, a process called "mean-item substitution". Three additional scales, not included in the calculation of the fatigue score, measured relief (perceived effectiveness of fatigue interventions), associated symptoms and evaluative dimensions (what the subject believed was contributing most to or causing the fatigue). These scales were thought to constitute a "planning index" for nursing care.

Each subscale item was measured by a horizontal, 100mm visual analogue scale anchored by verbal descriptors placed in the same direction to facilitate subject response (i.e., "none" to "a great deal"). In RT patients, reliability for the PFS-B (Cronbach's alpha) ranged from .69 for the associated symptom dimension to .95 for the sensory dimension. The reliability estimate for the total fatigue score, calculated on the basis of four subscales: temporal, severity, affective and sensory, was .85 (Piper et al, 1989a). In pregnant women, reliabilities ranged from .80 to .95 with a total alpha of .95 (Pitzer, 1991). Moderate evidence for convergent and divergent validity exists (Piper et al, 1989a).

Fatigue Symptom Checklist

The FSCL contains 30 items that measure three subscales or factors thought to be associated with fatigue: general and specific feelings of incongruity, and mental symptoms. It took subjects approximately two to three minutes to complete this instrument (Appendix F). For each item, subjects were asked to circle a number (1=absence of; 2=a little; 3=moderate amount; 4=quite a bit; and 5=a great deal) to indicate the presence and degree each symptom was experienced. Fatigue symptoms and intensities were summed for each subscale and for the instrument as a whole.

The FSCL has been validated by factor analytic studies in healthy Japanese industrial populations (Kogi, Saito, & Mitsuhashi, 1970; Saito, Kogi, & Kashiwagi, 1970; Yoshitake, 1969; 1971; 1978). In American clinical populations, subscale

reliability estimates range from .77 (specific incongruity) to .90 (general incongruity); reliability estimates for the total FSCL score ranges from .92-.94 (Pugh, 1990). Convergent validity estimates range from .61-.66 (Davis, 1983; Pugh, 1990) to .87 or higher (Srivastava, 1989).

POMS Fatigue-Inertia Subscale

There are seven items on the POMS F/I subscale: worn-out, listless, fatigued, exhausted, sluggish, weary and bushed. The subscale has been confirmed in six studies (McNair et al, 1971) (see reliability estimates below) and was used as a concurrent validity measure for the PFS and the FSCL in this study.

Profile of Mood States

The Profile of Mood States (POMS) was developed to measure six mood or affective states: tension-anxiety, anger-hostility, vigor-activity, fatigue-inertia, confusion-bewilderment, and depression-dejection (McNair et al, 1971)(Appendix G). It is a 65-item, five point adjective rating scale that can determine a total mood disturbance score by summing the first five mood scores and subtracting the vigor-activity score. The greater the score, the more the mood disturbance. The POMS is a standardized instrument that has reliability and validity estimates calculated in a variety of populations (McNair et al, 1971). Internal consistency reliabilities for the individual subscales are as follows: tension .90, anger .93, fatigue .93, confusion .84, vigor .87, and depression .95 (McNair et al, 1971). Normative data exist for cancer patients (Cassileth et al, 1986). It took subjects approximately 5-10 minutes to complete the POMS. The POMS has been used in a previous study conducted by the investigator to examine the relationship between depression and fatigue and determine convergent and construct validity estimates for the Piper Fatigue Scale (Piper et al, 1989a; 1991).

Recalculated Total Mood Disturbance Score

In order to determine the unique contributions of vigor, depression, and mood disturbance in predicting fatigue in these women, the POMS Total Mood Disturbance

Score (TMD) was recalculated for the regression analysis only. Items on the fatigue/inertia, vigor/activity, and depression/dejection subscales were removed from the originally calculated TMD, and the TMD was recalculated on the basis of the remaining three subscales: confusion/bewilderment, anxiety/hostility, and tension/anxiety. The POMS fatigue/inertia subscale score could not be used as an independent variable in the multiple regression analysis because of redundancy and potential multicolinearity with the fatigue dependent measures (total number of symptoms and intensity scores) (FSCL). Thus, for descriptive data analysis only, the originally calculated TMD was used; for the regression analysis, the recalculated TMD score was used (RTMD).

Norbeck Social Support Questionnaire

The Norbeck Social Support Questionnaire (NSSQ) (Appendix H) is a self-report questionnaire that measures three functional components of social support: affect, affirmation, and aid; three network properties through which social support is provided: size or number in the network; stability or duration of the relationship; and availability or frequency of contact; and recent losses of network members and degree of support previously provided. Subjects are asked to list all significant persons in their life at this point in time (up to 20) on one side of the NSSQ (number in network). Individuals listed on the NSSQ are identified according to nine sources of support categories: spouse/partner, family member/relative, friends, work/school associates, neighbors, health care provider, counselor/therapist, religious person, or other. On the opposite side of the form, 10 questions are asked on a series of half-pages that ask the subject to rate each network member on a "1 not at all" to "5 a great deal" scale as to how much affect, affirmation, or aid this person provides (six questions); the duration and frequency of contact (2 questions); and recent losses and loss of support (2 questions). For questions 1-6, the 5-point rating scale was converted to a 0-4 rating scale by the computer to avoid artificially inflating the total amount of support. Test-

retest reliabilities for the NSSQ in healthy subjects range from .58-.92 (Norbeck et al., 1981). Concurrent validity estimates range from .24-.41; indicating moderate evidence for construct validity (Norbeck, et al, 1983).

The average time to complete the NSSQ in this sample was 10 minutes (range: 5-20 minutes). The NSSQ can be scored directly or responses can be transferred onto a one page scoring sheet, as was done in this study. Responses to the first eight questions were added; recent losses were scored dichotomously (yes or no response), and quality of the losses was rated by a 100mm visual analogue scale.

Medical Record Form

The Medical Record Form (Appendix I), developed by the investigator was completed periodically throughout the course of the study by the investigator. Data were recorded from subjects' charts to determine what influence selected medical characteristics such as treatment regimen, weight, and hematocrit values might have had on subjective fatigue.

Data Analyses

Data Management

Descriptive statistics, reliabilities of the measures, Pearson correlations, repeated measures ANOVA, independent t-tests and Chi Square statistical tests were performed using the CRUNCH statistical software program (Crunch, 1991). The Statistical Program for the Social Sciences (Norusis, 1990) was used to conduct the forward, stepwise multiple regression analysis and determine whether the model's statistical assumptions had been met.

Descriptive statistics (means and frequencies), were run on all data files in an effort to insure the accuracy of data entry before merging the files. A random check of data collection forms also was performed and revealed no data entry errors.

For subjects who had answered at least 75% of the individual subscale items on the Profile of Mood States (POMS), the Fatigue Symptom Checklist (FSCL) and the

Piper Fatigue Scale (PFS), the mean value of the answered subscale items was substituted for each of the missing item values, a process known as "mean item substitution." Missing values for individual items on the remaining instruments that did not have subscales, were treated as bonafide missing data. Variations in the sample sizes reflect these missing values.

Reliability of the Measures

Table 3 summarizes the internal consistency reliabilities (Cronbach's alpha coefficients) for the fatigue measures over time. Total scale reliabilities for the Fatigue Symptom Checklist (FSCL) and the Piper Fatigue Scale (PFS) total fatigue score (calculated on the basis of the temporal, sensory, severity and affective items) ranged from .91-.96 to .92-.98 respectively.

Individual subscale reliabilities for the FSCL were highest for the mental fatigue subscale (.88-.94), followed by the general incongruity (.84-.92) and specific incongruity subscales (.62-.84). Reliability estimates for the PFS fatigue subscales (temporal, sensory, severity and affective) were highest for the sensory and severity subscales (.92-.97), followed by the affective (.91-.96) and temporal subscales (.68-.94). Alpha coefficients for the Profile of Mood States Fatigue/Inertia subscale (POMS F/I) ranged from .94-.97. Thus, with the exception of Time 1 and 8 coefficients for the FSCL specific incongruity subscale (alphas=.75 and .62 respectively) and Time 1 and 3 coefficients for the PFS temporal subscale (alphas=.68 and .79), all coefficients for subscales used to calculate the total fatigue scores for the instruments were within the acceptable reliability range of .80 or above.

Table 4 summarizes the alpha coefficients for the POMS subscales over time. With the one exception of an alpha coefficient of .77 for the confusion subscale at Time 1, all remaining subscale coefficients were at .80 or above. Reliability coefficients were not calculated for the Norbeck Social Support Questionnaire (NSSQ) since individual items on this scale are not expected to be internally consistent.

Table 3: Internal Consistency Reliabilities of the Fatigue Measures Over Time

Instrument/ Sub-scale	No. of Items	Time 1 n*	Time 1 Alpha**	Time 2 n	Time 2 Alpha	Time 3 n	Time 3 Alpha	Time 4 n	Time 4 Alpha	Time 5 n	Time 5 Alpha	Time 6 n	Time 6 Alpha	Time 7 n	Time 7 Alpha	Time 8 n	Time 8 Alpha
Fatigue Symptom Checklist																	
• Total scale	30	63	.94	63	.91	63	.95	55	.96	54	.93	52	.93	47	.96	41	.94
• General Incongruity Subscale	10	68	.87	68	.84	65	.88	62	.91	57	.88	57	.88	48	.92	44	.91
• Mental Fatigue Subscale	10	68	.91	68	.89	64	.93	64	.94	59	.90	57	.88	50	.92	44	.91
• Specification Congruity	10	67	.75	63	.70	64	.82	59	.84	56	.73	54	.69	49	.80	41	.62
Piper Fatigue Scale																	
• Temporal***	7	24	.68	22	.85	20	.79	30	.90	16	.89	22	.88	19	.94	13	.89
• Sensory***	19	59	.92	51	.96	52	.96	58	.97	37	.94	43	.96	40	.95	32	.97
• Severity	11	66	.92	59	.96	57	.93	54	.96	51	.93	51	.93	42	.92	39	.93
• Affective	5	67	.91	58	.95	62	.92	61	.95	54	.94	54	.92	44	.95	40	.96
• Total Fatigue Scale**	42	21	.92	18	.98	16	.97	28	.98	12	.98	17	.97	14	.98	12	.98
• Evaluative	12	69	.87	65	.80	64	.81	63	.78	56	.80	56	.79	47	.83	42	.83
• Associated Symptoms	11	73	.84	66	.71	62	.72	63	.78	58	.67	57	.82	48	.85	43	.81
• Relief	6	70	.60	49	.85	51	.88	49	.90	43	.93	58	.91	38	.91	31	.89
• Total Scale	71	17	.90	12	.95	9	.94	23	.96	8	.94	14	.92	12	.95	10	.96
Profile of Mood States																	
• Fatigue/Inertia Subscale	7	69	.94	68	.95	66	.95	58	.97	59	.95	53	.95	49	.97	43	.97

NOTE: * n = number of subjects
** Raw Item Alphas
*** For Time 1 only the Baseline Piper Fatigue Scale has two additional items in the temporal subscale and one additional item in the sensory subscale. Thus, for Time 1, the total number of items in the Fatigue Score is 45 in the total scale 74.
NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

Table 4: Internal Consistency Reliabilities of the Profile of Mood States Over Time

POMS Subscales	No. of Items	Time 1 n*	Time 1 Alpha**	Time 2 n	Time 2 Alpha	Time 3 n	Time 3 Alpha	Time 4 n	Time 4 Alpha	Time 5 n	Time 5 Alpha	Time 6 n	Time 6 Alpha	Time 7 n	Time 7 Alpha	Time 8 n	Time 8 Alpha
• Tension	9	66	.83	69	.93	64	.93	61	.93	59	.91	56	.93	51	.94	42	.95
• Depression	15	67	.94	67	.92	66	.92	61	.97	59	.94	53	.93	51	.93	43	.96
• Anger	12	64	.88	66	.84	64	.92	62	.93	59	.93	53	.96	50	.92	44	.96
• Vigor	8	68	.90	68	.89	64	.93	61	.95	59	.93	52	.92	50	.94	44	.91
• Fatigue	7	69	.94	68	.95	66	.95	58	.97	59	.95	53	.95	49	.97	43	.97
• Confusion	7	65	.77	68	.85	66	.86	62	.86	59	.80	54	.85	51	.86	44	.84

NOTE: * n = number of subjects
** Raw Item Alphas

NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

Validity of the Fatigue Measures

Subjective fatigue was measured by three instruments in this study; the FSCL, PFS and the POMS F/I. The FSCL produced two fatigue scores: total number of symptoms and total intensity of symptoms. The PFS and the POMS F/I each produced one fatigue score. Table 5 summarizes the correlation coefficients among four measures over time. They ranged from .48 to .93, providing moderate to strong evidence for the concurrent validity of these four fatigue measures. Appendices J-Q show the correlation coefficients among the four fatigue measures at each time period (Times 1-8).

To determine whether a composite score of the fatigue measures should be used in subsequent analyses, a principal axis factor analysis was conducted on the four fatigue measures at each time period (Times 1-8). Only one factor emerged consistently, and this one factor explained 73.8 to 83.9% of the variance among the fatigue measures over time. Unrotated factor loadings for each of the four fatigue measures ranged from .64 to .96, with the majority loading at .80 or higher. Since only one factor emerged to explain such a high percent of the variance at each time, it was concluded that any one of the four measures could be used in the final regression analyses.

Therefore, a repeated measures analysis of variance (ANOVA) was run to determine which fatigue measure had the greatest rate of same subject completion over time (Times 1-8). A greater number of the same women completed the FSCL over all eight time periods (n=37) than for the POMS F/I (n=32) or the PFS (n=29). Thus, the number and intensity of fatigue symptoms (FSCL) were used as the dependent variables in the final regression analyses.

Chi square and independent t-tests were run to determine if the women who completed the FSCL (n=37) Times 1-8 differed in any respect from the remaining women in the sample (n=37/74). The women were found to differ significantly only on one variable, Karnofsky Performance Status Score (KPS) and only at one point in time

Table 5: Summary of Pearson Product Moment Correlations Between the Four Fatigue Measures Over Time (T_{1-8})

Fatigue Measure	1	2	3	4
1. Intensity of Fatigue Symptoms (FSCL)	1.0	.68-.84	.52-.80	.80-.93
2. Fatigue/Inertia Subscale (POMS)		1.0	.67-.84	.61-.73
3. Total Fatigue Score (PFS)			1.0	.48-.80
4. Total Number of Fatigue Symptoms (FSCL)				1.0

NOTE: All significant at $p < .0001$

Sample Range Over Time: n=40-63

(Time 7). Subjects who completed the FSCL were significantly more likely to have a better KPS at Time 7 (i.e. 90 or above)(Fisher's Exact Test, one-tailed; $p < .03$) than those who did not complete the instrument.

Testing Assumptions of the Statistical Procedures

Tests were conducted to check for violations in all statistical assumptions. For example, to conduct a repeated measures analysis of variance (ANOVA), the following assumptions must be met. First, in the population, the variances in all groups (between and within) need to be equal (homogeneity of variance). Secondly, each group has to be a random, non-biased sample from a normal population (Burns & Grove, 1987; Norusis, 1986; Schott, 1990). Variances were computed by length of chemotherapy cycle (21-Day vs 28-Day) and by inclusion of adriamycin in the treatment regimen (between group variances). Within group variances were computed for over time differences and the interactions between cycle, adriamycin and time. Since ANOVA is considered to be a "robust" procedure even if the normality assumption is not met, histograms were not computed to examine normal distribution (Norusis, 1986). However, when the statistical assumption for the within groups homogeneity of variance was not met, the more stringent Huynh-Feldt p value was used.

Graphic residual analyses, scatterplots, colinearity diagnostics, and determinants for the correlation matrices Norusis (1990) were conducted to verify the statistical assumptions of the forward, stepwise multiple regression analysis (i.e., homogeneity of variance, normality, and linearity), and determine if multicollinearity among the independent variables was present (Schroeder, 1990; Verran & Ferketich, 1987). In reviewing the scatterplots, a check for homogeneity of variance revealed residuals constant over a range of dependent values. No heteroscedasticity was noted; homogeneity was assumed. There was no evidence of curvilinear relationships between subjective fatigue and the independent variables.

Several methods were used to explore whether multicollinearity among the

independent variables was present (Burns & Grove, 1987; Cohen & Cohen, 1983; Norusis, 1986; Schroeder, 1990; Shott, 1990). Multicollinearity indicates that the independent variables are interdependent. When this occurs, little confidence can be placed in the parameter estimation of the model, and thus generalizability of the model is reduced (Schroeder, 1990). Ideally, independent variables should have strong correlations with the dependent variables but only weak correlations with one another in order to avoid the problems associated with multicollinearity.

First, the bivariate correlation tables were examined for a high degree of relationship (> .85) between the independent variables (Schroeder, 1990; Tabachnick & Fidell, 1989). Tables 6-13 summarize the significant correlation coefficients between the independent and dependent variables over time. Four correlation coefficients were found to be greater than .85; each involved the relationship between the POMS depression scores and the POMS recalculated total mood disturbance score (RTMD). At Time 3 (Table 8) a .92 correlation coefficient was found; at Times 4, 6, and 7 (Tables 9, 11, and 12), correlations of .86 were found; and at Time 8 (Table 13), a .85 correlation was found. While these high correlations are suggestive of multicollinearity, they are not diagnostic (Schroeder, 1990).

Next the multivariate relationships between the independent variables were examined for evidence of multicollinearity by calculating the determinant and the condition indices of each of the bivariate correlational matrices over time (Times 1-8). None of the determinants equaled zero, and none of the condition indices were 10 or greater (Schroeder, 1991; Norusis, 1990). Based on these analyses, there was little concern for multicollinearity.

