Original Article

Measuring Fatigue and Other Anemia-Related Symptoms with the Functional Assessment of Cancer Therapy (FACT) Measurement System

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Abstract

This paper reports the development and validation of a questionnaire assessing fatigue and anemia-related concerns in people with cancer. Using the 28-item Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire as a base, 20 additional questions related to the symptoms and concerns of patients with anemia were developed. Thirteen of these 20 questions dealt with fatigue, while the remaining 7 covered other concerns related to anemia. Using semi-structured interviews with 14 anemic oncology patients and 5 oncology experts, two instruments were produced: The FACT-Fatigue (FACT-F), consisting of the FACT-G plus 13 fatigue items, and the FACT-Anemia (FACT-An), consisting of the FACT-F plus 7 nonfatigue items. These measures were, in turn, tested on a second sample of 50 cancer patients with hemoglobin levels ranging from 7 to 15.9 g/dL. The 41-item FACT-F and the 48 item FACT-An scores were found to be stable (test-retest r = 0.87 for both) and internally consistent (coefficient alpha range = 0.95-0.96). The symptom-specific subscales also showed good stability (test-retest r range = 0.84-0.90), and the Fatigue subscale showed strong internal consistency (coefficient alpha range = 0.93-0.95). Internal consistency of the miscellaneous nonfatigue items was lower but acceptable (alpha range = 0.59-0.70), particularly in light of their strong relationship to patient-rated performance status and hemoglobin level. Convergent and discriminant validity testing revealed a significant positive relationship with other known measures of fatigue, a significant negative relationship with vigor, and a predicted lack of relationship with social desirability. The total scores of both scales differentiated patients by hemoglobin level ($p < 0.05$) and patient-rated performance status ($p < 0.0001$). The 13-item Fatigue subscale of the FACT-F and the 7 nonfatigue items of the FACT-An also differentiated patients by hemoglobin level ($p < 0.05$) and patient-rated performance status ($p \leq 0.001$). The FACT-F and FACT-An are useful measures of quality of life in cancer treatment, adding more focus to the problems of fatigue and anemia. The Fatigue Subscale may also stand alone as a very brief, but reliable and valid measure of fatigue. J Pain Symptom Manage *1997;13:63-74.* © *U.S. Cancer Pain Relief Committee, 1997.*

Key Words

Anemia, fatigue, quality of life, measurement, cancer

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Introduction

The multiple burdens of disease and treatment are often physically, functionally, socially, and emotionally debilitating in the cancer patient, and can have a profound impact on quality of life across the illness trajectory. One symptom of significant concern to cancer patients is fatigue.[1-17] Because fatigue is common byproduct of increasingly aggressive chemotherapy regimens, information about fatigue as a consequence of treatment has gained higher priority recently. Over the past decade, attention has been directed towards defining and measuring fatigue in cancer patients.[1-4,6-9,11,13-19] However, measuring fatigue has been difficult due, in part, to the complex and interactive nature of potential underlying etiological factors, among them mood disturbance, anemia, anorexia/cachexia, infection/fever, pain, sleep disturbance, diffuse chemotherapy and radiotherapy effects, surgical recovery, tumor burden, and prolonged stress.[3,4,7,9,10,14,15] Although the specific etiology of cancer treatment-induced fatigue is complex and poorly understood, its prevalence is high, with estimates ranging from 80% to 96%.[4]

Similar to fatigue, anemia in the cancer patient can be the result of either advanced disease or aggressive therapy.[5,20] Clinical symptoms include fatigue, shortness of breath, chest pain, weakness, loss of appetite, and headache.[5,20] A decline in the subjective sense of well-being and functional impairment defined as a reduction in exercise tolerance, ability to work, social interaction, and the pursuit and enjoyment of leisure activities have been commonly identified as the quality-of-life domains most significantly disrupted by symptoms of anemia.[20] If one wished to measure the impact of anemia on the quality of life in cancer patients, a fatigue questionnaire would most certainly be included. However, there are symptoms other than fatigue that are relevant in anemia. Existing measures of fatigue do not survey the full spectrum of anemia-related symptoms.

Anemia is defined as a deficiency of either red blood cells (RBCs) or lack of hemoglobin, which leads to a reduction in the oxygen-carrying capacity of blood. In cancer treatment, anemia is thought to result from the myelosuppressive effects of therapy. It is generally reversible and does not carry significant post-treatment morbidity although its associated fatigue can be quite disruptive to patients lives. Anemia can also result from other causes, among them folate or Vitamin B_{12} deficiencies, chronic blood loss from the gastrointestinal tract, renal failure, or from myelosuppression of stem cells by tumor cell products.