Multiple Regression Analysis

Forward, stepwise multiple regression was used to determine the percent of explained variance and unique contributions made by the independent variables (IV) to predicting the number of fatigue symptoms and their intensities over time. For each

Table 6: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 1 (n=33)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9	10	11
A. Dependent Variables											
1. Number of Fatigue Symptoms (FSCL)	1.0	.90***	-.54**	.50**	.65***	---	---	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.54**	.51**	.71***	---	---	---	---	---	---
B. Independent Variables											
3. Vigor (POMS)			1.0	-.41*	-.54**	---	---	---	-.43*	---	---
4. Depression (POMS)				1.0	.76***	---	---	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	-.36*	---	---	---	---	---
6. Age						1.0	---	---	---	---	---
7. Stage							1.0	-.36*	---	---	-.55**
8. Total Functional Support								1.0	---	---	---
9. Karnofsky Performance Level									1.0	---	---
10. Cycle										1.0	---
11. Adriamycin											1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$ ** $p < .005$ *** $p < .0001$

Table 7: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 2 (n=29)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9	10
A. Dependent Variables										
1. Number of Fatigue Symptoms (FSCL)	1.0	.95***	-.56**	.55**	.71***	---	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.57**	.63***	.78***	---	---	---	---	---
B. Independent Variables										
3. Vigor (POMS)			1.0	-.47**	-.41*	---	-.40*	---	---	---
4. Depression (POMS)				1.0	.78***	---	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	---	---
6. Age						1.0	---	---	---	---
7. Stage							1.0	---	---	-.56
8. Hematocrit								1.0	---	---
9. Cycle									1.0	---
10. Adriamycin										1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 8: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 3 (n=35)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9	10
A. Dependent Variables										
1. Number of Fatigue Symptoms (FSCL)	1.0	.92***	-.42*	.69***	.75***	---	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.40*	.76***	.82***	---	---	---	---	---
B. Independent Variables										
3. Vigor (POMS)			1.0	-.50**	-.49*	---	---	---	---	---
4. Depression (POMS)				1.0	.92	---	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	---	---
6. Age						1.0	---	---	---	---
7. Stage							1.0	---	---	-.52**
8. Karnofsky Performance Status								1.0	---	---
9. Cycle									1.0	---
10. Adriamycin										1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 9: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 4 (n=34)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9
A. Dependent Variables									
1. Number of Fatigue Symptoms (FSCL)	1.0	.95***	-.59**	.63***	.76***	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.56**	.76***	.79***	---	---	---	---
B. Independent Variables									
3. Vigor (POMS)			1.0	-.43*	-.41*	---	---	---	---
4. Depression (POMS)				1.0	.86***	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	---
6. Age						1.0	---	---	-.52**
7. Stage							1.0	---	---
8. Cycle								1.0	---
9. Adriamycin									1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 10: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 5 (n=33)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9	10	11
A. Dependent Variables											
1. Number of Fatigue Symptoms (FSCL)	1.0	.90***	-.51**	.50**	.72***	---	---	---	.37*	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.51**	.55**	.75***	---	---	---	.36*	---	---
B. Independent Variables											
3. Vigor			1.0	-.36*	---	---	---	---	---	---	---
4. Depression (POMS)				1.0	.71***	---	---	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	.43*	---	---
6. Age						1.0	---	---	---	---	---
7. Stage							1.0	.47**	---	---	-.53**
8. Total Functional Support								1.0	---	---	-.39*
9. Karnofsky Performance Status									1.0	---	---
10. Cycle										1.0	---
11. Adriamycin											1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 11: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 6 (n=33)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9
A. Dependent Variables									
1. Number of Fatigue Symptoms (FSCL)	1.0	.94***	-.54**	.80***	.80***	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.52**	.78***	.77***	---	---	---	---
B. Independent Variables									
3. Vigor (POMS)			1.0	-.53**	-.57***	---	---	---	---
4. Depression (POMS)				1.0	.86***	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	-.36	---	---	---
6. Age						1.0	---	---	---
7. Stage							1.0	---	-.42*
8. Cycle								1.0	---
9. Adriamycin									1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 12: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 7 (n=34)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9	10	11
A. Dependent Variables											
1. Number of Fatigue Symptoms (FSCL)	1.0	.78***	-.48**	.58**	.70***	---	---	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.66***	.59**	.79***	---	---	---	---	---	---
B. Independent Variables											
3. Vigor (POMS)			1.0	-.57**	-.63***	---	---	---	---	---	---
4. Depression (POMS)				1.0	.86***	---	---	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	---	---	---
6. Age						1.0	---	---	---	---	---
7. Stage							1.0	---	---	---	-.52**
8. Total Functional Support								1.0	---	---	---
9. Karnofsky Performance Status									1.0	---	---
10. Cycle										1.0	---
11. Adriamycin											1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

Table 13: Significant Pearson Product Moment Correlations Between the Dependent Variables--Intensity and Number of Fatigue Symptoms (FSCL) and the Independent Variables--Time 8 (n=35)

Dependent/Independent Variables	1	2	3	4	5	6	7	8	9
A. Dependent Variables									
1. Number of Fatigue Symptoms (FSCL)	1.0	.92***	-.56**	.70***	.81***	---	---	---	---
2. Intensity of Fatigue Symptoms (FSCL)		1.0	-.48**	.71***	.86***	---	---	---	---
B. Independent Variables									
3. Vigor (POMS)			1.0	---	-.40*	---	---	---	---
4. Depression (POMS)				1.0	.85***	---	---	---	---
5. Mood Disturbance (POMS) (Recalculated)					1.0	---	---	---	---
6. Age						1.0	---	---	---
7. Stage							1.0	---	-.53**
8. Cycle								1.0	---
9. Adriamycin									1.0

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p < .05$
** $p < .005$
*** $p < .0001$

time period (Times 1-8), the IVs were entered in the following order: depression and vigor were entered as the first set; the POMS recalculated total mood disturbance, as the second set; total functional support (Times 1, 5 & 7 only), as the third set; age, as the fourth set; and stage of disease, cycle, adriamycin, hematocrit (Time 2 only), and KPS (Times 1, 3, 5, & 7 only) as the fifth and final set.

Threats to Validity

The major threat to validity in this study concerned the lack of power to detect significant differences between the groups should they exist (statistical conclusion validity; Cook & Campbell, 1979). A power analysis was performed to determine the approximate sample size needed for the multiple regression analysis. Power was set at .80, alpha was set at .05, and the effect size was set at a moderate level ($r=.42$; $r^2=.18$).

Under these conditions, a sample size of 80 was needed to detect statistically significant findings; 37 women constituted the final sample in this study. Thus, the following results need to be viewed cautiously and within this context.

CHAPTER FOUR

RESULTS

The Sample

Demographic Characteristics

Table 14 summarizes the baseline demographic characteristics of the 37 women who completed the FSCL Times 1-8. The average woman was married and Caucasian, 50 years old, with an average annual income of more than $30,000/year and had completed at least part of college.

Medical Characteristics

Almost all of the women (92%) had been treated with a modified radical mastectomy and an auxiliary node dissection (Table 15); most had Stage II (49%) or Stage I Breast Cancer (40.5%). The most common chemotherapy regimen was Cytoxan, Methotrexate, and 5-Fluorouracil (5-FU)(CMF; 77.8%) given on a 21-Day treatment cycle (56.8%), without "sandwich" radiation therapy or Tamoxifen therapy. The 21-day CMF regimen consisted of Cytoxan (600mg/M^2), Methotrexate (40mg/M^2) and 5FU (600mg/M^2) given intravenously (IV), Days 1 & 8 of every cycle. The 28-Day regimen involved Cytoxan (100mg/M^2) orally, for the first 14 days of each cycle; and Methotrexate (40mg/M^2) and 5FU (600mg/M^2) given IV Day 1 of each cycle. The majority of women required no dosage modifications over time (Times 1-8).

Baseline (Time 1) Activity/Exercise Variables

Prior to beginning CT (Time 1), the majority or 78% were working at least 20 or more hours per week (Table 16) at a position that did not involve shift rotation (74%, n=27). In response to a question that asked the women what percentage of their daily activities, regardless of their occupational status involved a physical component (i.e., heavy lifting or strenuous physical activity); an emotional component (i.e., caring for others or dealing with emotionally-laden issues); or a mental component (i.e., intense concentration, memorization), the majority stated less than 25% of their time

Table 14: Baseline Demographic Characteristics (n=37)

Characteristic	n	Percent
Ethnicity		
Caucasian	33	97.1
Oriental	1	2.9
Marital Status		
Married	25	71.4
Separated/Divorced	6	17.1
Widowed	3	8.6
Single, Never Married	1	2.9
Income		
More than $30,000	20	60.6
$20,000 - $30,000	9	27.3
$10,000 - < $20,000	3	9.1
less than $10,000	1	3.1
Highest Educational Level		
Completed College	12	34.3
Partial College	12	34.3
Completed Graduate School	6	17.2
Completed High School	3	8.6
Other	2	5.8

Characteristic	n	M	SD	Range
Age (yrs)	35	49.74	9.37	30-71

Table 15: Medical Demographic Characteristics (n=37)

Characteristic	n	Percent
Stage		
1	15	40.5
2	18	48.7
3	2	5.4
4	2	5.4
Cycle		
21 Day	21	56.8
28 Day	16	43.2
Protocol		
CMF	28	77.8
FAC	4	11.1
Other	4	11.1
Radiation		
Yes	1	2.7
No	36	97.3
Adriamycin		
Yes	8	21.6
No	29	78.4
Tamoxifen		
Yes	4	10.8
No	33	89.2

Characteristic	n	Percent
Surgery		
• Modified Radical Mastectomy with A.N.D.*	34	91.9
• Lumpectomy with A.N.D.*	1	2.7
• Other	2	5.4

Characteristic	n	M	SD	Range
Hematocrit (Time 2)	32	36.52	3.47	30.8-43.40

* NOTE: A.N.D. = Axillary Node Dissection

Table 16: Activity and Exercise Variables–Time 1 (n=37)

Variable	n	Percent	Variable	n	Percent
Occupational Status			Usual Pattern of Exercise		
• Employed	23	65.7	• Walking	23	65.7
• Homemaker	9	25.7	• None	8	22.9
• Retired	2	5.7	• Other	4	11.5
• Unemployed	1	2.9			
			Frequency of Exercise/Week		
Hours Worked/Week			• 2 - 4 times/wk	16	50.0
• More than 40, less than 60	9	39.1	• More than 4 times/wk	9	28.1
• More than 20, less than 40	9	39.1	• None	5	15.6
• Less than 20 hrs/wk	4	17.4	• Less than 2 times/wk	2	6.3
• More than 60 hrs/wk	1	4.4			
			Change in Exercise Pattern Past 6 Months		
Karnofsky Performance Status			• No change	21	63.6
• 90 - 100	14	41.2	• Exercising less	9	27.3
• 80 - 89	14	41.2	• Exercising more	3	9.1
• 60 - 79	5	14.7			
• 20 - 39	1	2.9			

per day was spent in physical activities (n=37/75.7%), while 25-50% was spent on emotional activities (n=37/72.9%) and 25% on mental activities (n=36/48.7%). The majority (82.4%) described their self-perceived KPS to be at least 80% or greater (Table 16); and 63.6% denied any change in their exercise patterns during the 6 months prior to diagnosis. The most common form of exercise was walking two to four times per week.

Baseline (Time 1) Nutritional Variables

Table 17 summarizes baseline nutritional variables for these women. The majority (56.3%) stated that they had experienced a change in weight (both losses and gains were reported) in the 6 months prior to diagnosis; these changes were described as being unintentional by 75% of the women, and intentional by 25%. The average weight change was 8.4 pounds (range: 3-32lbs.). Appetite in general, was described as "good" with only 20.6% reporting a change during the previous 6 months. The average weight and height for these women was 142 pounds (range: 103-198lbs.) and 5'4" (range: 4'10"-5'9").

Baseline (Time 1) Sleep/Wake Cycles

Table 18 describes the baseline sleep/wake cycles of these women. The average woman slept 5-8 hours per night; described the overall quality of her sleep as "good to excellent" and reported no change in sleep cycle during the preceding 6 months (57.1%). However, 43% of the women reported sleeping either more or less in the preceding six months. Naps were seldom if ever taken, but were described as being generally "fair to good" when they were taken. A change in the number of naps was reported by 26.4% of the women.

Changes in Activity/Rest Variables

Table 19 describes changes in activity/exercise variables over time (Times 3, 5, & 7). At Time 1 (Table 16), only 82.4% of the women reported a Karnofsky Performance Status (KPS) of 80 or above. By Time 3 however, 94.3% described their

Table 17: Weight and Appetite Variables–Time 1 (n=37)

Variable	n	Percent
Weight Change Past 6 Months		
No	16	45.7
Loss	10	28.6
Gain	9	27.7
Intentional Weight Change		
No	18	75.0
Yes	6	25.0
Appetite		
Good	21	61.8
Excellent	10	29.4
Fair	3	8.8
Change in Appetite Past 6 Months		
No	27	79.4
Decrease	6	17.7
Increase	1	2.9

Variable	n	M	SD	Range
Weight (Time 1)	37	141.97	22.27	103-198

Table 18: Sleep/Wake Variables–Time 1 (n=37)

Variable	n	Percent
Usual Amount of Sleep in a 24 Hour Period		
• More than 5 hrs, less than 8	25	71.4
• More than 8 hrs, less than 12	8	22.9
• Less than 5 hrs	2	5.7
Quality of Sleep Pattern		
• Excellent	5	14.3
• Good	16	45.7
• Fair	11	31.4
• Poor	3	8.6
Change in Sleep Patterns Past 6 Months		
• No change	20	57.1
• Sleeping less	10	28.6
• Sleeping more	5	14.3
Usual Nap Pattern		
• Never	10	28.6
• Seldom	17	48.6
• Occasionally	5	14.3
• Frequently	2	5.7
• Always	1	2.9
Change in Number of Naps Past 6 Months		
• No change	25	73.5
• Napping more	8	23.5
• Napping less	1	2.9
Usual Nap Quality		
• Excellent	3	10.7
• Good	16	57.1
• Fair	8	28.6
• Poor	1	3.6

Table 19: Changes in Activity/Exercise Variables Over Time (n=37)

Variable	Time 3 n	Time 3 Percent	Time 5 n	Time 5 Percent	Time 7 n	Time 7 Percent
Karnofsky Performance Status						
• 90 - 100	12	34.3	13	37.1	18	51.4
• 80 - 89	21	60.0	22	62.9	17	48.6
• 60 - 79	2	5.7	--	--	--	--
Occupational Status						
• No change	16	45.71	24	68.6	24	68.6
• Now employed	1	2.9	--	--	1	2.9
• Now work part-time	7	20.0	7	20.0	3	8.6
• Now work full-time	4	11.4	2	5.7	4	11.4
• Other	6	17.1	1	2.9	2	5.7
• Now unemployed	1	2.9	1	2.9	1	2.9
Exercise						
• No change	17	48.6	19	54.3	19	54.3
• Walking less	9	25.7	9	25.7	6	17.1
• Walking more	5	14.3	4	11.4	7	20.0
• Jogging less	2	5.7	2	5.7	2	5.7
• Jogging more	--	--	1	2.9	1	2.9
• Bicycling more	1	2.9	--	--	--	--
• Other	1	2.9	--	--	--	--

NOTE: Time 3 = Day 1, Cycle 2; Time 5 = Day 1, Cycle 3; Time 7 = Day 1, Cycle 6

KPS at this level; and by the 3rd and final (6th) cycle, 100% of the women, described their KPS at 80 or above.

While 78.2% described working 20 or more hours a week at Time 1 (Table 16), the majority (54.3%) indicated that they had experienced some type of change in their occupational status by Day 1 of the second cycle (Time 3). Almost a quarter (22.9%) were either working part-time or were unemployed. This change held constant through Day 1 of the third cycle (Time 5); but had dropped to 11.5% by Time 7 (Day 1, cycle 6).

Most open-ended responses concerning occupational status were made at Time 3 only (Day 1, 2nd cycle). Three women commented that they had to go on a leave of absence, sick leave, or disability immediately following surgery. Two others stated that while they continued to work, they had to reduce the number of hours worked; the number of meetings attended; and refuse to accept new clients. After Time 3, the majority of women reported no change in their occupational status.

Exercise variables stayed relatively stable over time. Only two women volunteered comments about changes that had occurred in their exercise patterns over time. At Time 3, one women commented that prior to surgery she had been able to both walk and hike; since surgery, walking one hour a day was all she could undertake. Another woman commented that since her surgery, she was dancing less, but by Time 5 (Day 1, cycle 3) she had resumed her usual dance patterns.

Changes in Nutritional Variables

The nutritional variables of appetite and weight remained relatively stable over time (Times 3, 5, & 7) with the majority continuing to report their appetites as "good to excellent" (Table 20). Average weight (baseline: 141.97 lbs. see Table 17) increased by 4.4 pounds to 146.41 pounds by Time 6 (Day 10/14, cycle 3)(Table 20).

A few women volunteered nutritionally-related comments. At Time 3 (Day 1, cycle 2), two women stated that their appetites were "fair" while on CT, but improved

Table 20: Changes in Nutritional Weight and Appetite Variables Over Time (n=37)

Variable	Time 3 n	Time 3 Percent	Time 5 n	Time 5 Percent	Time 6 M	Time 6 SD	Time 6 Range	Time 7 n	Time 7 Percent
Appetite									
• Poor	2	5.7	--	--				1	2.9
• Fair	7	20.0	6	17.1				6	17.7
• Good	17	48.6	17	48.6				14	41.2
• Excellent	9	25.7	12	34.3				13	38.2
Weight (Time 6) (N=32)					146.4	21.61	105-196		

NOTE: Time 3 = Day 1, Cycle 2; Time 5 = Day 1, Cycle 3; Time 6 = Day 10/14, Cycle 3; Time 7 = Day 1, Cycle 6

to "good" when off CT. At Time 5 (Day 1, cycle 3), a third women stated a similar response: "My appetite is poor when I am taking CT; after two weeks off however, I'm feeling more normal, and my appetite, exercise, and energy all improve."

Changes in Sleep/Wake Cycles

Table 21 summarizes the changes in Sleep/Wake Cycles over time (Times 3, 5, & 7). The majority of women were sleeping and napping more at Time 3 (Day 1, 2nd cycle) than noted at other times. Concerns about sleep quality and quantity were the most common concerns expressed over the entire study, with 10 women volunteering comments about their sleep patterns at Time 3; seven at Time 5 and 3 at Time 7. The three most common concerns had to do with frequent night time awakenings, difficulty falling back to sleep once awakened, and a change in the quality of their sleep. For example, one woman stated that she "felt wired" and not rested after sleeping, since she was taking only "short naps" during the night. Another stated that she had to get up frequently in the middle of the night to go to the bathroom, because she was drinking a lot of fluids secondary to her CT. Once she was up, she had difficulty falling back to sleep because her mind would start to focus on "personal concerns and family issues." One woman commented that the quality of her sleep was worse especially for the first week following CT, with improvements noted during the two weeks she was off CT. Another woman stated that she had started to dream a lot and that her dreams had become very violent, active dreams. Later, at Time 5 this same woman observed that these vivid dreams were more frequent and pronounced during the first week following CT. Only one woman reported an improvement in her sleeping patterns and that occurred at Time 3 when she stated that she was sleeping "longer and better".