There is no known valid questionnaire assessing the full spectrum of anemia-related symptoms. Current measures of fatigue, a cardinal symptom of anemia, are hampered by problems of definition, limited reliability and validity data, and an absence of comprehensive assessment of symptoms on quality of life (QOL).[2,6,10,15,16,18] These considerations are important when selecting an outcome measure to assess change across the treatment trajectory. Accurate assessment of quality of life, including the component expressed as fatigue or influenced by fatigue, is important when evaluating comparative treatments, making decisions about future treatments, and in palliative care. The value of accurate QOL assessment is twofold: (a) it allows for an immediate understanding of an individual patient s current status (making it a potentially useful intervention tool); and (b) it allows for measurement of change over time, making it a useful outcome tool. A multidimensional assessment of QOL allows for a comprehensive understanding of the impact of cancer treatment and of the tumor itself. This is particularly true for those who suffer from the QOL consequences of anemia and/or fatigue.

The Functional Assessment of Cancer Therapy (FACT) Measurement System is a comprehensive compilation of questions which measure health-related QOL in patients with cancer and other chronic illnesses. There are currently over 250 questions in the FACT item bank, but any given patient is rarely asked to answer more than 60. This is done with the use of a 34-item general version of the ques-

[a] This publication presents validity data from the 32-item FACT-G, the 13-item Fatigue Scale and 20-item Anemia Scale. One question (question 25) has since been added to the FACT-G data bank ("I worry that my condition will get worse"), and is reflected in the final version of the FACT-An, making it a 55-item scale, of which 49 are scored.

tionnaire (FACT-G).[21] The general version serves as the foundation upon which questions are added to address concerns or problems specific to a given disease site, treatment, or symptom. For example, specific concerns related to lung cancer form the Lung Cancer Subscales (LCS) and are added to the FACT-G, forming the FACT-L.[22] Similarly, specific concerns related to anorexia/cachexia form an anorexia/cachexia subscale which, when added to the FACT-G forms the Functional Assessment of Anorexia/Cachexia Therapy (FAACT).[23]

We describe here the development and initial testing of a subscale for assessing specific problems related to anemia in cancer patients. It was understood at the outset that this subscale would be heavily represented by questions addressing the cardinal symptom of anemia—fatigue. Accordingly, it was anticipated that the Anemia Subscale would include questions related to fatigue as well as other miscellaneous problems associated with anemia. We therefore report data on two FACT subscales: Fatigue and Anemia. The FACT-Fatigue (FACT-F) is comprised of the FACT-G plus the Fatigue Subscale, and the FACT-Anemia (FACT-An) is comprised of the FACT-F plus additional miscellaneous non-fatigue items relevant to anemia in cancer patients.

Study Design and Overview

Scale Development

The Functional Assessment of Cancer Therapy–Fatigue (FACT-F) and FACT–Anemia (FACT-An) Subscales were developed between May 1994 and October 1994. The Functional Assessment of Cancer Therapy Scale–General (FACT-G)[21] served as the core "generic" health-related QOL instrument, to which the Fatigue and Anemia subscales were added.[a] The goal of the study was to identify a finite set of concerns specific to fatigue and anemia that were not adequately covered by the FACT-G. Development of the subscales occurred in two phases: item development and subscale validation. The item development phase involved item generation and item reduction. Item generation and reduction were accomplished using comprehensive semi-structured interviews with anemic cancer patients and medical care providers (item generation), followed by presentation to a second group of medical experts for comment and expert input (item reduction).

The subscale validation phase involved presentation of the FACT-An (that is, FACT-F plus miscellaneous anemia-related concerns), along with other measures, to a second sample of patients. Collected data allowed for determination of (a) internal consistency (Cronbach's alpha); (b) test–retest reliability; (c) revalidation of the FACT-G with cancer patients suffering from anemia and fatigue; (d) convergent and discriminant validation; and (e) assessment of the accuracy of the FACT-F and FACT-An in discriminating patients according to hemoglobin level and Eastern Cooperative Oncology Group (ECOG) Performance Status Rating (PSR).

Methods

In the item development phase, candidate items for the fatigue and anemia subscales of the FACT-G were generated using comprehensive semi-structured interviews with 14 anemic oncology patients (seven men and seven women) and five medical expert providers. Eligibility criteria for the patients required that they be (a) 18 years or older; (b) at least 1 month postdiagnosis of cancer; and (c) have a current hemoglobin level at or below 11.0 g/dL. Experts were defined as physicians or nurses who possessed a minimum of three years experience treating at least 100 patients with cancer-associated anemia and fatigue. This definition of an expert has been used in developing all other FACT items.[21]

The item-generation patient sample comprised both inpatients and outpatients. Age ranged from 42 to 80 years, and hemoglobin levels ranged from 6.3 to 11.0. Mean hemoglobin level for the sample was 8.9 g/dL. Eleven patients had a performance status rating of 2 or better (0–4, Zubrod scale[26]), and the sample was represented by a broad range of cancer diagnoses (for example, breast, lung, colorectal, and lymphoma).

Eligible oncology patients were approached and asked to participate in a brief interview designed to elicit a variety of information related to the degree to which their illness (and anemia in particular) affected their qual-

ity of life. Participation was voluntary, and verbal consent was obtained according to local institutional review board requirements. A total of eight medical experts (two MDs, six master's level RNs) were approached and interviewed by the second author. Two experts were involved in both the item-generation and item-reduction phases. Three experts participated only in the item-generation phase and the remaining three experts participated only in the item-reduction phase of the study.

Using a semi-structured interview format, pertinent sociodemographic, disease, and treatment information were gathered followed by a series of open-ended questions designed to elicit candidate items. The inquiry covered areas of information about personal definitions of quality of life, symptoms associated with anemia, and how disease- or treatment-related fatigue and anemia affected various dimensions of quality of life. Quality-of-life issues ranged from physical and functional status to emotional well-being, family issues, sexuality/intimacy, social relations, work status, and future orientation. Finally, patients rated the relevance of each FACT-G question to their quality of life on a scale ranging from 0 to 10 (0 = not at all; 10 = as much as I could imagine).

Validation Phase

The validation sample consisted of an initial pool of 50 previously untested patients (23 men and 27 women). These patients were receiving treatment at Rush–Presbyterian–St. Luke's Medical Center, Chicago, (N = 29), at Rush North Shore Medical Center, Skokie, (N = 20), and at Cook County Hospital, Chicago, (N = 1). There were four patient refusals (8%). Reasons for refusing to participate included lack of time or feeling too ill. One patient did not complete the retesting/validation phase of the study. The final sample of 49 patients ranged in age from 19 to 83 years (median age, 56 years), and represented a broad spectrum of cancer diagnoses (See Table 1). In order to obtain test–retest data from patients whose current performance status rating and hemoglobin level were not expected to change between baseline and retesting, eligibility criteria for this phase of instrument testing was fairly restrictive. Exclusion criteria included: (1) receiving cytotoxic chemotherapy or surgery either within the past week or expected within 1 week; (2) currently receiving radiation therapy; (3) having received either a blood transfusion or growth factor injection 3 days prior to data collection; (4) anticipating transfusion or a growth factor injection within one week after baseline data; (5) brain metastasis; or (6) pregnancy. The final sample consisted of 49 patients (98%) who provided evaluable baseline data and 44 (88%) who provided evaluable retest administrations.

Table 1
Demographic and Clinical Characteristics of the Validation Sample (N = 50)

Sample characteristic	N (range)	%
Gender		
Male	23	46%
Female	27	54%
Race/ethnicity		
White non-Hispanic	43	86%
Black non-Hispanic	4	8%
Hispanic	3	6%
Age		
Median	56 years	
Range	19–83 years	
Educational level		
Median	13 years	
Range	8–21 years	
Disease site		
Breast	12	24%
Lung	8	16%
Colorectal	11	22%
Lymphoma	5	10%
Leukemia	3	6%
Ovarian	3	6%
Prostate	2	4%
Myeloma	2	4%
Stomach	1	2%
Bladder	1	2%
Others	2	4%
Hemoglobin levels		
Median	12.5 g/dL	
Range	7–15.9 g/dL	
<11.0 g/dL	N = 14	28%
11.0–12.99 g/dL	N = 17	34%
≥13 g/dL	N = 19	38%
Performance status (patient-rated)		
0 (fully ambulatory without physical symptoms)	18	36%
1 (ambulatory with symptoms)	22	44%
2,3 (requiring bedrest during waking day)	10	20%

Patients were divided according to their hemoglobin level, which had been drawn less than 48 hours before baseline data collection. Fourteen patients had a hemoglobin level less than or equal to 11.0 g/dL, 17 patients with 11.0–12.99 g/dL, and 19 patients with hemoglobin levels greater than or equal to 13 g/dL. A complete description of the demographic

and clinical characteristics of the validation sample can be seen in Table 1.

Measures

The validation packet of questionnaires included the FACT-An, The Piper Fatigue Scale,[12] the Fatigue and Vigor subscales of the Profile of Mood States (POMS),[24] a ten-item short form of the Marlowe-Crowne Social Desirability Scale,[25] and the ECOG Performance Status Rating (PSR).[26] Sociodemographic, disease, and treatment information were also gathered.

The FACT-An is 55-item self-report instrument in which 48 items are scored. It includes the core FACT-G (version 3), 20 additional concerns items (the 13-item Fatigue Scale and 7 non-fatigue items), and one experimental item weighting the degree to which the additional concerns affect QOL. The FACT-G (version 3) is a 34-item self-report instrument, 29 items assessing quality of life across the domains of physical well-being (7 items), social/family well-being (7 items), relationship with the physician (2 items), emotional well-being (6 items), and functional well-being (7 items) using a five-point Likert-type scale ranging from 0 ("not at all") to 4 ("very much so").[21] The remaining five questions are experimental, reflecting weightings of the degree to which each domain affects quality of life. Scores are obtained for each of the specific domains as well as a total QOL score. The FACT-G has good test-retest reliability (r ranging from 0.82 to 0.92) and is sensitive to change over time. It also has been shown to possess good convergent and discriminant validity.[21]