Changes in Psychological Variables Over Time

Mean scores for the POMS total mood disturbance (TMD), the recalculated TMD, and individual subscale scores over time (Times 1-8) are shown in Table 22. Total mood disturbance scores were the highest at Time 1 ($\underline{M}$=26.89, SD=27.64) and

Table 21: Changes in Sleep/Wake Variables Over Time (n=37)

Variable	Time 3 n	Time 3 Percent	Time 5 n	Time 5 Percent	Time 7 n	Time 7 Percent
Sleep Pattern						
• No change	11	32.4	15	42.9	17	48.6
• Sleeping more	16	47.1	10	28.6	7	20.0
• Sleeping less	6	17.4	7	20.0	8	22.9
• Other	1	2.9	3	8.6	3	8.6
Sleep Quality						
• No change	18	51.4	20	54.1	23	65.7
• Better quality	5	14.3	6	17.1	4	11.4
• Worse quality	8	22.9	7	20.0	7	20.0
• Other	4	11.4	2	5.7	1	2.9
Awaken Refreshed						
• Seldom	1	2.9	1	2.9	2	5.9
• Occasionally	8	22.9	9	25.7	11	32.4
• Frequently	25	71.4	19	54.3	19	55.9
• Always	1	2.9	6	17.1	2	5.9
Amount of Naps						
• No change	14	40	20	54.1	24	68.6
• Napping more	15	42.9	6	17.1	7	20.0
• Napping less	6	17.1	9	25.7	4	11.4

NOTE: Time 3 = Day 1, Cycle 2; Time 5 = Day 1, Cycle 3; Time 7 = Day 1, Cycle 6

Table 22: Profile of Mood State Scores (POMS) Times 1-8 (n=37)

Affective State	Time 1			Time 2			Time 3			Time 4			Time 5			Time 6			Time 7			Time 8		
	n	M	SD	n	M	SD	n	M	SD	n	M	SD	n	M	SD	n	M	SD	n	M	SD	n	M	SD
• Depression	36	8.37	5.18	36	5.89	6.82	37	6.16	7.73	36	7.03	12.20	37	4.73	6.63	35	6.31	8.19	37	5.84	6.81	37	5.93	9.39
• Anger	36	6.60	5.11	36	4.28	5.02	37	4.87	6.33	36	5.17	8.70	37	3.73	7.66	35	6.09	9.14	37	4.65	6.76	37	3.89	7.86
• Vigor	36	16.97	6.49	36	17.17	7.18	37	17.00	7.14	36	15.88	7.21	37	16.81	7.28	35	14.88	6.51	37	16.76	7.39	37	15.43	6.79
• Fatigue	36	9.14	7.35	36	8.94	7.43	37	7.46	5.91	36	9.62	7.44	37	7.41	6.74	34	10.77	7.39	37	9.06	7.78	37	9.71	8.31
• Tension	36	12.39	6.03	36	9.42	8.11	37	7.61	6.16	36	7.45	7.17	37	6.46	5.80	36	7.22	6.74	37	7.46	7.76	37	7.24	7.77
• Confusion	36	7.36	3.95	36	5.53	4.77	37	5.37	4.17	37	5.37	4.17	37	4.95	4.60	35	5.46	4.47	37	5.54	4.79	37	5.30	4.74
• Total Mood Disturbance	36	26.89	27.64	35	17.63	30.24	37	13.72	30.57	35	19.57	38.49	35	11.58	29.88	33	22.61	36.13	34	17.97	35.00	36	17.35	37.23
• Recalculated Total Mood Disturbance*	33	27.14	12.70	29	19.28	16.08	35	17.39	14.59	34	16.16	14.68	33	13.61	10.16	33	16.52	13.80	34	16.82	15.42	35	14.11	12.53

NOTE: * Recalculated Total Mood Disturbance score includes Anger, Tension, and confusion scores only. Depression, Vigor and Fatigue scores are not included.

NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

the lowest at Time 5 (M=11.58, SD=29.88). Similar findings were noted for the subscales of depression, anger, tension, and confusion. Vigor remained relatively constant over time. Highest mean fatigue scores were reported at Time 6. However, there were no statistically significant changes in total mood disturbance or subscale scores over time or by length of CT cycle or by the inclusion of adriamycin in the CT regimen (repeated measures ANOVA).

Changes in Social Support Over Time

The mean scores for the Norbeck Social Support Questionnaire (NSSQ) are shown in Table 23. The total number of people identified in the woman's support network declined from Time 1 (M=12.14, SD=6.14) to Time 5 (M=10.11, SD=5.42). Similar declines over time (Times 5 & 7) were noted in total network and total functional support. Repeated measures ANOVA revealed that these were statistically significant declines over time but were not affected by length of CT cycle (Tables 24-26) or by the inclusion of adriamycin in the treatment regimen (Tables 27-29).

The one exception to these significant declines over time, occurred for the total number listed in the support network when adriamycin was included in the regimen (Table 27). This change was not significant. Thus, the total number of people identified in the network did not decline significantly for the group receiving adriamycin in the regimen.

Changes in Subjective Fatigue Over Time

Fatigue Symptoms

A maximum of 30 fatigue symptoms could be measured by the FSCL. At baseline, the average number of symptoms experienced by this sample was 8.81 (SD=7.20) (Table 30). This number stayed relatively stable at each time with the most symptoms occurring at Time 7 (M=10.03, SD=8.15). Symptoms measured by the general incongruity subscale were the most frequent and consistent symptoms reported

Table 23: Norbeck Social Support Questionnaire Scores (N.S.S.Q.) Over Time (N=37)

N.S.S.Q. Variable	Time 1* n	Time 1* M	Time 1* SD	Time 5 n	Time 5 M	Time 5 SD	Time 7 n	Time 7 M	Time 7 SD
• Number in Network	36	12.14	6.14	37	11.30	5.74	37	10.11	5.42
• Total Network Support	36	112.75	57.15	37	99.05	53.01	37	88.89	52.26
• Total Functional Support	36	219.31	120.81	35	199.66	105.08	36	175.89	104.16

* NOTE: Time 1 = Baseline
Time 5 = Day 1 of 3rd Cycle
Time 7 = Day 1 of 6th Cycle

Table 24: Repeated Measures Analysis of Variance: Number Listed in Social Support Network (NSSQ) Over Time by Length of Chemotherapy Cycle

Source	df	ss	MSS	F	p
• Between Subjects	35	3109.519			
• Cycle	1	8.189	8.189	.090	.77
• Error 1	34	3101.329	91.216		
• Within Subjects	72	516.667			
• Time ($T_{1,5,7}$)	2	77.840	38.920		.007*
• Interaction (Cycle x Time)	2	1.507	.753		.85*
• Error 2	68	436.808	6.424		

* NOTE: Huynh-Feldt

Table 25: Repeated Measures Analysis of Variance: Total Network Support (NSSQ) Over Time by Length of Chemotherapy Cycle

Source	df	ss	MSS	F	p
• Between Subjects	35	252142.296			
• Cycle	1	86.801	86.801	.012	.92
• Error 1	34	252055.496	7413.397		
• Within Subjects	72	69158.667			
• Time ($T_{1,5,7}$)	2	10855.119	5427.560	6.435	.003*
• Interaction (Cycle x Time)	2	660.268	330.134	.391	.68*
• Error 2	68	57357.492	843.493		

* NOTE: Huynh-Feldt

Table 26: Repeated Measures Analysis of Variance: Total Functional Support (NSSQ) Over Time by Length of Chemotherapy Cycle

Source	df	ss	MSS	F	p
• Between Subjects	33	1057541.294			
• Cycle	1	1452.494	1452.494	.04	.84
• Error 1	32	1056088.800	33002.775		
• Within Subjects	68	213332.667			
• Time ($T_{1,5,7}$)	2	42907.322	21453.661	8.219	.0009*
• Interaction (Cycle x Time)	2	1281.322	640.661	.245	.77*
• Error 2	64	167054.267	2610.223		

* NOTE: Huynh-Feldt

Table 27: Repeated Measures Analysis of Variance: Number Listed in Network (NSSQ) Over Time by Inclusion of Adriamycin in the Treatment Regimen

Source	df	ss	MSS	F	p
• Between Subjects	35	3109.519			
• Adriamycin	1	185.780	185.780	2.160	.15
• Error 1	34	2923.738	85.992		
• Within Subjects	72	516.667			
• Time ($T_{1,5,7}$)	2	27.763	13.882	2.300	.11
• Interaction (Ariamycin x Time)	2	27.874	13.937	2.309	.11
• Error 2	68	410.441	6.036		

Table 28: Repeated Measures Analysis of Variance: Total Network Support (NSSQ) Over Time by Inclusion of Adriamycin in the Treatment Regimen

Source	df	ss	MSS	F	p
• Between Subjects	35	252142.296			
• Adriamycin	1	18236.112	18236.112	2.651	.12
• Error 1	34	233906.185	6879.594		
• Within Subjects	72	69158.667			
• Time ($T_{1,5,7}$)	2	5597.343	2798.671	3.444	.04*
• Interaction (Ariamycin x Time)	2	2757.676	1378.838	1.697	.19*
• Error 2	68	55260.083	812.648		

* Huynh-Feldt

Table 29: Repeated Measures Analysis of Variance: Total Functional Support (NSSQ) Over Time by Inclusion of Adriamycin in the Treatment Regimen

Source	df	ss	MSS	F	p
• Between Subjects	33	1057541.294			
• Adriamycin	1	105528.105	105528.105	3.547	.07
• Error 1	32	952013.189	29750.412		
• Within Subjects	68	213332.667			
• Time ($T_{1,5,7}$)	2	21841.676	10920.838	4.434	.02*
• Interaction (Ariamycin x Time)	2	10687.676	5343.838	2.169	.13*
• Error 2	64	157647.912	2463.249		

* NOTE: Huynh-Feldt

Table 30: Number of Fatigue Symptoms as Measured by the Fatigue Symptom Checklist (F.S.C.L.) Times 1-8 (N=37)

Subscale and Total Number of Symptom Scores	Time 1		Time 2		Time 3		Time 4		Time 5		Time 6		Time 7		Time 8	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
• General Incongruity Score	3.68	2.99	3.32	2.98	3.60	3.02	4.00	2.67	3.78	3.26	4.43	3.05	4.22	3.17	4.16	3.24
• Mental Fatigue Score	3.60	3.28	2.54	2.95	3.22	3.09	2.87	2.87	2.49	2.94	2.97	2.92	3.62	3.39	3.05	2.90
• Specific Incongruity Score	1.54	1.79	1.95	1.79	1.62	1.89	2.05	2.26	2.11	2.15	1.60	1.88	2.19	2.55	1.46	1.73
• Total No. of Fatigue Symptoms	8.81	7.20	7.81	6.57	8.43	7.01	8.92	7.06	8.38	7.20	9.00	6.74	10.03	8.15	8.68	6.91

NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

over time, followed by mental and specific incongruity subscale symptoms (Table 31).

Fatigue Intensities

Intensity scores for the FSCL could range from 30-150. In this particular sample, mean intensity scores stayed relatively low (41.96-44.43) and stable over time (Table 32). Lowest intensities were reported at Time 5 (M=41.96, SD=13.65); highest intensities at Time 7 (M=44.43, SD=15.96). Fatigue symptoms consistently reported over time (Times 1-8) as being the most intense were the general incongruity symptoms of "tired over my whole body, tired in my legs, and wanting to lie down." (Table 31).

On the PFS, where scores could range from 0-100, the average total fatigue score at Time 1 also was low (M=38.90, SD=12.86) (Table 33). This score stayed relatively stable over time with the highest average score reported at Time 6 (M=39.40, SD=18.77). As expected, the highest scores for the temporal, severity and affective subscales occurred at Time 6 (Day 10/14, 3rd cycle), but this did not hold true for the sensory subscale, where Time 1 scores were the highest (M=69.96, SD=13.73).

Fatigue scores on the POMS Fatigue/Inertia subscale (POMS F/I) could range from 1 to 28. In this sample, the lowest fatigue scores occurred at Time 5 (M=7.41, SD=6.74); the highest at Time 6 (M=10.77, SD=7.39) (Table 22).

Fatigue Changes by Length of Cycle and by Inclusion of Adriamycin in the Regimen

To determine whether fatigue scores were affected by length of CT cycle (21-day versus 28-day), by inclusion of adriamycin in the regimen, or by time, multiple repeated measures ANOVAs were run on the four fatigue indicators. There were no significant changes found for any of the fatigue indicators over time, or by length of CT cycle, or by the inclusion of adriamycin in the treatment regimen.

In response to the open-ended question on the demographic profiles that asked

Table 31: Most Common and Intense Fatigue Symptoms Over Time (T_{1-8})

General Incongruity

1. Tired over my whole body*
2. Tired in my legs*
3. Want to lie down*
4. Drowsy
5. Feel like yawning
6. Eye strain

Mental Fatigue

1. Anxious
2. Forgetful

Specific Incongruity

1. Thirsty

NOTE: * Cited by at least a third of the sample as being moderate/greater in intensity during five or more CT cycles.

Table 32: Intensity of Fatigue Symptoms as Measured by the Fatigue Symptom Checklist (F.S.C.L.) Times 1-8 (N=37)

Subscale and Total Intensity Scores	Time 1		Time 2		Time 3		Time 4		Time 5		Time 6		Time 7		Time 8	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
• General Incongruity Score	15.40	5.68	15.14	5.81	15.32	6.68	15.89	5.38	15.57	6.62	16.83	6.29	16.61	7.40	16.76	7.47
• Mental Fatigue Score	15.79	7.20	14.24	5.93	14.62	6.16	14.10	5.28	13.53	5.31	14.14	4.85	15.22	7.22	14.57	6.13
• Specific Incongruity Score	12.60	3.78	13.14	3.58	12.32	3.94	13.00	3.85	12.89	3.17	12.03	2.5	12.63	3.68	12.03	2.80
• Total Fatigue Intensity Score	43.79	15.04	42.52	12.55	42.27	15.05	42.98	13.13	41.96	13.65	42.99	12.09	44.43	15.96	43.38	15.09

NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

Table 33: Subjective Fatigue as Measured by the Piper Fatigue Scale (PFS) Times 1-8 (N=37)

Subscale and Total Fatigue Scores	Time 1			Time 2			Time 3			Time 4			Time 5			Time 6			Time 7			Time 8		
	n	M	(SD)	n	M	(SD)	n	M	(SD)	n	M	(SD)	n	M	(SD)	n	M	(SD)	n	M	(SD)	n	M	(SD)
• Temporal	33	31.55	17.86	24	43.72	20.24	22	37.26	20.98	24	40.56	21.37	19	39.28	20.09	23	46.05	18.10	22	40.27	24.60	24	42.03	21.95
• Sensory	36	69.96	13.73	36	38.97	18.42	37	38.99	22.20	37	40.36	23.65	36	37.36	20.88	37	42.06	21.45	36	40.26	22.53	37	40.49	23.63
• Severity	36	18.05	12.50	37	23.43	20.58	37	19.13	15.70	37	23.06	20.17	37	22.25	20.34	37	24.33	17.24	34	23.24	19.99	37	21.24	19.88
• Affective	35	34.96	24.48	33	35.06	28.17	35	36.73	24.52	34	40.24	24.97	34	45.34	26.02	35	45.47	23.63	32	36.94	26.87	34	37.76	29.59
• Total Fatigue Score	36	38.90	12.86	32	35.49	19.72	35	32.23	18.34	35	35.55	21.14	33	35.60	19.89	35	39.40	18.77	32	34.69	21.92	34	35.61	20.98
• Evaluative	35	41.93	22.36	36	22.87	12.51	36	24.82	14.55	37	23.50	12.18	36	22.13	12.47	36	24.98	12.58	34	21.29	11.51	37	22.40	15.57
• Associated Symptoms	36	11.67	8.70	36	12.13	9.43	36	9.82	8.80	37	10.56	7.07	37	11.12	8.82	37	11.18	9.93	36	11.65	12.41	37	12.33	11.29
• Relief	35	61.57	13.76	29	58.47	20.35	30	54.11	25.20	31	53.72	24.40	30	54.15	28.07	32	54.63	23.79	29	48.04	25.44	32	48.41	22.63

NOTE: Times 1 & 2 = Cycle 1; Times 3 & 4 = Cycle 2; Times 5 & 6 = Cycle 3; Times 7 & 8 = Cycle 6

about "any other changes during the past month that may be of concern to you?", four women described being fatigued at Time 3 (Day 1, 2nd cycle); two were on 21-day regimens (one was receiving adriamycin); two were on 28-day CMF regimens. One woman stated that she was more tired the first week following CT; by the second week, her fatigue had improved slightly, and by the third week, she felt "almost normal" (21-Day CMF cycle). Another stated that her "energy level" routinely declined during the first two weeks of CT; during which time she also didn't think as clearly and was more impatient (28-Day CMF cycle).

By Time 5 (Day 1, cycle 3), five women volunteered concerns about fatigue; three were on 21-Day regimens, one with adriamycin; two were on 28-day CMF regimens. One woman stated that while she was "fully active", keeping that way required "more effort" (21-Day, adriamycin cycle). Another stated that while she usually did not feel the need to "rest or relax" much during the day, during the past month she had had to lay down each afternoon. "I'm trying to function at my normal level, and I am frustrated when I can't. (21-Day CMF cycle).

By Time 7 (Day1, cycle 6), five different women described feeling fatigued, three were on 21-day regimens; none were reciving adriamycin. Two described remaining tired longer after CT. They each commented about how the amount of time needed to recover from CT's side effects in general, had increased. Other concerns cited by these women over time (in addition to the previously discussed fatigue, work and sleep-related concerns), included hair loss (N=5), emotional concerns (N=4)(i.e., feeling like "being on a roller-coaster"; impatient, lacking in enthusiasm/depression); hot flashes and missed periods (N=2).

Interrelationships Among the Variables

The direction, strength, and statistical significance of the bivariate correlations over time between the intensity and number of fatigue symptoms (FSCL) and the independent variables (IV), vigor, depression, recalculated POMS Total Mood

Disturbance Score (RTMD), total functional support, age, stage, Karnofsky Performance Status (KPS), hematocrit, length of cycle and inclusion of adriamycin in the treatment regimen are shown in Tables 6-13. As expected, significant positive correlations between the fatigue indicators, intensity and number of fatigue symptoms occurred consistently over time. Correlations ranged from .78 at Time 7 (Table 12) to .95 Times 2 and 6 (Tables 7 & 9).

Intensity and number of fatigue symptoms correlated positively and significantly with POMS depression and RTMD scores over time. The correlations between the number of fatigue symptoms and depression ranged from .50 (Times 1 & 5, Tables 6 & 10) to .80 (Time 6, Table 11). For fatigue symptoms and the RTMD, the correlations ranged from .65 (Time 1, Table 6) to .81 (Time 8, Table 13). Correlations between fatigue intensity and depression ranged from .51 (Time 1, Table 6) to .78 (Time 6, Table 11); for the RTMD, the correlations ranged from .71 (Time 1, Table 6) to .86 (Time 8, Table 13).

Consistent and significant negative correlations were found between vigor and the intensity and number of fatigue symptoms, lending support for the divergent validity of the FSCL. For the number of fatigue symptoms, correlations ranged from -.42 (Time 3, Table 8) to -.59 (Times 4, Table 9). For fatigue intensities, correlations ranged from -.40 (Time 3, Table 8) to -.66 (Time 7, Table 12).

Significant negative correlations were found between vigor and POMS depression and RTMD scores over time. Correlations ranged from -.36 (Time 5, Table 10) to -.57 (Time 7, Table 12) for depression, and -.40 (Time 8, Table 13) to -.63 for the RTMD (Time 7, Table 12). Vigor failed to correlate significantly with depression at Time 8 only (Table 13), and with the RTMD, Time 5 only (Table 10).

The only consistent and significant correlations among the remaining IVs occurred between stage of disease and whether adriamycin was included in the regimen. Statistically significant negative correlations were found for seven of the eight time

frames (Tables 6-8, 10-13). Correlations ranged from -.42 (Time 6, Table 11) to -.56 (Time 2, Table 7).

Total Explained Variance and Unique Contributions of the Independent Variables on Fatigue Symptoms and Intensities

Tables 34 and 35 summarize the total explained variance (cumulative R^2) and unique contributions made by the independent variables to explaining the number of fatigue symptoms in these women at each time (Times 1-8). Taken as a group, the three independent variables of mood (vigor, depression and RTMD) explained 47-72% of the variance over time in the number of fatigue symptoms. No other variables entered the model.

Depression, when controlling for the effects of the other variables, made the most consistent contribution to the explained variance in the number of fatigue symptoms over time. It uniquely explained 10-64% of the variance in fatigue symptoms Times 1-8. The recalculated TMD uniquely contributed 8-22% of the variance, in seven of the eight time periods; vigor, 12-19% in five of the eight time periods. At no point did any of the remaining variables enter the model.

Tables 36 and 37 summarize the total explained variance and unique contributions made by the independent variables to explaining the intensities of fatigue symptoms over time (Times 1-8). Once again, the three mood variables, vigor, depression, and the recalculated TMD, as a group, explained 54-76% of the variance in fatigue intensity over time. Depression again uniquely contributed 7-58% of the variance over the eight time periods; the recalculated TMD, 7-60% of the variance, seven of the eight time periods; and vigor 7-44%, six of eight time periods. Stage of disease was the only other independent variable that made a unique contribution to the explained variance in fatigue's intensity. It uniquely contributed 5% of the variance at Time 7 only.

Figures 3-10 display the empirical models in this study that predicted fatigue

Table 34: Summary of Total Explained Variance and Significant Unique Contributions of Independent Variables to the Number of Fatigue Symptoms (FSCL) Over Time (T_{1-4})

Source	Time 1				Time 2				Time 3				Time 4			
	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p
• Total Explained Variance ($CumR^2$)	.47	3,29	8.496	***	.60	3,25	12.496	****	.57	2,32	21.035	****	.68	3,30	21.110	****
	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p
• Vigor	-.54	.29	12.565	**	-.56	.32	12.435	**					-.39	.12	7.946	*
• Depression	.34	.10	4.640	*	.37	.10	4.649	*	.69	.48	30.439	****	.63	.40	21.404	****
• Mood Disturbance	.48	.08	4.579	*	.69	.18	11.295	**	.76	.09	6.530	*	.77	.16	14.515	**
• Social Support																
• Age																
• Stage																
• Hematocrit																
• Karnofsky Performance Status																
• Cycle																
• Adriamycin																

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: Confusion/bewilderment, anger/hostility and tension/anxiety. Depression, Vigor, and Fatigue are not included.

NOTE: * $p \leq .05$
** $p \leq .005$
*** $p \leq .0005$
**** $p \leq .0001$

NOTE: Times 1 & 2 = Cycle 1
Times 3 & 4 = Cycle 2

Table 35: Summary of Total Explained Variance and Significant Unique Contributions of Independent Variables to the Number of Fatigue Symptoms (FSCL) Over Time (T_{5-8})

Source	Time 5				Time 6				Time 7				Time 8			
	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p
• Total Explained Variance ($CumR^2$)	.60	3,29	14.155	****	.64	1,31	54.767	****	.49	2,31	14.975	****	.72	3,31	26.352	****
	β	R^2 Change	F-value for Change	p	β	R^2 Change	F-value for Change	p	β	R^2 Change	F-value for Change	p	β	R^2 Change	F-value for Change	p
• Vigor	-.51	.26	10.971	**									-.38	.13	10.535	**
• Depression	.37	.12	5.563	*	.80	.64	54.767	****	.58	.33	16.038	***	.70	.49	31.604	****
• Mood Disturbance	.67	.22	15.528	**					.79	.16	9.601	**	.64	.10	11.293	**
• Social Support																
• Age																
• Stage																
• Hematocrit																
• Karnofsky Performance Status																
• Cycle																
• Adriamycin																

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, Vigor, and Fatigue are not included.

NOTE: * $p \leq .05$
** $p \leq .005$
*** $p \leq .0005$
**** $p \leq .0001$

NOTE: Times 5 & 6 = Cycle 3
Times 7 & 8 = Cycle 6

Table 36: Summary of Total Explained Variance and Significant Unique Contributions of Independent Variables to Fatigue Intensity (FSCL) Over Time (T_{1-4})

Source	Time 1				Time 2				Time 3				Time 4			
	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p
• Total Explained Variance ($CumR^2$)	.54	3,29	11.518	****	.69	3,25	18.230	****	.67	2,32	32.707	****	.71	3,30	24.091	****
	B	R^2 Change	F-value for Change	p	B	R^2 Change	F-value for Change	p	B	R^2 Change	F-value for Change	p	B	R^2 Change	F-value for Change	p
• Vigor	-.54	.29	12.800	**	-.35	.09	4.729	*					-.29	.07	5.742	*
• Depression	.36	.11	5.287	*	.63	.40	17.845	***	.76	.57	44.441	****	.76	.58	43.434	****
• Mood Disturbance	.64	.15	9.241	**	.71	.20	15.595	**	.80	.10	9.512	**	.49	.07	6.605	*
• Social Support																
• Age																
• Stage																
• Hematocrit																
• Karnofsky Performance Status																
• Cycle																
• Adriamycin																

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p \leq .05$
** $p \leq .005$
*** $p \leq .0005$
**** $p \leq .0001$

NOTE: Times 5 & 6 = Cycle 3
Times 7 & 8 = Cycle 6

Table 37: Summary of Total Explained Variance and Significant Unique Contributions of Independent Variables to Fatigue Intensity (FSCL) Over Time (T_{5-8})

Source	Time 5				Time 6				Time 7				Time 8			
	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p	$CumR^2$	df	F	p
• Total Explained Variance ($CumR^2$)	.64	3,29	17.344	****	.60	1,31	47.133	****	.76	4,29	23.203	****	.76	3,31	32.477	****
	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p	ß	R^2 Change	F-value for Change	p
• Vigor	-.36	.12	5.897	*					-.66	.44	25.293	****	-.28	.07	5.201	*
• Depression	.55	.30	13.231	**	.78	.60	47.133	****	.32	.07	4.245	*	.71	.51	33.840	****
• Mood Disturbance	.68	.23	18.463	***					.94	.20	21.173	****	.85	.18	23.543	****
• Social Support																
• Age																
• Stage									.24	.05	6.08	*				
• Hematocrit																
• Karnofsky Performance Status																
• Cycle																
• Adriamycin																

NOTE: Mood Disturbance is recalculated POMS score based on three subscales only: confusion/bewilderment, anger/hostility and tension/anxiety. Depression, vigor, and fatigue are not included.

NOTE: * $p \leq .05$
** $p \leq .005$
*** $p \leq .0005$
**** $p \leq .0001$

NOTE: Times 5 & 6 = Cycle 3
Times 7 & 8 = Cycle 6

symptoms and intensities Times 1-8. At no time did the variables social support, age, hematocrit, Karnofsky Performance Status, length of cycle or inclusion of adriamycin in the regimen, contribute to the model.

Summary of Findings in Relationship to the Research Questions

Four research questions were posed for this descriptive, prospective, and correlational study. Each research question is addressed in light of the above findings.

1) Does subjective fatigue increase in frequency and intensity over time in women receiving adjuvant CT for breast cancer?

The results of the repeated measures ANOVAs indicated that there were no significant increases in either the frequency of fatigue symptoms or the intensity of subjective fatigue, as measured by the Fatigue Symptom Checklist (FSCL) at each time. The changes reported for subjective fatigue as measured by the Piper Fatigue Scale (PFS) also were nonsignificant, and this held true for the POMS Fatigue/Inertia Subscale.

2) Do women receiving CT on a 28-Day treatment cycle experience more fatigue than women receiving CT on a 21-Day cycle?

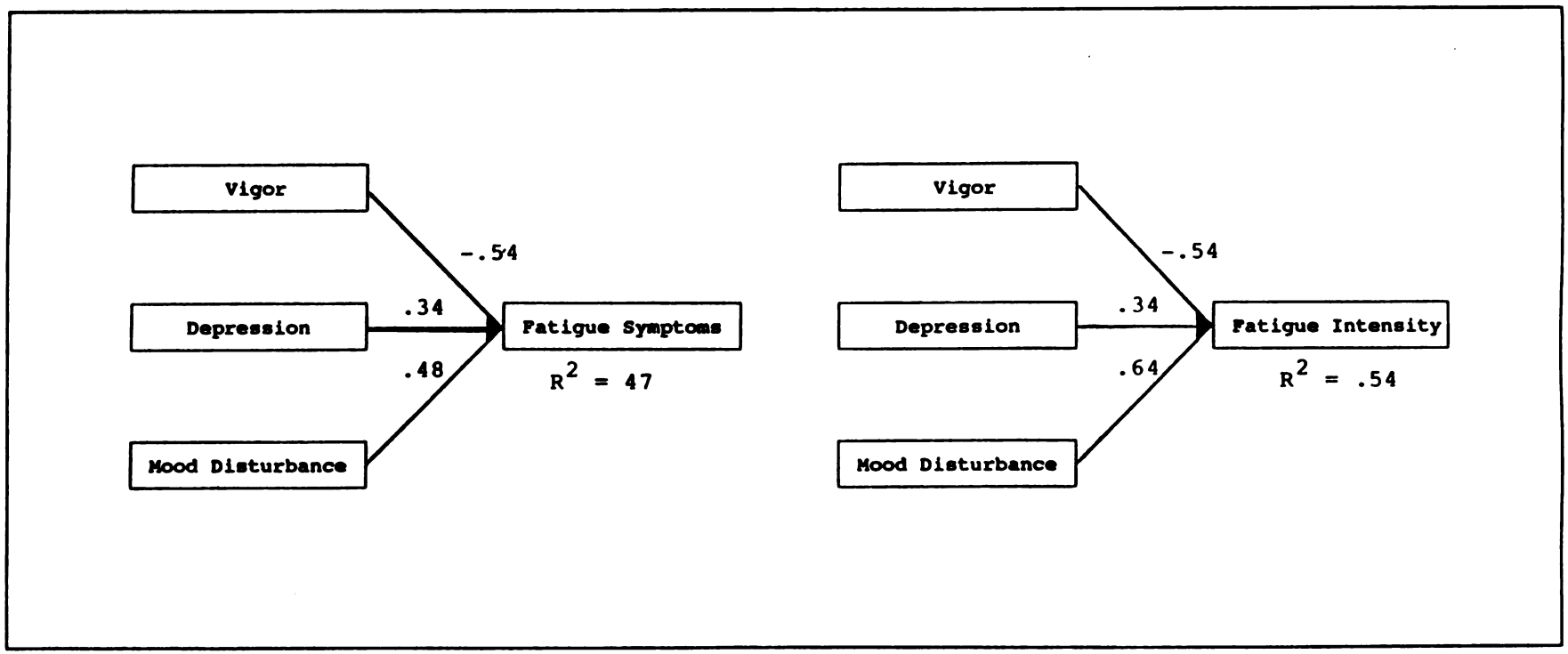
The results of the repeated measures ANOVAs indicated that there were no significant differences at any of the time periods by length of treatment cycle, in the number of fatigue symptoms or fatigue intensity as measured by the FSCL. The changes reported for the PFS and POMS F/I also were nonsignificant.

3) Do women receiving Adriamycin-containing regimens experience more fatigue?

The results of the repeated measures ANOVAs indicated that there were no significant differences in either the number or the intensity of fatigue symptoms at any time period (FSCL) whether or not adriamycin was included in the treatment regimen. Results for the PFS and the POMS F/I also were nonsignificant.

4. Do women experience more fatigue when they have less vigor, are more

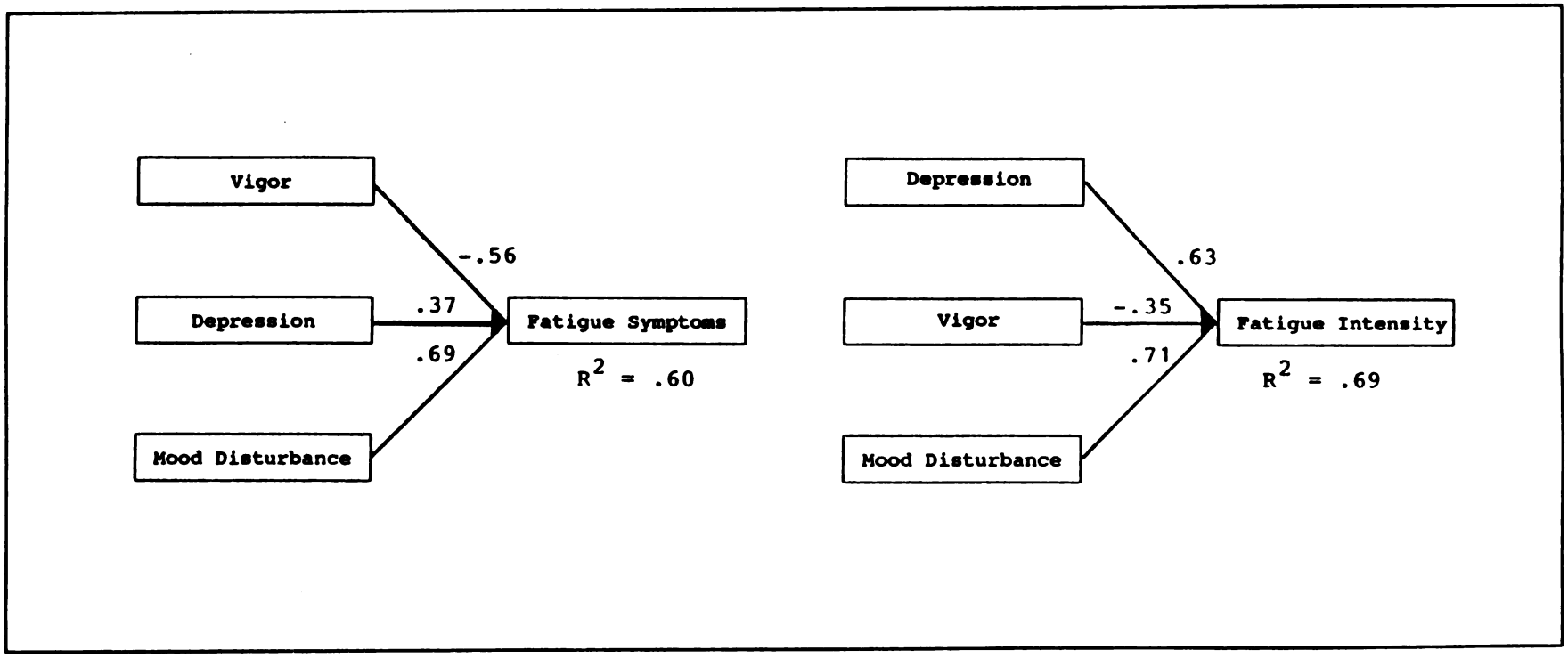
Figure 3: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 1 (n=33)



NOTE: All Beta weights are standardized estimates and are significant at $p \leq .05$.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

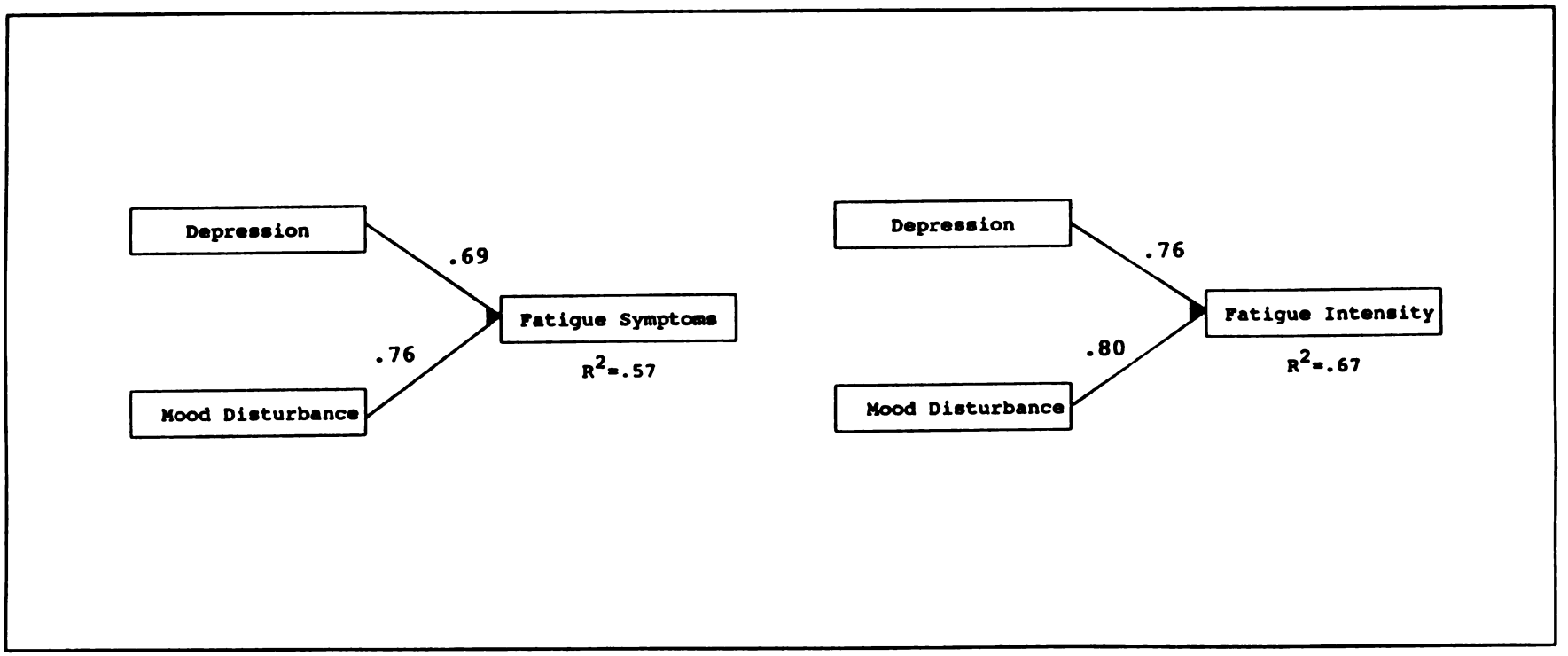
Figure 4: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 2 (n=29)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