The Piper Fatigue Scale (PFS) assesses subjective fatigue using responses to a 46-item visual analogue scale.[12] The PFS was selected because it is a frequently used "criterion" instrument measuring fatigue, to which the FACT-F and FACT-An could be compared to assess concurrent validity. Only the first 41 items of the PFS were used in this study because they did not include open-ended questions, and they provided information about the temporal, intensity/severity, affective, and sensory dimensions of fatigue, along with a total score. Piper and colleagues[12] report good internal consistency (alpha = 0.85 for the total score), and the baseline form shows some evidence of discriminant and convergent validity. More recent studies using the PFS have found significant negative correlations with clinician-rated Karnofsky Performance Status scores and quality of life as measured by the Quality of Life Index for Patients with Cancer.[27]

The Profile of Mood States (POMS) is a widely utilized 65-item self-report measure of subjective mood states. Adjectives are rated on a five-point rating scale ranging from 0 ("not at all") to 4 ("extremely"), and responses are summed to yield both subscale scores and a total mood disturbance score. The eight-item Vigor subscale of the POMS is defined by adjectives suggesting vigorousness, cbullience, and high energy; the seven-item Fatigue subscale is defined by weariness, inertia, and low energy. These two subscales were included to gather evidence for convergent validity of the FACT-F and FACT-An. The Vigor and Fatigue subscales have been shown to demonstrate good internal consistency ($K\text{-}R_{20}$ = 0.89 and 0.94, respectively), adequate test-retest reliability (r = 0.65 and 0.66, respectively, over an average 20-day period), and good construct validity in multiple empirical investigations.[28]

The Marlowe-Crowne Social Desirability Scale—Short Form (MC-1) is a ten-item measure of conformity with socially desirable traits. It is an indirect measure of a person s need for social acceptance. The MC-1 was added for evidence of divergent validity. The ten-item short form is a homogeneous condensation of its lengthier parent version, which demonstrates good internal consistency ($K\text{-}R_{20}$ ranging from 0.66 to 0.70 in a university sample), and is significantly correlated with the longer form (r ranging from 0.80 to 0.90).[25] In all forms, higher scores reflect a greater social desirability response bias. Because such a response bias should not be related to QOL, the Marlowe-Crowne was predicted to have, at best, a weak correlation with the The FACT-F and FACT-An.

The ECOG Performance Status Rating (PSR) is a single-item rating of the degree to which patients are able to participate in customary activities without the need for rest. The ECOG PSR item was included because it is a familiar, if somewhat global, index by which patients could be divided for known-groups validation. It is widely used in cancer clinical trials to assess functional capability of patients as they undergo treatment. The PSR

Table 2
Descriptive Statistics for Functional Assessment of Cancer Therapy (FACT) Scales and Item Totals

FACT Subscales (Number items)	Subscale Means ($N = 49$)[a]	Standard Deviations ($N = 49$)[a]	Subscale Range ($N = 49$)[a]	Cronbach's Alpha Initial/ Retest[b]	Test-Retest Correlations ($N = 44$)[c]
FACT-Fatigue (FACT-F) (41)	121.74	23.18	59–163	0.95/0.95	0.87
FACT-Anemia (FACT-An) (48)	141.59	26.78	67–190	0.96/0.96	0.87
FACT-G (28)	84.98	14.84	48–111	0.88/0.90	0.82
Fatigue subscale (13)	36.76	10.49	6–52	0.93/0.95	0.90
Non-fatigue items (7)	19.85	4.40	8–28	0.59/0.70	0.84

[a] N based on initial administration.
[b] N for internal consistency analyses vary as a function of missing data within each subscale.
[c] N based on retest administration.

score ranges from 0 ("I have normal activity without symptoms") to 4 ("I am unable to get out of bed").[26] This rating was obtained directly from patients.

The validation of the FACT-An and FACT-F involved administration of 49 baseline assessments and 44 retest administrations of the FACT-An within 3–7 days. Patients who agreed to participate completed the initial validation packet at the time they were approached. They were required to complete only the FACT-An again within 3–7 days. Each patient was given a copy of the FACT-An and a self-addressed stamped envelope in which to return it within the 3–7 days. Frequent telephone contact was used to monitor and maintain adherence to the 3- to 7-day window.

Results

Scale Development Phase

Candidate items were initially summarized as identifiable issues or symptoms related to fatigue versus other anemia-related concerns, and then tabulated to determine frequencies. The five medical experts produced 32 candidate items and the 14 anemic cancer patients produced 221 candidate items. As expected, there was a high degree of redundancy among items generated by patients, between patients and the medical experts, and between newly generated items and pre-existing items from the FACT-G. The redundancy allowed for a sharp reduction of the initial pool of items. Another factor that helped reduce the initial candidate pool was the lack of specificity of certain items to anemia concerns. Many items tapped general health-related quality of life rather than anemia. Thus, of the initial 253 items, 39 were given consideration as second-round candidates. This pool of items was presented again to the second group of medical experts for comment and assistance, allowing for further simplification and reduction to a final pool of 20 anemia-specific questions.

Careful content review of the final 20 items confirmed two main components: 13 items assessing fatigue and 7 dealing with non-fatigue concerns relating to anemia. The 13-item Fatigue and 20-item Anemia subscales were then formatted with response choices compatible with the FACT-G, comprising two scales: the 48-item FACT–Fatigue (FACT-F) in which 41 items are scored, and the 55-item FACT-Anemia (FACT-An), in which 48 items are scored. The seven non-scored items are experimental in nature and ask for ratings of the impact of specific domains on quality of life, using a ten-point rating scale. The FACT-F and FACT-An items can be found in the appendix. The FACT-An, reported in the appendix, uses the most recent version of the FACT-G core to which a new emotional well-being question (item 25) has been added.

Validation Phase

FACT-Fatigue (FACT-F). The 41-item FACT-F scores in the validation sample are reported in Table 2. This measure was stable over a 3- to 7-day window (test–retest $r = 0.87$) and had excellent internal consistency (alphas = 0.95 on both initial and retest administrations). The 13-item Fatigue subscale of the FACT-F independently demonstrated good test–retest reliability ($r = 0.90$), internal consistency (alphas = 0.93 and 0.95) on initial and test–retest administrations, suggesting an ability to be used as an independent, brief, unidimensional measure of fatigue (See Table 2).

FACT-Anemia (FACT-An). Similarly, the

Table 3
Convergent/Divergent Validity of the Functional Assessment of Cancer Therapy (FACT) Scales and Subscales ($N = 49$)[a]

Scale (Number of items)	FACT-F (41)	FACT-An (48)	FACT-G (28)	Fatigue subscale (13)	Non-fatigue items (7)	POMS fatigue (7)	POMS vigor (8)	Piper fatigue (41)
Fatigue subscale	0.66[b]	0.73[b]	0.66					
Non-fatigue items	0.79	0.79[b]	0.68	0.77				
POMS fatigue	−0.74	−0.77	−0.57	−0.83	−0.77			
POMS vigor	0.66	0.65	0.59	0.61	0.52	−0.52		
Piper fatigue	−0.75	−0.75	−0.58	−0.77	−0.57	0.75	−0.43	
Marlowe-Crowne	0.04	−0.06	0.10	−0.07	0.18	−0.11	0.15	0.28

[a] Sample size was $N = 49$ for all comparisons except for those on the Piper fatigue scale, where sample size was $N = 30$ due to missing data.
[b] Correlations corrected for item overlap.
Note: Because the FACT is scored so that a high score signifies good quality of life, positive associations with the Piper and POMS fatigue scales are indicated by negative coefficients, and negative associations with the POMS vigor scales are indicated by positive coefficients.
Correlations >0.35 significant at $P = 0.05$.
POMS, Profile of Mood States.

FACT-An (FACT-F plus 7 non-fatigue items) was found to possess good psychometric properties (See Table 2). Test–retest reliability over the 3- to 7-day window was high ($r = 0.87$), with more than adequate internal consistency on both initial and retest administrations. The additional non-fatigue items also showed good stability (test–retest $r = 0.84$), but marginal internal consistency (alpha range, 0.59–0.70).

Convergent-divergent validity. Pearson correlation coefficients assessed the strength of relationships between the FACT subscale and aggregate, and other measures expected to be positively related, negatively related, or unrelated to fatigue and anemia. Because a number of questions on the Piper Fatigue Scale regarding the degree of fatigue experienced was not applicable to all subjects ($N = 19$ in the high hemoglobin group), there were only 30 questionnaires with complete responses to all measures. In order to maximize the sample size for each combination of measures in the correlation matrix, pairwise deletions were used. Thus, sample sizes for each correlation coefficient ranged from a low of $N = 30$ for the Piper Fatigue Scale to $N = 49$. Pearson correlation coefficients can be found in Table 3.

Both the Fact-F and FACT-An are significantly related to similar concepts (convergent validity) and are unrelated to concepts not assumed to be associated with either fatigue or anemia (divergent validity). Because answers to the FACT-F, FACT-An, and the 13-item Fatigue subscale are scored so that high scores reflect fewer problems (good QOL), it was expected that there would be a strong negative relationship with the POMS Fatigue and Piper Fatigue Scales and a positive relationship with the POMS Vigor scale. Expectations were confirmed by these data. Further, the FACT-F, FACT-An, and Fatigue subscales are unrelated to social desirability, as measured by the short-form of the Marlowe–Crowne Social Desirability Scale (see Table 3).