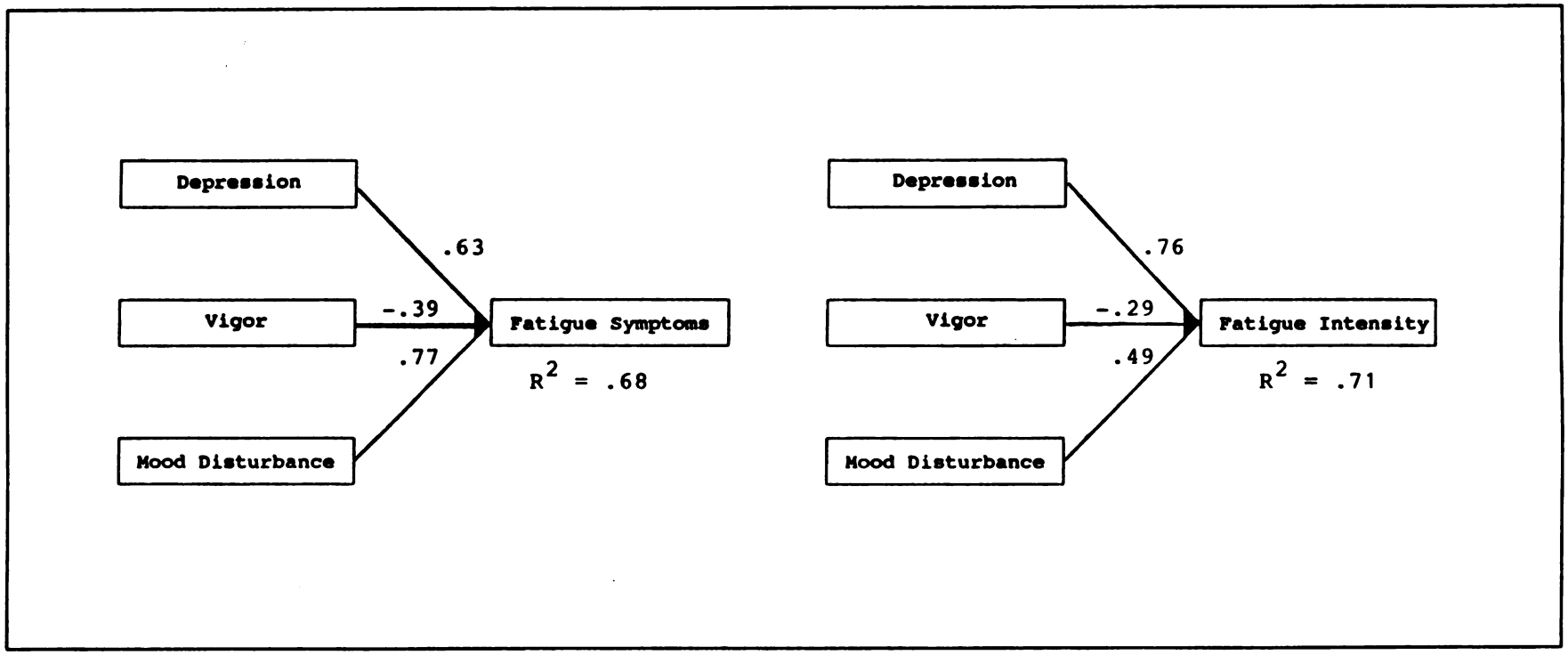
Figure 5: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 3 (n=35)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

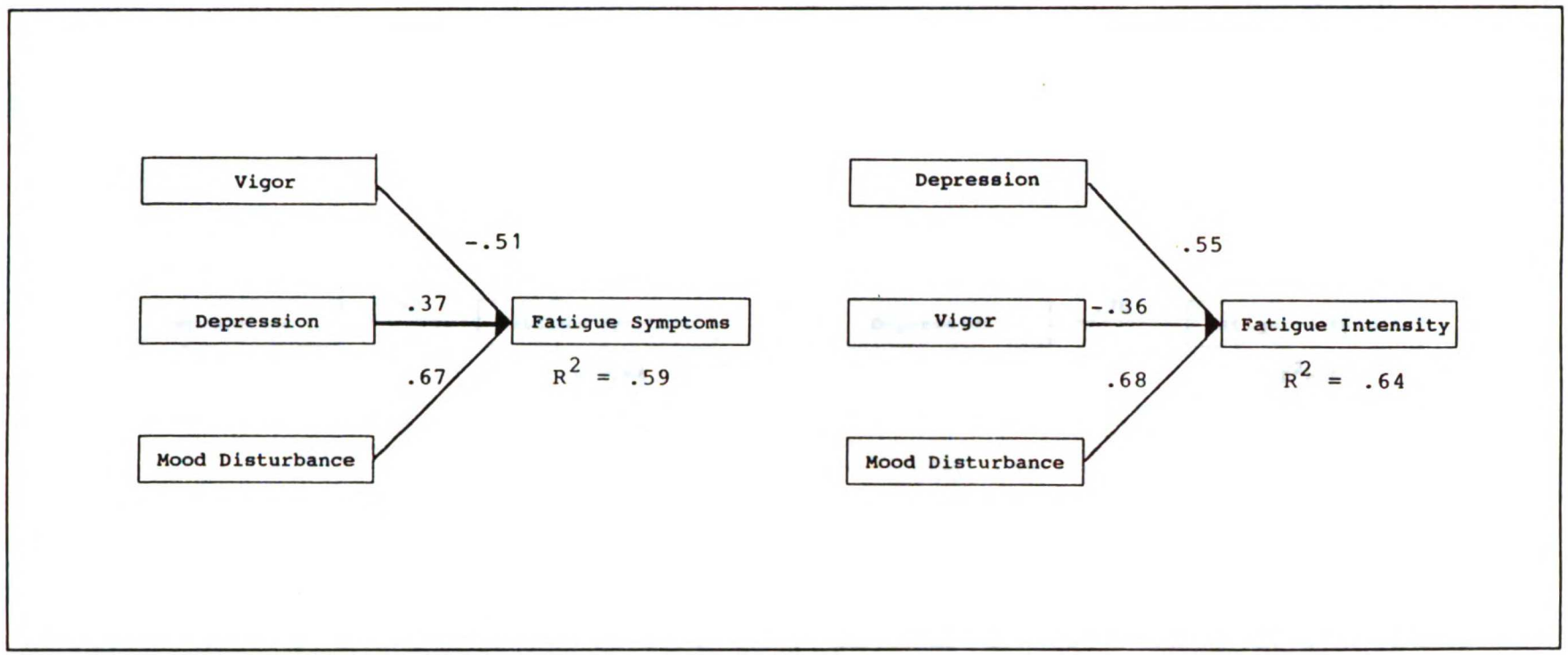
Figure 6: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 4 (n=34)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

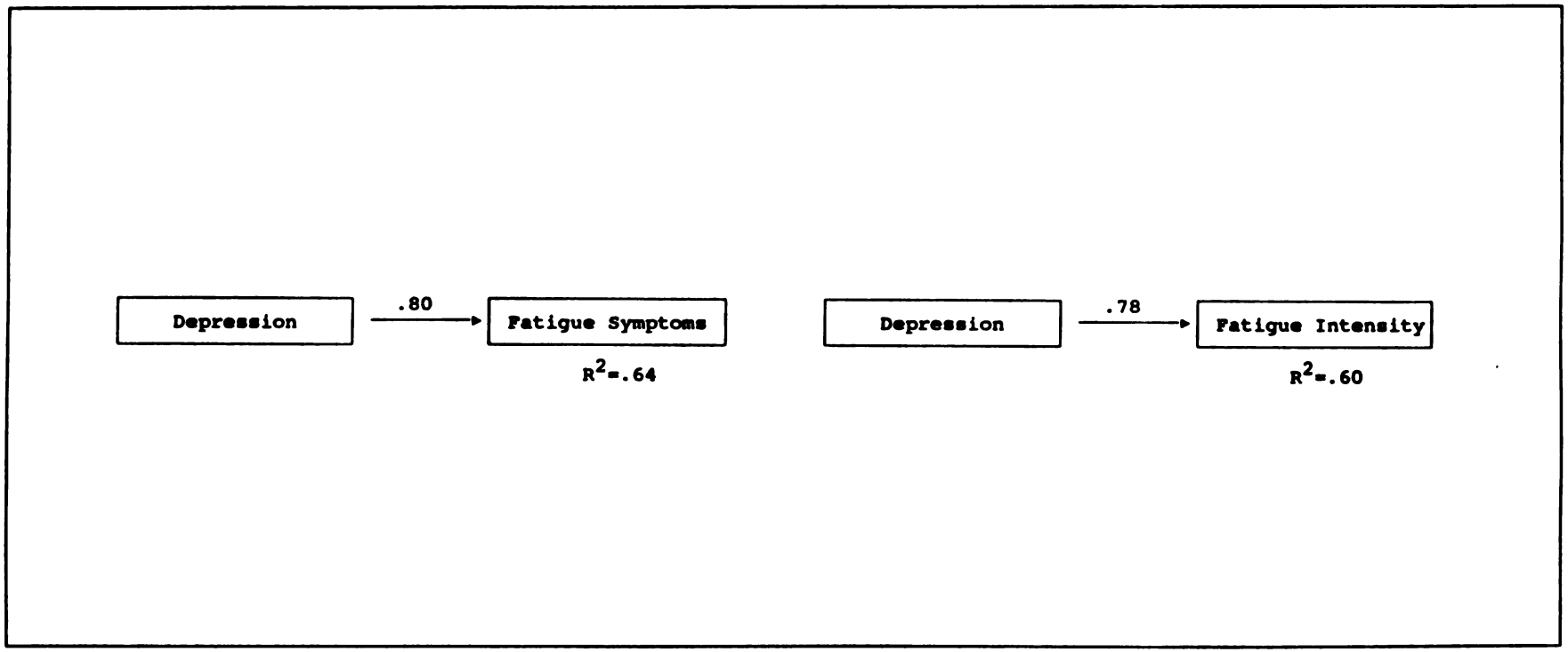
Figure 7: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 5 (n=33)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

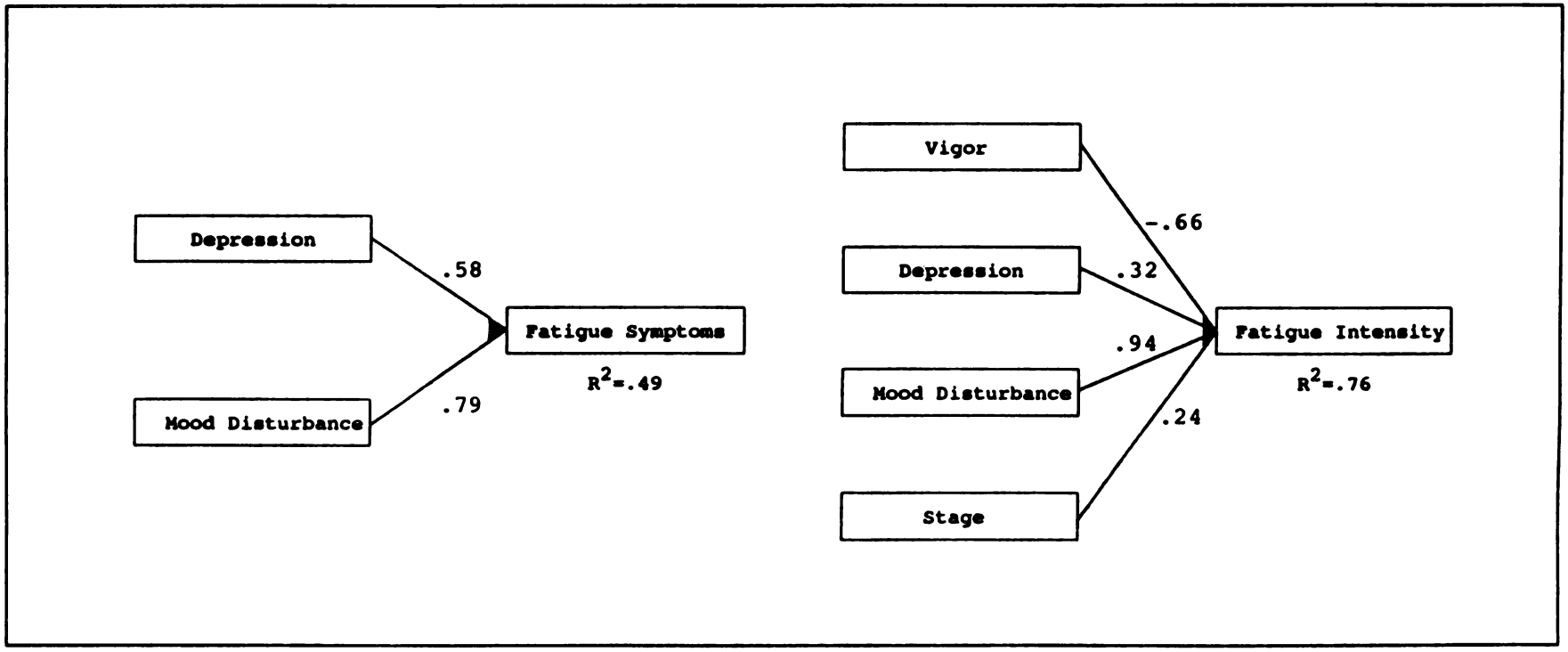
Figure 8: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 6 (n=33)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

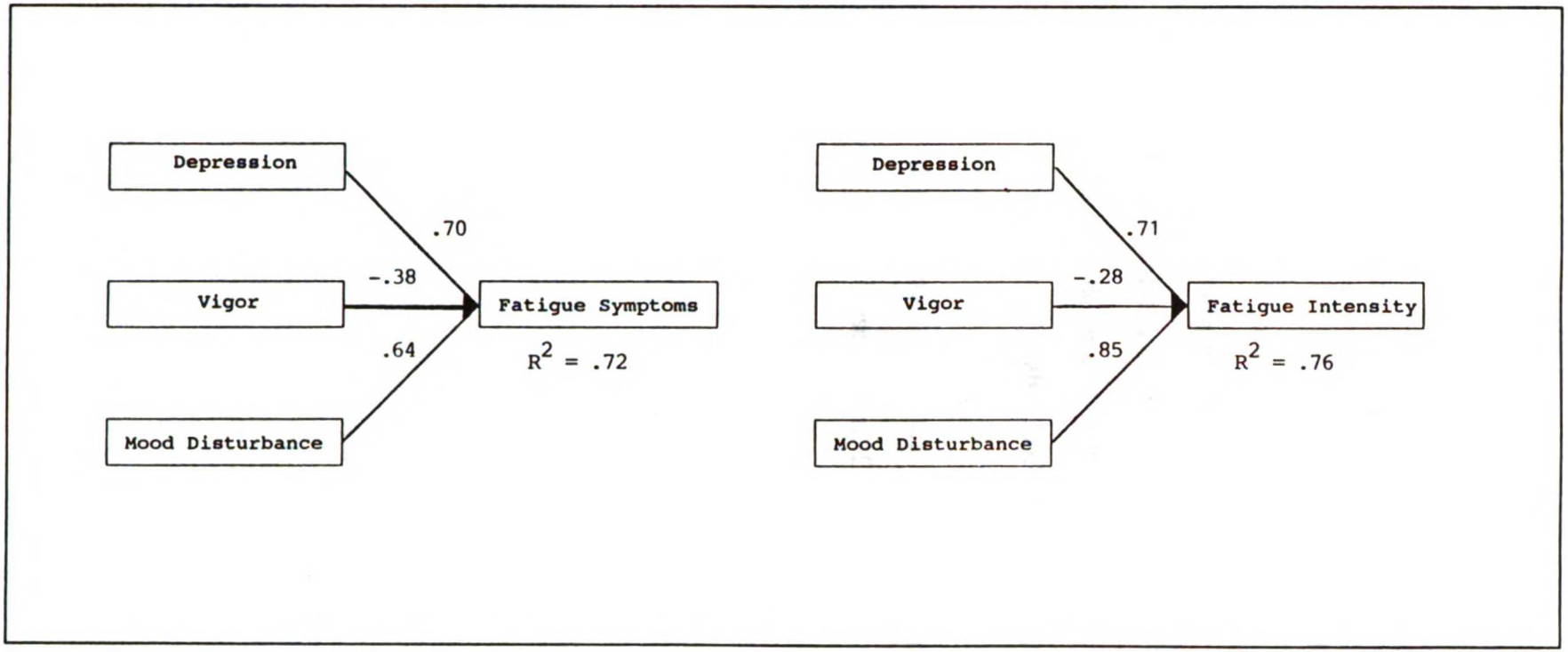
Figure 9: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 7 (n=34)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

Figure 10: Empirical Models for Fatigue Symptoms and Intensity (FSCL) Time 8 (n=35)



NOTE: All Beta weights are standardized estimates and are significant at p≤.05.

NOTE: Variables are displayed in descending order of explained variance (see Tables 34-37).

depressed, have more mood disturbance, less social support, are older, have more extensive disease, are anemic, have a poorer perceived Karnofsky Performance Status (KPS), a longer CT cycle or the inclusion of adriamycin in the treatment regimen?

The results of the forward, stepwise multiple regression analyses did indicate that less vigor, more depression, and more mood disturbance were able to predict with a 47-76% degree of accuracy, increased fatigue in these women at each time (Tables 34-37). At no time however, did age, social support, anemia, KPS, cycle, or adriamycin contribute to the increased risk for chronic fatigue. More extensive disease did enter the model, but only once at Time 7 (Table 37). Thus, stage was not a consistent predictor of fatigue over time.

Of the three mood variables, depression was the single most consistent predictor of chronic fatigue over time in these women. Depression was able to predict fatigue with a 7-64% degree of accuracy over time (Times 1-8).

CHAPTER 5

DISCUSSION

Sample

Age, ethnicity, level of education, occupational status, stage of disease, and treatment characteristics of this sample were comparable to women diagnosed nationally with early stage breast cancer (Knobf, 1991) and women described in studies documenting symptom occurrence in general, in breast cancer (Hughson, Cooper, McArdle, & Smith, 1986; Knobf, 1986; Meyerwitz, et al, 1979; 1983), and fatigue in particular (Cimprich, 1990; Piper, et al, 1991). Thus, this sample was comparable to samples reported in the literature and to the general population of early stage breast cancer women.

In previously published studies, length of CT cycle and total length of time on CT either was not specified (i.e., 21-day vs 28-Day cycle; Greene, et al, 1992) or varied from 21-Day (Cimprich, 1990) to 28-Day CMF regimens, given over 12 cycles (Meyerwitz, et al, 1979; Hughson, et al, 1986). Other agents, in addition to or instead of CMF such as Adriamycin, Mitoxantrone [Greene, et al, 1992], Vincristine, Prednisone [Knobf, 1986] or BCG were used [Meyerwitz, et al, 1979; 1983]).

Activity/Exercise Variables

For the majority of women, self-perceived KPS at baseline was at least 80%, improving to 90-100% by Day one of the sixth and final CT cycle (Time 7). Changes in occupational status were reported infrequently (n=5/35), but for women who did report changes, the time from surgery to day one of the second cycle (Time 3) was a particular period of change.

The low incidence of occupationally-related changes in this sample is in stark contrast to the findings reported by Meyerwitz and Associates (1979; 1983), where the majority of women (n=50 or 74%) experienced a decrease in work-related activity during CT. This disruption in work-related activities used to be quite common when

adjuvant CMF regimens were 12 months or longer, as in the Meyerwitz study (1979; 1983). Once treatment efficacy was shown to be unaffected by reducing the length of treatment from 12 to 6 months however (Hughson, et al, 1986), shorter regimens became the norm, and work-related disruptions became infrequent (Knobf, 1986).

Nutritional Variables: Weight Change

The majority of women experienced an average change in weight of 8.4 pounds from 6 months preceding diagnosis to diagnosis; losses and gains occurred equally. Average weight increased only 4.4 pounds from baseline to Time 6, in contrast to Knobf's findings where the majority of women gained 17 pounds ($\pm$ 10) during treatment (1986). Actual office weights were recorded in both studies. Differences may be attributable to different lengths in treatment regimens. In the Knobf study (1986), subjects received an average of 10 months of CT compared to 6 months in the current study. Weight generally increases an average of one to two pounds per month on adjuvant CT (M.T. Knobf, personal communication, August 10, 1992). Thus, the longer the treatment regimen, the more the gain in weight.

Sleep/Wake Cycles

The majority of women were sleeping and napping more by Time 3. Changes in sleep quality and quantity were common. Frequent night time awakenings, difficulty falling back to sleep once awakened, and hot flashes may have been contributing factors. Insomnia and an increased need to sleep and nap have been noted by others in this population (Hughson, et al, 1986; Knobf, 1986; Nail, Jones, Greene, Schipper & Jensen, 1991).

In general, while there is controversy about how age may affect the sleep cycle (Kedas, Lux, & Amodeo (1989), sleep disorders are quite common in adults, particularly in older females (Bixler, Kales, Soldatos, Kales, & Healy, 1979). The presence of hot flashes also has been associated with decreased sleep quality and increased time spent in bed (Lee, In review; Shaver, Giblin, Lentz, & Lee, 1988).

Clearly, more research is needed to document the presence of hot flashes and other symptoms that may be contributing to decreased quality of sleep and increased fatigue in this population.

Psychological Variables

Women experienced the most mood disturbance at the beginning of CT (M=26.89, Time 1), and the least at Time 5 (M=11.58). This would be anticipated since the start of CT is considered to be very stressful. The decline in mood disturbance over time is consistent with Dodd's findings suggesting that adaptation to the diagnosis and treatment of breast cancer does occur over time (1990). While demographic characteristics were similar between these two groups, mood disturbance scores in Dodd's study (1990) for women with breast cancer were consistently higher than noted for this sample. Variations in sample size may be responsible for these differences (n=37 vs n=48). In Dodd's study (1990), the 48 women with breast cancer were a subgroup of 100 patients with various types of malignancies.

Mood disturbance was significantly higher for this sample of newly diagnosed, early stage breast cancer women, than that noted for women with metastatic breast disease (Speigel, Bloom, & Gottheil, 1983; Speigel, Bloom, & Yalom, 1981; M=16.1 and 11.8 respectively). Perhaps women with metastatic disease have had more time to adapt to the diagnosis of breast cancer than women who are newly diagnosed. Scores were significantly lower at Time 1 however, than scores noted for women diagnosed with other forms of cancer (Cella, et al, 1989, M=37); female psychiatric patients (M=80.6); and female college students (M=44.8, McNair, et al, 1971).

Depression followed a similar pattern with the highest average scores noted at Time 1 (M=8.37) and the lowest at Time 5 (M=4.73). This depression was less than that noted for women in Dodd's study (1990) and for women with other forms of cancer (M=11.5, Cella, et al, 1989), female psychiatric patients (M=28), and female college students (M=14.8)(McNair, et al, 1971). Suggesting that depression had a

relatively low occurrence in this sample. Consistent with these findings is that vigor (Time 1) was higher in this sample than noted in women with other forms of cancer (M=12.6, Cella, et al, 1989); female college students (M=15.6); and female psychiatric patients (M=9.3).

Social Support Variables

In this sample, the total number of people in the woman's support network declined significantly over time. Significant declines occurred similarly in total network and total functional support. This was not an unanticipated finding as family and friends often provide support initially in the face of a new diagnosis or treatment, but begin to withdraw support as treatment continues; the woman is expected to adapt or to cope; and family and friends return to their own day-to-day activities and concerns (Lindsey, et al, 1981). At the same time, these declines in social support over time may simply reflect the "artificially inflated" level of support at the time of the initial diagnosis (M.J. Dodd, personal communication, August 14, 1992).

Declines in social support can occur as women become less interested (Lindsey, et al, 1981) or less able to expend the energy during therapy that is required to maintain the social support network. Thus, demands of treatment and fatigue may contribute to the declines noted. Few studies have documented changes in social support over time using the NSSQ, however the declines noted in this study are comparable to the significant declines in total functional support experienced by women with breast cancer in Dodd's study (1990).

In Dodd's study, mean total functional support during the first cycle of chemotherapy in women with breast cancer was 234.93 (n=45; SD=99.14) (1990). Six months later, total functional support had declined significantly to 210.18 (n=38, SD=103.17) (Dodd, 1990). In contrast to the current study, however, no significant declines in network size or total network support were reported over time by the women in Dodd's study (1990). Of interest, women in Dr. Dodd's study consistently

reported higher support scores in general over time than those reported by the women in this current study.

Subjective Fatigue

Despite anecdotal evidence to the contrary, cumulative fatigue did not occur in this study; the number and intensity of fatigue symptoms did not increase over time. In fact, the average number of fatigue symptoms was found to be relatively low ($\underline{M}$=8.81) when compared to the total number of symptoms that could have been experienced (n=30). Fatigue intensities also were surprisingly low ($\underline{M}$=41.96) considering the intensity range that was possible (30-150). Knobf found similarly unexpected low ratings for fatigue and insomnia, despite these two symptoms being the most distressing in her sample (1986).

Similarly, no significant changes in PFS or POMS fatigue scores occurred over time. Average POMS F/I scores ranged from 7.41 to 10.77, again relatively low when one considers the total possible range that can occur (0-28). These findings are comparable to those documented by Dodd in women with breast cancer (1990), and by others in women with other forms of malignancy (Cella, et al, 1989) and in female college students (McNair, et al, 1971). No significant differences in fatigue scores occurred as a function of length of cycle (21-Day vs 28-Day) or by the inclusion of adriamycin in the regimen.

In contrast to the lack of change demonstrated in POMS F/I scores over time in the Dodd study (1990), more qualitative data analyses revealed an increasing incidence and concern about fatigue over time (Piper, et al, 1991). This suggests that the more quantitative measures of fatigue may not detect some of the more subtle changes that occur over time in perceptions of subjective fatigue. Triangulation of methods, both quantitative and qualitative, may be needed to better capture the fatigue experience (Morse, 1991).

While women in this sample were asked to complete the fatigue measures when

they were most tired, the timing of measurement might have varied. As a consequence, fatigue forms could have been completed by the women when they were less fatigued, resulting in the unexpectedly low scores found in this and other studies. Secondly, subjects in longitudinal studies tend to drop out over time for multiple reasons. In this study, the 37 subjects who completed data for all 8 data collection points had a higher Karnofsky Performance Status at Time 7 than did the 37 women who failed to complete the study. Thus, the very subjects most at risk for chronic fatigue over time may not be the ones able to complete the studies designed to capture and document these patterns.

Significant positive correlations were documented between the intensity and number of fatigue symptoms, depression, and the recalculated TMD. As depression and mood disturbance scores increased, subjective fatigue increased. In addition, consistent and significant negative correlations were found between fatigue and vigor over time. As vigor increased, the number and intensity of fatigue symptoms decreased.

Hematocrit failed to correlate with the fatigue measures, despite the fact that anemia is linked to fatigue in the literature (Piper et al, 1987). Factors that might have contributed to this finding include the lack of variability in the hematocrit levels in this sample (Table 15) and the fact that hematocrits were drawn only during the first cycle's nadir. Thereafter, levels were drawn only if there were complications. Correlating a biological measure, such as hematocrit, with a subjective phenomenon such as fatigue, may prove difficult because of the changing nature of the variables; their natural circadian patterns; and the need to time the measures to be taken as close to one another as possible.

Results of the forward, stepwise multiple regression analyses indicated that approximately 47-76% of the variance in fatigue symptoms and intensity could be explained by the combination of three mood variables: vigor, depression and mood disturbance. Thus, these factors, when taken together, constitute high risk factors for the development of chronic fatigue over time. Depression uniquely explained between

7-64% of the variance in fatigue scores at each time. Depression therefore constitutes a consistent and significant risk factor for the development of chronic fatigue over time in women receiving adjuvant CT for breast cancer.

Relationship of the Findings to the Hypothesized Model

The results of the regression analysis indicated that vigor, depression, and mood disturbance were predictive of chronic fatigue (Psychological Variables) (Figure 2). Age (host variable), total functional support (social support), hematocrit (oxygenation variable), stage of disease (disease variable), Karnofsky Performance Status (activity/exercise), length of cycle and adriamycin (treatment variables) were not.

Results of the repeated measures ANOVAs also did not support the factors of length of treatment cycle (21-Day vs 28-Day) or the inclusion of Adriamycin in the treatment regimen as predictors of fatigue. The results of the power analysis indicated that a sample size of 80 was required to detect statistically significant differences in fatigue scores in relation to these two treatment variables. Perhaps a larger sample size could have achieved statistical significance. Anecdotally, the clinical significance of these two factors in relationship to side effects in general is reported to be significant.

Limitations

Limitations of the study include the small sample size; the lack of control over when the women completed the fatigue questionnaires; the inability to control when blood work was drawn in relation to the subjective fatigue measures; and the inability to obtain serial blood work at nadirs over time. The low fatigue scores documented in this study call into question whether these women were, in fact, fatigued at all. Secondly, this study relied primarily on the subjective measurement of fatigue. The failure to use a variety of physiological measures that could have been correlated with the subjective reports of fatigue is a major limitation to this study.

Implications for Practice

The results of this study suggest that if a nurse knows the degree of vigor,

depression and mood disturbance of the woman with breast cancer receiving adjuvant CT, the nurse may be able to predict the risk for developing fatigue at each time with a 47-76% accuracy. Knowledge about the woman's depression status is the single most important risk factor over time in predicting chronic fatigue in these women. Should these risk factors be confirmed by other studies, the timing and selection of fatigue interventions can be tailored to those at high risk.

Significant insomnia and declines in social support occurred in this sample over time. Intervening clinically to initiate social service referrals, patient/family conferences and doing anticipatory teaching about these potential effects may lessen their impact over time. The nurse has a significant role to play in modulating these events.

Implications for Research

Given the fact that only 37 women completed the FSCL, and fewer still completed the POMS and the PFS, greater attention needs to be given to developing and testing shorter, more user-friendly scales to measure fatigue in clinical populations. Secondly, a triangulation of quantitative and qualitative measures needs to be used in future studies to better capture the more subtle changes in fatigue patterns that may occur over time. Third, few biological measures have been correlated with subjective fatigue. Problems inherent in documenting the circadian rhythmicity and coordinating the timing and the serial measurement of these variables must be addressed. Lastly, more attention needs to be given to "teasing" out the differences that exist between depression and fatigue.

Most depression scales contain somatic symptoms of fatigue that confound the measurement of fatigue with depression. This was not the case in this study. The POMS depression items did not contain somatic symptoms of fatigue as measured by the FSCL. Future studies need to address this measurement issue and explore the relationships that may exist between depression, sleep disorders, menopausal symptoms

(i.e., hot flashes), and fatigue in these women. Since severity of fatigue was rated low in this and other breast cancer studies (Piper, et al, 1991; Knobf, 1976), future studies should consider using a healthy, age-matched control group to determine whether women with breast cancer experience more fatigue than controls.

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APPENDIX A

University of California, San Francisco
School of Nursing
Department of Physiological Nursing

CONSENT TO BE A RESEARCH SUBJECT

While fatigue is experienced by everyone at one time or another, very little is known about how fatigue may be experienced; how it may vary from person to person, or how it may be alleviated once it occurs. The purpose of this nursing study is to determine how individuals perceive their fatigue, how and under what conditions it may occur, and how the fatigue experience may vary over time. This study is being conducted by Barbara F. Piper, R.N., M.S. and Dr. Marylin J. Dodd, R.N., Ph.D. from the Department of Physiological Nursing, U.C.S.F. School of Nursing in collaboration with your office oncology nurse.

If I decide to participate in this nursing study, I will be asked to complete three to four short forms at different periods of time during my first three cycles of chemotherapy and during my sixth treatment cycle. There will be five forms for me to complete initially. Ideally these forms should be completed before I receive my first chemotherapy treatment. It has taken other individuals approximately 20-25 minutes to complete these forms. I will be asked to complete three to four of these same forms at approximately two week intervals thereafter, at the midpoint in each of my treatment cycles (either on day 10 or day 14), and on the day before each subsequent treatment cycle. It has taken previous individuals 12-15 minutes to complete these forms. All forms will need to be completed at approximately the same time of day.

My oncology nurse will give me these forms in advance so that I may complete them at home. She also will call me in between treatment cycles to see how I am doing, and to remind me to complete and return the forms at the appropriate times. My oncology nurse will be available to help me complete these forms if needed, and to answer any questions that I may have concerning the study. Additional information needed for the study will be collected by one of the nurse investigators, Barbara F. Piper, R.N., M.S. from my medical records.

Every effort will be made to maintain my confidentiality as is possible under the law. My name will not appear on any of the forms and when results of the study are reported, responses will be summarized so that no one individual can be identified. I may be

slightly inconvenienced by having to complete the forms at the appropriate time intervals and by having to mail the mid-cycle forms back to the office in the self-addressed, pre-stamped envelop given to me. I may refuse to participate or withdraw my consent at any time without jeopardizing my treatment. If I find that certain questions strongly affect me and I feel that I need to discuss these reactions, I can contact my oncology nurse or Ms. Piper.

There will be no direct benefit to me from my participation on this study. However, future benefits may include a better understanding of how fatigue is experienced and alleviated.

Should I have any questions about this study, I may contact my oncology nurse_____during the daytime at_____or I may call Ms. Piper collect during the evenings at (415) 388-5581. If for some reason I do not wish to do this, I may contact the Committee on Human Research which is concerned with the protection of volunteers in research projects. I may reach the committee's office between 8:00am and 5:00pm, Monday through Friday by calling (415) 476-1814, or by writing to the Committee on Human Research, Laurel Heights, Suite 11, University of California, San Francisco, San Francisco, CA. 94143.

I have read the above and agree to participate in this nursing study.

Signature_____Date_____

Signature of the oncology nurse who obtained this consent_____Date_____

APPENDIX B

DEMOGRAPHIC PROFILE

SECTION A: TO BE COMPLETED BY THE REGISTERED NURSE

Subject Number: _____ _____ Clinical Site Code: _____

Medical Record Number: _____

Date of Entry: _____/_____/_____
(Month) (Day) (Years)

SECTION B: TO BE COMPLETED BY THE SUBJECT

DIRECTIONS:

Time Now _____/_____
(Hour) (Minutes)

For each of the following questions you will be asked to either 1) fill in the blank or 2) place a check mark (✓) in the appropriate space. For each question, please select the one best response.

1. Birthdate: _____/_____/_____
(Month) (Day) (Years)

2. Age in years: _____

3. Sex (1) Male _____
(2) Female _____

4. Ethnic Background:
(1) Caucasian: _____
(2) Mexican-American: _____
(3) Oriental: _____
(4) Black: _____
(5) Other (Specify): _____

5. Marital Status:
(1) Single, Never Married: _____
(2) Married: _____
(3) Separated/Divorced: _____
(4) Widowed: _____

6. **Living Arrangements:**
   - (1) **Live Alone:** _____
   - (2) **Live with Spouse/Partner:** _____
   - (3) **Other (Specify):** _____

7. **Number of children living at home:**
   - (1) **No children:** _____
   - (2) **No children living at home:** _____
   - (3) **1-2 children:** _____
   - (4) **3-4 children:** _____
   - (5) **More than 4 children:** _____

8. **Age(s) (in years) of each child living at home:**
   - (1) **None:** _____ (6) _____
   - (2) _____ (7) _____
   - (3) _____ (8) _____
   - (4) _____ (9) _____
   - (5) _____

9. **Annual income level:**
   - (1) **Less than $10,000:** _____
   - (2) **More than $10,000 but less than $20,000:** _____
   - (3) **More than $20,000 but less than $30,000:** _____
   - (4) **More than $30,000:** _____

10. **Highest educational level achieved:**
    - (1) **Completed elementary school only** _____
    - (2) **Completed part of high school** _____
    - (3) **Completed high school** _____
    - (4) **Completed part of college** _____
    - (5) **Completed college** _____
    - (6) **Completed graduate school** _____

11. **Current occupational status: (Select the one best response)**
    - (1) **Employed** _____
    - (2) **Unemployed** _____
    - (3) **Retired** _____
    - (4) **Homemaker** _____
    - (5) **Student** _____

12. **Please specify your current type of occupation/position. If you are currently unemployed, retired, student or homemaker, please specify your most recent employed position:**

_____

13. If you are employed, how many hours a week do you "work":
    (1) Less than 20 hrs./week _____
    (2) More than 20 but less than 40 hrs./week _____
    (3) More than 40 hrs./week but less than 60 hrs./week _____
    (4) More than 60 hrs./week _____

14. Does this "work" involve shift work? (Check the one best response)
    (1) No _____
    (2) Day shift _____
    (3) Evening shift _____
    (4) Night shift _____
    (5) Rotating shifts _____

15. Regardless of your occupational status, what percent of your daily activities involves a physical component (i.e., heavy lifting or strenuous physical activity)?
    (1) Less than 25% per day _____
    (2) More than 25% but less than 50% per day _____
    (3) More than 50% but less than 75% per day _____
    (4) More than 75% per day _____

16. What percent of your daily activities involves an emotional component (i.e., caring for others or dealing with emotionally ladened issues)?
    (1) Less than 25% per day _____
    (2) More than 25% but less than 50% per day _____
    (3) More than 50% but less than 75% per day _____
    (4) More than 75% per day _____