Known-groups (discriminant) validity. Hemoglobin level. The sample was divided into groups of high (≥13.0 g/dL), moderate (11–12.99 g/dL), and low (<11 g/dL) hemoglobin levels. It was expected that higher hemoglobin levels would be associated with better QOL, and that group membership could be predicted by the FACT-F and FACT-An. As can be seen in Table 4, hemoglobin levels were indeed associated with QOL as measured by both the FACT-F ($F(2,46) = 4.28$, $P = 0.02$) and FACT-An ($F(2,46) = 4.76$, $P = 0.013$. Post hoc comparisons of groups (Tukey Test) indicated that the effect was greatest in differentiating the very low hemoglobin group (<11 g/dL) from the highest group (≥13 g/dL) ($P = 0.01$). The 13-item Fatigue subscale and 7 non-fatigue items were also successful in discriminating hemoglobin group membership (See Table 4). Post hoc comparison of groups (Tukey Test) indicated that the Fatigue subscale differentiated the very low from the very high group ($P = 0.04$), whereas the non-fatigue items differentiated the low and middle groups from the high group (Table 4).

Performance status. All specific subscales

Table 4
Mean Functional Assessment of Cancer Therapy (FACT) Total and Subscale Scores by Hemoglobin Level (g/dL)

FACT scales and subscales (Number of items)	Mean hemoglobin level <11 g/dL N = 14	11–12.99 g/dL N = 16	≥13 g/dL N = 19	
FACT-Fatigue (FACT-F) (41)	110.29a SD = 24.7	119.25 SD = 22.5	132.28[a] SD = 18.6	F(2,46) = 4.28 $P < 0.020$
FACT-Anemia (FACT-An) (48)	128.70[b] SD = 29.0	137.30 SD = 24.8	154.70[b] SD = 21.5	F(2,46) = 4.76 $P < 0.013$
FACT-General (FACT-G) (28)	77.64[c] SD = 15.1	84.44 SD = 15.4	90.84[c] SD = 12.1	F(2,46) = 3.54 $P < 0.037$
Fatigue subscale (13)	32.60[d] SD = 12.6	34.80 SD = 9.5	41.40[d] SD = 8.1	F(2,46) = 3.59 $P < 0.036$
Non-fatigue items (7)	18.40[e] SD = 5.0	18.0f SD = 3.7	22.40[e,f] SD = 3.2	F(2,46) = 6.76 $P < 0.003$

Note: Superscript letters in each row reflect significant post hoc Tukey comparisons at the following significance levels: [a] $P = 0.017$; .013; [c] $P = 0.029$; [d] $P = 0.041$; [b] $P = 0.016$; and [b] $P = 0.005$.

and total scores discriminated levels of performance status in a sample divided into three levels (PS = 0 versus 1 versus 2,3). It was expected that better performance status would be associated with higher QOL scores and that group membership would be predicted by both the FACT-F, FACT-An, and FACT-G. Higher scores on both instruments were associated with better performance status. (See Table 5 for details and statistical information). Post hoc comparisons (Tukey Test) suggested that all subscales and total scores were able to successfully discriminate between PS = 0 versus 2,3 (P ranging from 0.001 to 0.003) and PS = 1 versus 2,3 (P ranging from 0.003 to 0.039). The FACT-G was the only scale able to discriminate between PS = 0 versus 1 ($P = 0.025$).

Discussion

The goal of this study was to develop subscales of the FACT Measurement System that could accurately assess quality of life in cancer patients suffering from fatigue and other anemia-related symptoms. To this end, the FAC T-An and FACT-F are offered as reliable and valid measures to obtain this information. The 48-item FACT-An demonstrates high internal consistency, good test-retest reliability, convergent validity, divergent validity, and has been found to successfully discriminate patients based upon hemoglobin level and performance status. Patients with higher hemoglobin levels and better performance status reported significantly higher scores on these instruments (including the newly created subscales) than did those with lower hemoglobin levels and poorer performance status. Likewise, the 41-item FACT-F is internally consistent, has good test-retest reliability, and predicted group membership for both hemoglobin level and performance status. It is an appropriate measure for use in clinical tri-

Table 5
Mean Functional Assessment of Cancer Therapy (FACT) Total and Subscale Scores by Performance Status Rating (PSR)

FACT scales and subscales (Number of items)	Performance status rating (PSR) PSR = 0 N = 17	PSR = 1 N = 22	PSR = 2,3 N = 10	
FACT-Fatigue (FACT-F) (41)	136.18[a] SD = 21.7	121.79[b] SD = 17.1	97.10[a,b] SD = 16.6	F(2,46)=13.66 $P < 0.000$
FACT-Anemia (FACT-An) (48)	158.29[c] SD = 24.8	141.67[d] SD = 19.0	138.00[c,d] SD = 21.4	F(2,46)=13.81 $P < 0.000$
FACT-General (FACT-G) (28)	94.59[e,f] SD = 13.1	83.64[e,g] SD = 13.3	71.60[f,g] SD = 8.7	F(2,46) = 10.89 $P < 0.000$
Fatigue subscale (13)	41.59[h] SD = 10.5	38.15[i] SD = 5.3	25.50[h,i] SD = 11.6	F(2,46) = 10.97 $P < 0.000$
Non-fatigue items (7)	22.12[j] SD = 4.1	19.88[k] SD = 2.8	15.90[j,k] SD = 5.3	F(2,46) = 8.18 $P < 0.001$