17. What percent of your daily activities involves a mental component (i.e., intense concentration, memorization)?
    (1) Less than 25% per day _____
    (2) More than 25% but less than 50% per day _____
    (3) More than 50% but less than 75% per day _____
    (4) More than 75% per day _____

18. How tall are you? _____ (feet) _____ (inches)

19. What is your usual weight in pounds?_____

20. What do you weigh (in pounds) now? _____

21. Have you experienced a change in your weight during the past six months?
    (1) No _____
    (2) Yes, a gain in weight _____
    (3) Yes, a loss in weight _____

22. If you experienced a change in weight during the past six months was this change intentional?
    (1) No _____
    (2) Yes _____

23. Indicate in pounds the amount of weight change: _____

24. I usually sleep:
    (1) Less than 5 hrs. per day _____
    (2) More than 5 hrs. but less than 8 hrs./24 hrs. _____
    (3) More than 8 hrs. but less than 12 hrs./24 hrs. _____
    (4) More than 12 hrs per day _____

25. Have you experienced a change in the number of hours you are sleeping over the past 6 months?
    (1) No change _____
    (2) Sleeping more _____
    (3) Sleeping less _____

26. Usually the quality of my sleep is:
    (1) Poor _____
    (2) Fair _____
    (3) Good _____
    (4) Excellent _____

27. My usual pattern for taking naps (lying down for short periods of time) during the day is:
    (1) Never _____
    (2) Seldom _____
    (3) Occasionally _____
    (4) Frequently _____
    (5) Always _____

28. Have you experienced a change in the number of naps you are taking during the day during the past 6 months?
    (1) No change _____
    (2) Napping more _____
    (3) Napping less _____

29. Usually the quality of my nap is:
    (1) Poor _____
    (2) Fair _____
    (3) Good _____
    (4) Excellent _____

30. My primary form of planned exercise includes:
    (1) No planned exercise _____
    (2) Walking _____
    (3) Jogging _____
    (4) Bicycling _____
    (5) Other/Specify _____

31. How many times per week do you usually engage in this activity?
    (1) None _____
    (2) Less than 2 times/week _____
    (3) 2 to 4 times/week _____
    (4) More than 4 times/week _____

32. Have you experienced a change in the number of times per week you engage in planned exercise during the past six months?
    (1) No change _____
    (2) Exercising more _____
    (3) Exercising less _____

33. How many cans of soft drink do you usually drink during a day?
    (1) None _____
    (2) 1-2 _____
    (3) 3-4 _____
    (4) More than 4 _____

34. Is this soft drink diet and/or decaffeinated?
    (1) Does not apply _____
    (2) Don't know _____
    (3) Diet only _____
    (4) Decaffeinated only _____
    (5) Both diet and decaffeinated _____

35. How many cups of coffee do you drink/day?
    (1) None _____ (Skip to Question 37)
    (2) Less than 2 cups/day _____
    (3) More than 2 cups but less than 4 cups/day _____
    (4) More than 4 cups per day _____

36. Is the coffee you drink:
    (1) Don't drink coffee _____
    (2) Caffeinated _____
    (3) Decaffeinated _____
    (4) Don't know _____
    (5) Both caffeinated and decaffeinated _____

37. How many cups of tea do you drink/day?
    (1) None _____
    (2) Less than 2 cups/day _____
    (3) More than 2 cups but less than 4 cups/day _____
    (4) More than 4 cups/day _____

38. Is the tea you drink:
    (1) I don't drink tea _____
    (2) Caffeinated _____
    (3) Decaffeinated _____
    (4) Don't know _____
    (5) Both caffeinated and decaffeinated _____

39. How frequently do you drink an alcoholic beverage each day?
    (1) None _____
    (2) 1-2 drinks per day _____
    (3) 3-4 drinks per day _____
    (4) More than 4 drinks per day _____

40. How would you describe your usual appetite?
    (1) Poor _____
    (2) Fair _____
    (3) Good _____
    (4) Excellent _____

41. Have you experienced a change in your appetite during the past six months?
    (1) No change _____
    (2) Yes, I've noticed an increased appetite _____
    (3) Yes, I've noticed a decreased appetite _____

42. How many cigarettes a day do you smoke?
    (1) None _____
    (2) Less than ½ pack per day _____
    (3) Between ½ pack and 1 pack per day _____
    (4) More than 1 pack per day but less than 2 packs per day _____
    (5) More than 2 packs per day _____

43. How many years have you been smoking?
    (1) None _____
    (2) Less than 5 years _____
    (3) More than 5 but less than 10 years _____
    (4) More than 10 but less than 20 years _____
    (5) More than 20 years _____ Specify actual number of years _____

44. How would you define your activity level for this past month? Select the best response.
    _____ (1) 90-100 No symptoms, fully active; able to carry out all activities without restriction.
    _____ (2) 80-89 Some symptoms, fully ambulatory and able to carry out work of a light or sedentary nature (i.e., housework, office work)
    _____ (3) 60-79 Symptomatic; unable to carry out work activities and in bed less than 50% of the day
    _____ (4) 40-59 Symptomatic; able to care for self; in bed 50% or more during the day
    _____ (5) 20-39 Symptomatic; unable to care for self without help; bedridden

45. Time Now: _____ (Hours) / _____ (Minutes)

APPENDIX C

Current Demographic Profile

Subject Number: _____ Clinical Site Code:

Date: _____

For each of the following questions, please place a check mark (✓) in the appropriate space. For each question, please select the one best response.

1. During the past month, has your occupational status changed at all?

   (1) No change _____
   (2) Now employed _____
   (3) Now unemployed _____
   (4) Now working part-time _____
   (5) Now working full-time _____
   (6) Other, please describe _____

   _____

2. During the past month, has the amount of time you spend sleeping changed at all?

   (1) No change _____
   (2) Sleeping more _____
   (3) Sleeping less _____
   (4) Other, please describe _____

   _____

3. During the past month, has the quality of your sleep changed in any way?

   (1) No change _____
   (2) The quality is better _____
   (3) The quality is worse _____
   (4) Other, please describe _____

   _____

4. Do you usually awake from your sleep feeling refreshed?

   (1) Never _____
   (2) Seldom _____
   (3) Occasionally _____
   (4) Frequently _____
   (5) Always _____

Subject Number _____

Date: _____ Clinical Site Code: _____

5. During the past month, have you experienced a change in the number of naps you are taking during the day (lying down for short periods of time)?

(1) No change _____
(2) Napping more _____
(3) Napping less _____

6. During the past month, have you changed your usual exercise pattern in any way?

(1) No change _____
(2) Walking less _____ Walking more _____
(3) Jogging less _____ Jogging more _____
(4) Bicycling less _____ Bicycling more _____
(4) Other, describe _____

7. How would you describe your appetite during this past month?

(1) Poor _____
(2) Fair _____
(3) Good _____
(4) Excellent _____

8. How would you define your activity level for this past month?

_____ (1) 90-100 No symptoms; fully active; able to carry out all activities without restriction
_____ (2) 80-89 Some symptoms, fully ambulatory and able to carry out work of a light or sedentary nature (i.e. housework, office work)
_____ (3) 60-79 Symptomatic; unable to carry out work activities and in bed less than 50% of the day
_____ (4) 40-59 Symptomatic; able to care for self; in bed 50% or more during the day
_____ (5) 20-39 Symptomatic; unable to care for self without help; bedridden

9. During this past month, have you experienced any other changes that may be of concern to you?

_____

_____

_____

_____

Thank you very much for completing this form for us.

11/01/86, BFP

APPENDIX D

FATIGUE SELF-REPORT SCALE: BASELINE DATA

DIRECTIONS:

Each of the following questions addresses some activity or feeling which may be related to your fatigue. For each of these questions you will be asked to place an "X" through a line. This "X" should be placed through the exact spot on this line which best indicates the degree to which you are experiencing the activity or feeling. For example, if you really like to sleep late in the mornings, and you were asked the following question, you might answer:

1. To what degree do you usually like to sleep late in the mornings?
   Not at all _____ (Example) _____X_____ A great deal

Another example would include the following: If you could only sleep late in the mornings on Saturday and Sunday, and you were asked the following question, you might answer:

2. How frequently are you able to sleep in the mornings during each week, including weekends?
   Seldom _____X_____ (Example) _____ Often

FATIGUE SELF-REPORT SCALE: BASELINE DATA

SUBJECT NUMBER _____ Clinical Site Code: _____

DATE ____/____/____

TIME NOW ____/____
(Hour) (Minutes)

For each of the following questions, place an "X" through the line at the exact spot which best describes your usual pattern of fatigue.

1. When during the morning are you most likely to experience fatigue?
   1 A.M. _____ 12 Noon
2. When during the afternoon/evening ae you most likely to experience fatigue?
   1 P.M. _____ 12 Midnight
3. How frequently do you usually experience fatigue?
   Seldom _____ Often
4. How long do you usually experience fatigue?
   Minutes _____ Hours
5. Days _____ Weeks
6. How would you describe your usual pattern of fatigue?
   Intermittent _____ Continuous
7. Acute _____ Chronic
8. Localized _____ Generalized
   (To a specific muscle group/extremity) (Whole body is fatigued)
9. To what degree has your usual pattern of fatigue changed during the past six months?
   Decreased _____ Increased

For each of the following questions, place an "X" through each line at the exact spot which best indicates the degree of distress or interference you usually experience in your daily activities as a result of your fatigue.

10. The degree of distress you usually experiencé in your daily activities as a result of your fatigue is:
    No Distress _____ A great deal of distress
11. How much does the fatigue you usually experience interfere with your ability to clean your house?
    None _____ A great deal
12. How much does the fatigue you usually experience interfere with your ability to cook for yourself?
    None _____ A great deal

13. How much does the fatigue you usually experience interfere with your ability to bathe or wash yourself?

None _____ A great deal

14. How much does the fatigue you usually experience interfere with your ability to read?

None _____ A great deal

15. How much does the fatigue you usually experience interfere with your ability to dress yourself?

None _____ A great deal

16. How much does the fatigue you usually experience interfere with your ability to complete your work or school activities?

None _____ A great deal

17. How much does the fatigue you usually experience interfere with your ability to visit or socialize with your friends?

None _____ A great deal

18. How much does the fatigue you usually experience interfere with your ability to engage in sexual activity?

None _____ A great deal

19. Overall, how much does the fatigue you usually experience interfere with your ability to engage in the kind of activities you enjoy doing?

None _____ A great deal

20. Overall, how would you describe the intensity or severity of the fatigue you usually experience?

Mild _____ Severe

21. To what degree would you describe the fatigue you usually experience as being:

Pleasant _____ Unpleasant

22. Agreeable _____ Disagreeable

23. Protective _____ Destructive

24. Positive _____ Negative

25. Normal _____ Abnormal

26. To what degree do you believe illness or disease usually contributes to or causes your fatigue?

Not at all _____ A great deal

27. To what degree do you believe medical treatment usually contributes to or causes your fatigue?

Not at all _____ A great deal

28. To what degree do you believe the lack of adequate sleep usually contributes to or causes your fatigue?

Not at all _____ A great deal

29. To what degree do you believe the lack of adequate rest usually contributes to or causes your fatigue?

Not at all _____ A great deal

30. To what degree do you believe the lack of exercise usually contributes to or causes your fatigue?

Not at all _____ A great deal

31. To what degree do you believe too much noise usually contributes to or causes your fatigue?

Not at all _____ A great deal

32. To what degree do you believe too much work usually contributes to or causes your fatigue?

Not at all _____ A great deal

33. To what degree do you believe too much stress usually contributes to or causes your fatigue?

Not at all _____ A great deal

34. To what degree do you believe eating too little usually contributes to or causes your fatigue?

Not at all _____ A great deal

35. To what degree do you believe depression usually contributes to or causes your fatigue?

Not at all _____ A great deal

36. To what degree do you believe too much exercise usually contributes to or causes your fatigue?

Not at all _____ A great deal

37. To what degree do you believe eating too much usually contributes to or causes your fatigue?

Not at all _____ A great deal

38. Overall, what do you believe most directly contributes to or causes the fatigue you usually experience? _____

_____

_____

_____

_____

_____

People feeling fatigued may experience certain feelings which indicate to them that they are fatigued. For each of the following questions, place an "X" through the line at the exact spot which best indicates the degree to which each feeling generally is experienced by you when you are fatigued.

39. When I am fatigued, I usually feel:
Refreshed _____ Exhausted
40. When I am fatigued, I usually feel:
Strong _____ Weak
41. When I am fatigued, I usually feel:
Awake _____ Sleepy
42. When I am fatigued, I usually feel:
Lively _____ Listless
43. When I am fatigued, I usually feel:
Alert _____ Drowsy
44. When I am fatigued, I usually feel:
Refreshed _____ Tired
45. When I am fatigued, I usually feel:
Energetic _____ Unenergetic
46. When I am fatigued, I usually feel:
Vigorous _____ Sluggish
47. When I am fatigued, I usually feel:
Interested _____ Bored
48. When I am fatigued, I usually feel:
Calm _____ Nervous
49. When I am fatigued, I usually feel:
Patient _____ Impatient
50. When I am fatigued, I usually feel:
Motivated _____ Unmotivated
51. When I am fatigued, I usually feel:
Happy _____ Sad
52. When I am fatigued, I usually feel:
Relaxed _____ Tense

53. When I am fatigued, I usually feel:

Exhilarated _____ Depressed

54. When I am fatigued, I usually feel:

Able to Concentrate _____ Unable to Concentrate

55. When I am fatigued, I usually feel:

Able to Remember _____ Unable to Remember

56. When I am fatigued, I usually feel:

Able to Think clearly _____ Unable to Think clearly

57. Are there other feelings that you experience when you are fatigued?

(1) No ☐

(2) Yes ☐ Please describe _____

When people feel fatigued they also may experience other signs or symptoms. For each of the following signs and symptoms, place an "X" through the line at the exact spot which best indicates the degree to which each sign or symptom is experienced when you are fatigued.

58. When I am fatigued, I usually am in pain.

No pain _____ Severe pain

59. When I am fatigued, I usually have a headache.

No Headache _____ Severe Headache

60. When I am fatigued, I usually am nauseated (sick to my stomach).

No Nausea _____ Severe Nausea

61. When I am fatigued, I usually vomit (throw up).

No vomiting _____ Severe vomiting

62. When I am fatigued, I usually have eye strain.

No eye strain _____ Severe eye strain

63. When I am fatigued, I usually am constipated (hard, infrequent bowel movements).

No Constipation _____ Severe Constipation

64. When I am fatigued, I usually have diarrhea (loose, frequent bowel movements).

No diarrhea _____ Severe diarrhea

65. When I am fatigued, I usually have shortness of breath.

No shortness of breath _____ Severe shortness of breath

66. When I am fatigued, I usually have difficulty in breathing.

No difficulty _____ Severe difficulty

67. When I am fatigued, I usually am coughing.

No coughing _____ Severe coughing

68. When I am fatigued, I usually have a fever.

No fever _____ Severe fever

69. Do you experience any other symptoms when you are fatigued?

(1) No ☐

(2) Yes ☐ Please describe _____

People who are fatigued may try certain activities to reduce the amount of fatigue they are experiencing. For each of the following questions, place an "X" through the line at the exact spot which best indicates the degree of relief each activity usually provides you in reducing the amount of fatigue.

70. To what degree does sleep usually relieve your fatigue?

No relief _____ Complete relief

71. To what degree do planned rest periods between activities usually relieve your fatigue?

No relief _____ Complete relief

72. To what degree does exercise usually relieve your fatigue?

No relief _____ Complete relief

73. To what degree does distraction usually relieve your fatigue?

No relief _____ Complete relief

74. To what degree does eating usually relieve your fatigue?

No relief _____ Complete relief

75. To what degree does lying down for short periods of time (napping) usually relieve your fatigue?

No relief _____ Complete relief

76. Overall, when you experience fatigue, the best thing you can do to relieve your fatigue is:

_____

_____

77. To what degree are you experiencing fatigue now?

No fatigue _____ A great deal of fatigue

78. How severe is the fatigue which you are experiencing now?

No fatigue _____ Worst fatigue ever experienced

79. How would you describe your current fatigue?

Localized _____ Generalized
(To a specific muscle group/extremity) (Whole body is fatigued)

80. Is there anything else you would like to add that would describe your fatigue better to us?

_____

_____

81. This is the last question we would like to ask you. Do the words "tired" and "fatigued" mean the same to you or do they have different meanings? (There are no right or wrong answers. Your response will simply add to our understanding about fatigue experience.) Thank you.

_____

_____

82. Time Now: _____ / _____
(Hours) (Minutes)

APPENDIX E

FATIGUE SELF-REPORT SCALE: CURRENT DATA

DIRECTIONS:

Each of the following questions addresses some activity or feeling which may be related to your fatigue. For each of these questions you will be asked to place an "X" through a line. This "X" should be placed through the exact spot on this line which best indicates the degree to which you are experiencing the activity or feeling. For example, if you really like to sleep late in the mornings, and you were asked the following question, you might answer:

1. To what degree do you usually like to sleep late in the mornings?

   Not at all _____ (Example) _____X_____ A great deal

Another example would include the following: If you could only sleep late in the mornings on Saturday and Sunday, and you were asked the following question, you might answer:

2. How frequently are you able to sleep in the mornings during each week, including weekends?

   Seldom ___X___ (Example) _____ Often

FATIGUE SELF-REPORT SCALE: CURRENT DATA

SUBJECT NUMBER _____ Clinical Site Code:

DATE ____/____/____

TIME NOW ____/____
(Hours) (Minutes)

For each of the following questions, place an "X" through the line at the exact spot which best describes the fatigue you are experiencing now. If you are not now experiencing fatigue, describe what you experienced today.

1. To what degree are you experiencing fatigue now?
   No fatigue _____ A great deal of fatigue
2. How severe is the fatigue which you are experiencing now?
   No fatigue _____ Worst fatigue ever experienced
3. How long have you been feeling fatigue?
   Minutes _____ Hours
4. Days _____ Weeks
5. How would you describe the fatigue which you are feeling now?
   Intermittent _____ Continuous
6. Acute _____ Chronic
7. Localized _____ Generalized
   (To a specific muscle group/extremity) (Whole body is fatigued)
8. To what degree has your fatigue changed in the past week?
   Decreased _____ Increased

For each of the following questions, place an "X" through each line at the exact spot which best indicates the degree of distress or interference you are experiencing in today's activities as a result of your fatigue.

9. The degree is the fatigue you are feeling causing you distress?
   No Distress _____ A great deal of distress
10. To what degree is the fatigue you are feeling interfering with your ability to clean your house?
    None _____ A great deal
11. To what degree is the fatigue you are feeling interfering with your ability to cook for yourself?
    None _____ A great deal

12. To what degree is the fatigue you are feeling interfering with your ability to bathe or wash yourself?

None _____ A great deal

13. To what degree is the fatigue you are feeling interfering with your ability to read?

None _____ A great deal

14. To what degree is the fatigue you are feeling interfering with your ability to dress yourself?

None _____ A great deal

15. To what degree is the fatigue you are feeling interfering with your ability to complete your work or school activities?