Note: Superscript letters in each row reflect significant post hoc Tukey comparisons at the following significance levels: [a] $P = 0.000$; [b] $P = 0.003$; [c] $P = 0.000$; [d] $P = 0.003$; [e] $P = 0.025$; [f] $P = 0.000$; [g] $P = 0.039$; [h] $P = 0.000$; [i] $P = 0.001$; [j] $P = 0.001$; and [k] $P = 0.025$.

als and in treatment of disease-related and treatment-related fatigue. Both the FACT-An and FACT-F were positively correlated with other measures of fatigue, negatively correlated with measures of vigor, and unrelated to a measure of social desirability.

The 13-item Fatigue subscale has strong psychometric properties and apparent utility independent of the core FACT-G. The Fatigue Subscale demonstrated excellent internal consistency and test-retest reliability over the 3- to 7-day window, and predicted group differences in hemoglobin level and performance status. The non-fatigue items, while less unidimensional than the fatigue items (alpha range, 0.59–0.70), also possessed good test–retest reliability and discriminative ability with respect to hemoglobin level and performance status. The somewhat lower internal consistency of the non-fatigue items is not surprising, given that they cover a broad range of content areas, including headaches, shortness of breath, appetite, chest pain, and interest in sex. Like the FACT-G, FACT-An, and FACT-F, both the Fatigue subscale and non-fatigue items were related in meaningful ways to other measures of fatigue (Piper Fatigue Scale and POMS Fatigue subscale) and vigor (POMS Vigor subscale), and unrelated to social desirability.

The FACT-F and 13-item Fatigue subscale measure a construct conceptually similar to that measured by the Piper Fatigue Scale and the POMS Fatigue and Vigor subscales, but differ from these measures in important ways. First, they are briefer than the other measures, making them easier to administer and score. Second, patients do not necessarily have to experience fatigue to be able to answer all the questions on the FACT-F and Fatigue subscale, as they would in the Piper Fatigue Scale. Finally, the Fatigue and Vigor subscales of the POMS are intended to reflect mood states only, rather than a broader spectrum of symptom experience and the impact of symptoms upon functional well-being. These new subscales address the implications or consequences of fatigue in addition to symptom expression. Importantly, the FACT-F has its greatest utility in delineating both the physical and functional consequences of fatigue, which in turn, have important implications for overall quality of life in cancer. Researchers and clinicians interested only in assessing fatigue as a symptom might choose to use the 13-item Fatigue subscale, whereas those interested in assessing both fatigue and quality of life would use the 41-item FACT-F.

When considering anemia and fatigue together, several factors should be considered in selection of the most appropriate instrument, among them: (a) burden to the patient; (b) literacy level; (c) whether anemia and fatigue is an acute or chronic problem; and (d) sensitivity to change over time.[16] With respect to the first issue, both the FACT-An and the FACT-F are brief instruments, rarely taking more than 10 min to complete. Second, literacy level is important when selecting questionnaires. Consistent with development of the core FACT-G instrument, a sixth grade reading level is sufficient for patients to understand and respond accurately to all items, and can be reliably administered either in an interview or pencil-and-paper format.[21] A third issue raised by Varricchio[16] involves acute versus chronic fatigue states. The etiology of fatigue in cancer is still unknown. Its chronicity varies from person to person, and is related to factors such as hemoglobin level, time elapsed since termination of active treatment, and tumor burden. Similarly, the perception of the impact of fatigue can vary tremendously from person to person. Because fatigue and quality of life are *subjective* states, it may be critical to select an instrument that measures not only fatigue, but fatigue in the context of other dimensions of well-being, such as the physical, functional, social, and emotional well-being. This can best be accomplished with the FACT Measurement System, by measuring symptoms of anemia as well as other more general quality-of-life domains. Finally, measures of fatigue and anemia should not only be stable and reliable, but also sensitive to changes in health status over time. While longitudinal data have not yet been collected to directly address this question, changes in health status as measured by the FACT-G are known to be associated with performance status.[21] Both the FACT-An and FACT-F were found to be sensitive to group differences in performance status. Given the known relationship between performance status and quality of life, it is expected that sensitivity of the FACT Measurement System to changes in health status will be confirmed in longitudinal follow-up. Studies

to test sensitivity to change are currently underway.

The FACT-An and FACT-F are offered as two reliable and valid components to the FACT Measurement System. Because this measurement system uses a component approach, it offers tremendous flexibility in choice of which subscales can be added to best address a specific research or clinical question. For example, a clinical question addressing fatigue in a lung cancer patient or population might utilize the core FACT-G with the lung and fatigue subscales, yielding information about general quality of life (29-item core FACT-G), disease specific concerns (9-item Lung Subscale), and symptom concerns (13-item Fatigue Subscale) for a total of 51 items. Because there are currently 13 disease-specific subscales, 3 treatment subscales, and 13 non-cancer-specific symptom or disease subscales currently within the FACT Measurement System, the clinician or researcher can choose to add various combinations of subscales to the core in order to answer a question. The main constraint is test length and the ability of the patient population to bear the added burden.