None _____ A great deal

16. To what degree is the fatigue you are feeling interfering with your ability to visit or socialize with your friends?

None _____ A great deal

17. To what degree is the fatigue you are feeling interfering with your ability to engage in sexual activity?

None _____ A great deal

18. Overall, how much is the fatigue which you are experiencing now interfering with your ability to engage in the kind of activities you enjoy doing?

None _____ A great deal

19. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

Mild _____ Severe

20. To what degree would you describe the fatigue which you are experiencing now as being:

Pleasant _____ Unpleasant

21. Agreeable _____ Disagreeable

22. Protective _____ Destructive

23. Positive _____ Negative

24. Normal _____ Abnormal

25. To what degree do you believe illness or disease is contributing or causing your fatigue?

Not at all _____ A great deal

26. To what degree do you believe medical treatment is contributing or causing your fatigue?

Not at all _____ A great deal

27. To what degree do you believe the lack of adequate sleep is contributing to or causing your fatigue?

    Not at all _____ A great deal

28. To what degree do you believe the lack of adequate rest is contributing to or causing your fatigue?

    Not at all _____ A great deal

29. To what degree do you believe the lack of exercise is contributing to or causing your fatigue?

    Not at all _____ A great deal

30. To what degree do you believe too much noise is contributing to or causing your fatigue?

    Not at all _____ A great deal

31. To what degree do you believe too much work is contributing to or causing your fatigue?

    Not at all _____ A great deal

32. To what degree do you believe too much stress is contributing to or causing your fatigue?

    Not at all _____ A great deal

33. To what degree do you believe eating too little is contributing to or causing your fatigue?

    Not at all _____ A great deal

34. To what degree do you believe depression is contributing to or causing your fatigue?

    Not at all _____ A great deal

35. To what degree do you believe too much exercise is contributing to or causing your fatigue?

    Not at all _____ A great deal

36. To what degree do you believe eating too much is contributing to or causing your fatigue?

    Not at all _____ A great deal

37. Overall, what do you believe is most directly contributing to or causing the fatigue you are now experiencing? _____

    _____

    _____

    _____

People feeling fatigued may experience certain feelings which indicate to them that they are fatigued. For each of the following questions, place an "X" through the line at the exact spot which best indicates the degree to which each feeling generally is being experienced by you now.

38. To what degree are you now feeling:
Refreshed _____ Exhausted
39. To what degree are you now feeling:
Strong _____ Weak
40. To what degree are you now feeling:
Awake _____ Sleepy
41. To what degree are you now feeling:
Lively _____ Listless
42. To what degree are you now feeling:
Alert _____ Drowsy
43. To what degree are you now feeling:
Refreshed _____ Tired
44. To what degree are you now feeling:
Energetic _____ Unenergetic
45. To what degree are you now feeling:
Vigorous _____ Sluggish
46. To what degree are you now feeling:
Interested _____ Bored
47. To what degree are you now feeling:
Calm _____ Nervous
48. To what degree are you now feeling:
Patient _____ Impatient
49. To what degree are you now feeling:
Motivated _____ Unmotivated
50. To what degree are you now feeling:
Happy _____ Sad
51. To what degree are you now feeling:
Relaxed _____ Tense

52. To what degree are you now feeling:

Exhilarated _____ Depressed

53. To what degree are you now feeling:

Able to Concentrate _____ Unable to Concentrate

54. To what degree are you now feeling:

Able to Remember _____ Unable to Remember

55. To what degree are you now feeling:

Able to Think clearly _____ Unable to Think clearly

56. Are there other feelings that you are now experiencing?

(1) No ☐

(2) Yes ☐ Please describe _____

When people feel fatigued they also may be experiencing other signs or symptoms. For each of the following signs and symptoms, place an "X" through the line at the exact spot which best indicates the degree to which each sign or symptom is being experienced by you now.

57. To what degree are you experiencing pain?

No pain _____ Severe pain

58. To what degree are you experiencing a headache?

No Headache _____ Severe Headache

59. To what degree are you experiencing nausea (sick to my stomach)?

No Nausea _____ Severe Nausea

60. To what degree are you experiencing vomiting (throwing up)?

No vomiting _____ Severe vomiting

61. To what degree are you experiencing eye strain?

No eye strain _____ Severe eye strain

62. To what degree are you constipated (hard, infrequent bowel movements).

No Constipation _____ Severe Constipation

63. To what degree are you experiencing diarrhea (loose, frequent bowel movements).

No diarrhea _____ Severe diarrhea

64. To what degree are you experiencing shortness of breath.

No shortness of breath _____ Severe shortness of breath

65. To what degree are you experiencing difficulty in breathing?

No difficulty _____ Severe difficulty

66. To what degree are you experiencing coughing?

No coughing _____ Severe coughing

67. To what degree are you experiencing a fever?

No fever _____ Severe fever

68. Are you experiencing any other symptoms right now?

(1) No ☐

(2) Yes ☐ Please describe _____

People who are fatigued may try certain activities to reduce the amount of fatigue they are experiencing. For each of the following questions, place an "X" through the line at the exact spot which best indicates the degree of relief each activity has provided you in reducing the amount of fatigue you have experienced today.

69. To what degree has sleep relieved your fatigue today?

No relief _____ Complete relief

70. To what degree have planned rest periods between activites relieved your fatigue today?

No relief _____ Complete relief

71. To what degree has exercise relieved your fatigue today?

No relief _____ Complete relief

72. To what degree has distraction relieved your fatigue today?

No relief _____ Complete relief

73. To what degree has eating relieved your fatigue today?

No relief _____ Complete relief

74. To what degree has lying down for short periods of time (napping) relieved you today? fatigue today?

No relief _____ Complete relief

75. Overall, when you experienced fatigue today, the best thing you found which relieved your fatigue was: _____

_____

_____

76. Is there anything else you would like to add that would describe your fatigue better to us?

_____

_____

77. Time Now: _____ / _____
(Hours) (Minutes)

APPENDIX F

FATIGUE SYMPTOM CHECKLIST

SUBJECT NUMBER _____ Clinical Site Code: _____

DATE ____/____/____

TIME NOW ____/____
(Hour) (Minutes)

PLEASE CIRCLE ONLY ONE NUMBER FOR EACH OF THE FOLLOWING SYMPTOMS

At the moment I feel	Absence of	A Little	Moderate Amount	Quite A Bit	A Great Deal
1. Heavy headed	1	2	3	4	5
2. Tired over my whole body	1	2	3	4	5
3. Tired in my legs	1	2	3	4	5
4. Like yawning	1	2	3	4	5
5. My thoughts are muddled	1	2	3	4	5
6. Drowsy	1	2	3	4	5
7. Eye strain	1	2	3	4	5
8. Awkward or clumsy	1	2	3	4	5
9. Unsteady on my feet	1	2	3	4	5
10. Want to lie down	1	2	3	4	5
11. Difficulty thinking	1	2	3	4	5
12. Tired of talking	1	2	3	4	5
13. Nervous	1	2	3	4	5
14. Unable to concentrate	1	2	3	4	5
15. Unable to take interest in things	1	2	3	4	5
16. Forgetful	1	2	3	4	5
17. Lacking in self-confidence	1	2	3	4	5
18. Anxious	1	2	3	4	5
19. I can't straighten my posture	1	2	3	4	5
20. Impatient	1	2	3	4	5
21. A headache	1	2	3	4	5
22. Stiff shoulders	1	2	3	4	5
23. Back pain	1	2	3	4	5
24. Difficulty breathing	1	2	3	4	5
25. Thirsty	1	2	3	4	5
26. Voice is husky	1	2	3	4	5
27. Dizzy	1	2	3	4	5
28. Twitching eyes	1	2	3	4	5
29. Twitching limbs	1	2	3	4	5
30. Feel ill	1	2	3	4	5
31. Time Now: ____:____ (Hour) (Minutes)					

APPENDIX G

NCS Trans-Optic® MOD-70410-3

NAME _____ DATE _____

SEX: Male (M) Female (F)

IDENTIFICATION

Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE circle under the answer to the right which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.

The numbers refer to these phrases.

0 = Not at all
1 = A little
2 = Moderately
3 = Quite a bit
4 = Extremely

Col (C) O.P. (O)

	NOT AT ALL	A LITTLE	MODERATELY	QUITE A BIT	EXTREMELY
1. Friendly	0	1	2	3	4
2. Tense	0	1	2	3	4
3. Angry	0	1	2	3	4
4. Worn out	0	1	2	3	4
5. Unhappy	0	1	2	3	4
6. Clear-headed	0	1	2	3	4
7. Lively	0	1	2	3	4
8. Confused	0	1	2	3	4
9. Sorry for things done	0	1	2	3	4
10. Shaky	0	1	2	3	4
11. Listless	0	1	2	3	4
12. Peeved	0	1	2	3	4
13. Considerate	0	1	2	3	4
14. Sad	0	1	2	3	4
15. Active	0	1	2	3	4
16. On edge	0	1	2	3	4
17. Grouchy	0	1	2	3	4
18. Blue	0	1	2	3	4
19. Energetic	0	1	2	3	4
20. Panicky	0	1	2	3	4
21. Hopeless	0	1	2	3	4
22. Relaxed	0	1	2	3	4
23. Unworthy	0	1	2	3	4
24. Spiteful	0	1	2	3	4
25. Sympathetic	0	1	2	3	4
26. Uneasy	0	1	2	3	4
27. Restless	0	1	2	3	4
28. Unable to concentrate	0	1	2	3	4
29. Fatigued	0	1	2	3	4
30. Helpful	0	1	2	3	4
31. Annoyed	0	1	2	3	4
32. Discouraged	0	1	2	3	4
33. Resentful	0	1	2	3	4
34. Nervous	0	1	2	3	4
35. Lonely	0	1	2	3	4
36. Miserable	0	1	2	3	4
37. Muddled	0	1	2	3	4
38. Cheerful	0	1	2	3	4
39. Bitter	0	1	2	3	4
40. Exhausted	0	1	2	3	4
41. Anxious	0	1	2	3	4
42. Ready to fight	0	1	2	3	4
43. Good natured	0	1	2	3	4
44. Gloomy	0	1	2	3	4
45. Desperate	0	1	2	3	4
46. Sluggish	0	1	2	3	4
47. Rebellious	0	1	2	3	4
48. Helpless	0	1	2	3	4
49. Weary	0	1	2	3	4
50. Bewildered	0	1	2	3	4
51. Alert	0	1	2	3	4
52. Deceived	0	1	2	3	4
53. Furious	0	1	2	3	4
54. Efficient	0	1	2	3	4
55. Trusting	0	1	2	3	4
56. Full of pep	0	1	2	3	4
57. Bad-tempered	0	1	2	3	4
58. Worthless	0	1	2	3	4
59. Forgetful	0	1	2	3	4
60. Carefree	0	1	2	3	4
61. Terrified	0	1	2	3	4
62. Guilty	0	1	2	3	4
63. Vigorous	0	1	2	3	4
64. Uncertain about things	0	1	2	3	4
65. Bushed	0	1	2	3	4

MAKE SURE YOU HAVE ANSWERED EVERY ITEM.

POM 021

APPENDIX H

SOCIAL SUPPORT QUESTIONNAIRE

PLEASE READ ALL DIRECTIONS ON THIS PAGE BEFORE STARTING.

Please list each significant person in your life on the right. Consider all the persons who provide personal support for you or who are important to you.

Use only first names or initials, and then indicate the relationship, as in the following example:

Example:

	First Name or Initials	Relationship
1.	MARY T.	FRIEND
2.	BOB	BROTHER
3.	M.T.	MOTHER
4.	SAM	FRIEND
5.	MRS. R.	NEIGHBOR

etc.

Use the following list to help you think of the people important to you, and list as many people as apply in your case.

- spouse or partner
- family members or relatives
- friends
- work or school associates
- neighbors
- health care providers
- counselor or therapist
- minister/priest/rabbi
- other

You do not have to use all 24 spaces. Use as many spaces as you have important persons in your life.

WHEN YOU HAVE FINISHED YOUR LIST, PLEASE TURN TO PAGE 2.

For each person you listed, please answer the following questions by writing in the number that applies.

1 = not at all
2 = a little
3 = moderately
4 = quite a bit
5 = a great deal

Question 1:

How much does this person make you feel liked or loved?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

Question 2:

How much does this person make you feel respected or admired?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

GO ON TO NEXT PAGE

1 = not at all
2 = a little
3 = moderately
4 = quite a bit
5 = a great deal

Question 3:

How much can you confide in this person?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

Question 4:

How much does this person agree with or support your actions or thoughts?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

GO ON TO NEXT PAGE

1 = not at all
2 = a little
3 = moderately
4 = quite a bit
5 = a great deal

Question 5:

If you needed to borrow $10, a ride to the doctor, or some other immediate help, how much could this person usually help?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

Question 6:

If you were confined to bed for several weeks, how much could this person help you?

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____
17. _____
18. _____
19. _____
20. _____
21. _____
22. _____
23. _____
24. _____

GO ON TO NEXT PAGE

Number _____ [1-4]

Clinical Site

Date _____

PERSONAL NETWORK

First Name or Initials	Relationship	Question 7: How long have you known this person? (1 = less than 6 months, 2 = 6 to 12 months, 3 = 1 to 2 years, 4 = 2 to 5 years, 5 = more than 5 years)	Question 8: How frequently do you usually have contact with this person? (Phone calls, visits, or letters) (5 = daily, 4 = weekly, 3 = monthly, 2 = a few times a year, 1 = once a year or less)
1. _____	_____ [32]	1. _____	1. _____
2. _____	_____ [33]	2. _____	2. _____
3. _____	_____ [34]	3. _____	3. _____
4. _____	_____ [35]	4. _____	4. _____
5. _____	_____ [36]	5. _____	5. _____
6. _____	_____ [37]	6. _____	6. _____
7. _____	_____ [38]	7. _____	7. _____
8. _____	_____ [39]	8. _____	8. _____
9. _____	_____ [40]	9. _____	9. _____
10. _____	_____ [41]	10. _____	10. _____
11. _____	_____ [42]	11. _____	11. _____
12. _____	_____ [43]	12. _____	12. _____
13. _____	_____ [44]	13. _____	13. _____
14. _____	_____ [45]	14. _____	14. _____
15. _____	_____ [46]	15. _____	15. _____
16. _____	_____ [47]	16. _____	16. _____
17. _____	_____ [48]	17. _____	17. _____
18. _____	_____ [49]	18. _____	18. _____
19. _____	_____ [50]	19. _____	19. _____
20. _____	_____ [51]	20. _____	20. _____
21. _____	_____ [52]	21. _____	21. _____
22. _____	_____ [53]	22. _____	22. _____
23. _____	_____ [54]	23. _____	23. _____
24. _____	_____ [55]	24. _____	24. _____

[5-6]

PLEASE BE SURE YOU HAVE RATED EACH PERSON ON EVERY QUESTION. GO ON TO THE LAST PAGE.

[25-27]

[28-30]

9. During the past year, have you lost any important relationships due to moving, a job change, divorce or separation, death, or some other reason? [57]

_____ 0. No
_____ 1. Yes

IF YES:

9a. Please indicate the number of persons from each category who are *no longer available* to you.

_____ spouse or partner [58]
_____ family members or relatives [59-60]
_____ friends [61-62]
_____ work or school associate: [63-64]
_____ neighbors [65-66]
_____ health care providers [67]
_____ counselor or therapist [68]
_____ minister/priest/rabbi [69]
_____ other (specify) _____ [70] [71-72]

9b. Overall, how much of your support was provided by these people who are no longer available to you? [73]

_____ 0. none at all
_____ 1. a little
_____ 2. a moderate amount
_____ 3. quite a bit
_____ 4. a great deal

10. Overall, how adequate is your social support for your current illness and treatment? Please put an "X" at the appropriate spot on the horizontal line below.

Not at all adequate _____ Very adequate

Clinical Site Code:

APPENDIX I

MEDICAL RECORD FORM I.D. No. _____

Dx: _____ Stage: _____

VARIABLES / Date	Time 1	Time 2	Time 3	Time 4	Time 5	Time 6
1. Weight (kg/lbs)						
2. Temperature						
3. Karnofsky Performance Status by M.D., record actual percentage						
4. Total white blood cell count						
5. Hemoglobin/Hematocrit						
6. Disease Response as measured by:						
a. _____						
b. _____						
c. _____						
d. _____						
7. Additional Lab values						
a. _____						
b. _____						
c. _____						
d. _____						

8. CHEMOTHERAPY PROTOCOL

Drug(s)	Dose	Route	Cycle Information:	Date Started
a. Cytoxan				
b. Methotrexate				
c. 5-FU				
d.				
e.				
f.				

Clinical Site Code:

MEDICAL RECORD FORM I.D. No. _____

9. CHEMOTHERAPY TREATMENT Date	Time 1	Time 2	Time 4	Time 5	Time 6
a. Cytoxan b. Methotrexate c. 5-FU d. e. f. Indicate whether a) protocol followed b) treatment not given c) dosage modification made					
VARIABLES					

10. Other medications:

11. Previous form(s) of treatment for cancer (Describe date and type of treatment):

12. Concurrent form(s) of treatment for cancer (Describe date and type of treatment if any):

13. Other illnesses, past and present (Describe dates and type of treatment):

Clinical Site Code: _____

I.D. No. _____

MEDICAL RECORD FORM

Karnofsky Performance Status Codes

(1) 90-100 No symptoms; fully active; able to carry out all activities without restriction

(2) 80-89 Some symptoms, fully active; able to carry out work of a light or sedentary nature (i.e. housework, office work)

(3) 60-79 Symptomatic; unable to carry out work activities and in bed less than 50% of the day

(4) 40-59 Symptomatic; able to care for self; in bed 50% or more during the day

(5) 20-39 Symptomatic; unable to care for self without help; bedridden

Disease Response Codes

(1) Complete response

(2) Partial response

(3) Disease progression

(4) Other (specify parameters used) _____

_____

Progress Notes: (Note any significant symptoms and/or occurrence while on study):

Date:

Date:

Date:

APPENDIX P

Pearson Product Moment Correlations Between the Four Fatigue Measures Time 7 (n=44)

Fatigue Measure	1	2	3	4
1. Intensity of Fatigue Symptoms (FSCL)	1.0	.76	.64	.80
2. Fatigue/Inertia Subscale (POMS)		1.0	.74	.62
3. Total Fatigue Score (PFS)			1.0	.53
4. Total Number of Fatigue Symptoms (FSCL)				1.0

NOTE: All significant at $p < .0001$