In conclusion, the FACT-F and FACT-An perform at a level that exceeds standards of acceptability in terms of reliability and validity of measurement. As such, both are worthwhile measures to consider when assessing quality of life, fatigue, and anemia in cancer patients. Because the 13-item scale alone is psychometrically sound, it should prove useful as an independent, brief assessment of fatigue. Studies with the FACT-F and FACT-An are currently underway to replicate psychometric properties of the measures in larger populations and to assess the impact of growth factors (for example, erythropoetin) on anemia and fatigue states. Future studies are needed to assess the validity of the FACT-F for different cancer treatments, symptoms, and survival. We anticipate that findings from these ongoing studies will lend additional support to the FACT-F, the FACT-An, the Fatigue subscale and non-fatigue anemia-related concerns as useful additions to the FACT Measurement System.

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Appendix

Functional Assessment of Cancer Therapy–Anemia (FACT-An) (Version 3)

Below is a list of statements that other people with your illness have said are important. **By circling one number per line, please indicate how true each statement has been for you *during the past 7 days.***

	Not at all	A little bit	Some-what	Quite a bit	Very much
PHYSICAL WELL-BEING					
1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. Looking at the above 7 questions, how much would you say your PHYSICAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so
SOCIAL/FAMILY WELL-BEING					
9. I feel distant from my friends	0	1	2	3	4
10. I get emotional support from my family	0	1	2	3	4
11. I get support from my friends and neighbors	0	1	2	3	4
12. My family has accepted my illness	0	1	2	3	4
13. Family communication about my illness is poor	0	1	2	3	4
14. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
15. Have you been sexually active during the past year? **Y/N** If yes: I am satisfied with my sex life	0	1	2	3	4
16. Looking at the above 7 questions, how much would you say your SOCIAL/FAMILY WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so
RELATIONSHIP WITH DOCTOR					
17. I have confidence in my doctor(s)	0	1	2	3	4
18. My doctor is available to answer my questions	0	1	2	3	4
19. Looking at the above 2 questions, how much would you say your RELATIONSHIP WITH THE DOCTOR affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so
EMOTIONAL WELL-BEING					
20. I feel sad	0	1	2	3	4

21.	I am proud of how I'm coping with my illness	0		1		2		3		4	
22.	I am losing hope in the fight against my illness	0		1		2		3		4	
23.	I feel nervous	0		1		2		3		4	
24.	I worry about dying	0		1		2		3		4	
25.	I worry that my condition will get worse	0		1		2		3		4	
26.	Looking at the above 6 questions, how much would you say your EMOTIONAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all								Very much so	

		Not at all	A little bit	Some-what	Quite a bit	Very much
	FUNCTIONAL WELL-BEING					
27.	I am able to work (include work in home)	0	1	2	3	4
28.	My work (include work in home) is fulfilling	0	1	2	3	4
29.	I am able to enjoy life	0	1	2	3	4
30.	I have accepted my illness	0	1	2	3	4
31.	I am sleeping well	0	1	2	3	4
32.	I am enjoying the things I usually do for fun	0	1	2	3	4
33.	I am content with the quality of my life right now	0	1	2	3	4
34.	Looking at the above 7 questions, how much would you say your FUNCTIONAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so
	ADDITIONAL CONCERNS					
*35.	I feel fatigued	0	1	2	3	4
*36.	I feel weak all over	0	1	2	3	4
*37.	I feel listless ("washed out")	0	1	2	3	4
*38.	I feel tired	0	1	2	3	4
*39.	I have trouble starting things because I am tired	0	1	2	3	4
*40.	I have trouble finishing things because I am tired	0	1	2	3	4
*41.	I have energy	0	1	2	3	4
42.	I have trouble walking	0	1	2	3	4
*43.	I am able to do my usual activities	0	1	2	3	4
*44.	I need to sleep during the day	0	1	2	3	4
45.	I feel lightheaded (dizzy)	0	1	2	3	4
46.	I get headaches	0	1	2	3	4
47.	I have been short of breath	0	1	2	3	4
48.	I have pain in my chest	0	1	2	3	4
*49.	I am too tired to eat	0	1	2	3	4
50.	I am interested in sex	0	1	2	3	4
51.	I am motivated to do my usual activities	0	1	2	3	4
*52.	I need help doing my usual activities	0	1	2	3	4
*53.	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
*54.	I have to limit my social activity because I am tired	0	1	2	3	4
55.	Looking at the above 20 questions, how much would you say these ADDITIONAL CONCERNS affect your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so

* These items comprise the 13-item fatigue subscale.