

# Fatigue and psychological distress – exploring the relationship in women treated for breast cancer

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## Abstract

Disabling fatigue and psychological symptoms of depression or anxiety are commonly reported by women with treated breast cancer. However, most instruments designed to assess fatigue do not assess concurrent psychological symptoms. This study compared the characteristics of two conceptually different, self-report instruments assessing fatigue to determine the extent to which common psychological symptoms co-exist with the symptom of fatigue in women treated for breast cancer. Women attending an oncology day-care facility for adjuvant treatment of breast cancer or ongoing surveillance post-treatment, completed two self-report questionnaires. The Somatic and Psychological Health REport-34 items (SPHERE) and the Functional Assessment of Cancer Therapy-Fatigue (FACT-F subscale-13 items). One hundred and nine women (mean age 52.8 years) completed both questionnaires and total scores on both fatigue assessment scales, FACT-F and SOMA-6, were highly correlated ( $r = 0.72$ ,  $P < 0.001$ ). Using the SPHERE case criteria, prolonged fatigue (37% [40/109]) and psychological distress 31% (34/109) were common in women treated for breast cancer. However, those who reported fatigue were much more likely to also report psychological symptoms (22/40 vs. 12/69,  $\chi^2 = 16.7$ : degrees of freedom (df) = 1;  $P < 0.001$ ) and the levels of fatigue on the FACT-F were not significantly different between those who reported ‘fatigue only’ and those who reported ‘psychological distress only’ (18.8 vs. 17.8,  $P = 0.79$ ). Thus the recent emphasis on recording fatigue during and following treatments for cancer needs to be accompanied by concurrent measurement of psychological symptoms.

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**Keywords:** Depression; Fatigue; Breast cancer; Psychological distress

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## 1. Introduction

Earlier diagnosis and improved treatments have led to a reduction in mortality for women with breast cancer [1,2]. However, with larger numbers of women surviving, previously unrecognised chronic morbidity has

emerged. Persistent fatigue is now reported as one of the most common, disabling and chronic symptoms following successful treatment [3–7].

Although cancer-related fatigue is now proposed for inclusion in the International Classification of Diseases 10th Revision-Clinical Modification (ICD-10 CM) [8], there remain significant problems with the current criteria [9]. Importantly, the notion of ‘fatigue’ is variably interpreted by both patients and doctors. In addition to uncertainties in the definition of the central symptom, debate has also ensued as to the relative merits of the ‘symptom’ versus ‘syndrome’ approach in the evaluation of cancer-related fatigue [6,10–12]. Findings of a

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**Abbreviations:** SPHERE = Somatic and Psychological Health REport; FACT-F = Functional Assessment of Cancer Therapy-Fatigue; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

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consistent co-occurrence of symptoms occurring in association with specifically characterised fatigue would support the construct of cancer-related fatigue syndrome. In this context, it is important to note that the ICD-10 CM definition of cancer-related fatigue includes “decreased motivation or interest in engaging in usual daily activities” in the symptom criteria (which is distinctly reminiscent of anhedonia) as well as several items potentially overlapping with other Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for depression, including sleep and neuro-cognitive disturbances.

As the aetiology of prolonged fatigue following treatment for breast cancer remains unresolved, there is a strong case for measuring broader clusters of relevant somatic symptoms (sleep–wake cycle disturbance, neuro-cognitive complaints, mood and musculoskeletal pain), rather than simply the individual symptom of fatigue. The 2002 National Institutes of Health (NIH) Conference on Symptom Management in Cancer [13], noted that ‘*Research is needed to validate approaches for screening and assessing cancer patients for fatigue in clinical practice*’.

A further issue in need of exploration is whether the fatigue experienced by patients with cancer is qualitatively or quantitatively different from the common forms of fatigue reported in the wider community. Fatigue is commonly the presenting symptom of psychological disorders, such as depression and anxiety [14–16]. Several large studies have assessed the incidence of depression in patients with breast cancer. While up to 47% of patients experience depression post-treatment [17–20], the presence of a physical disorder such as breast cancer and the adverse effects of adjuvant therapy (including anaemia) make psychiatric diagnoses particularly difficult [17,21]. If mood disturbances and fatigue commonly co-occur then the issue of ensuring reliable measurement of this comorbidity is critical for a etiological and treatment research.

To date, the studies investigating cancer-related fatigue have used a variety of assessment tools, and evaluated patients at varied times after treatment, making comparisons across studies difficult [11]. Fatigue assessment is also commonly incorporated into quality-of-life instruments used in the evaluation of clinical oncology treatment trials, usually as a small number of items (e.g. 1–3) in a battery of questions [22–24].

Therefore, the aims of the present study were, two-fold:

- (a) to compare the characteristics of two validated, but conceptually different, self-report instruments for the assessment of fatigue;
- (b) to determine the extent to which common psychological symptoms (indicative of depression and anxiety) co-exist with the symptom of fatigue in women treated for breast cancer.

Table 1

Clinical characteristics of patients ( $n = 109$ )

Median age (years)	52 (range 36–77)
Median time post-treatment (months)	4 (range 0–45)
<i>Surgical treatment</i>	
Mastectomy	55%
Lumpectomy	45%
Adjuvant treatment in progress	11%
<i>Adjuvant treatment</i>	
Chemotherapy	40%
Radiotherapy	10%
Combined chemotherapy and radiotherapy	39%

## 2. Patients and methods

Women following surgical treatment for breast cancer who were either currently receiving adjuvant treatment, or who had completed such treatment, were invited to complete two self-report questionnaires (Table 1). The women were recruited from consecutive attendances at the Medical Oncology Centre at the Prince of Wales Hospital, Sydney, Australia. Since the main aim of this cross-sectional study was to investigate the utility of two conceptually different questionnaires, no attempt was made to stratify women according to treatment stage or type. All women were diagnosed with stages I or II (TNM stages: T0 – 3N1M0 to T2–3N0M0) breast cancer [25]. The sample excluded women who were unable to read English, or those with concurrent major medical (e.g., severe cardiac, renal or endocrine disorders) illnesses identified by the clinician. There was no attempt to identify and exclude those with psychological disorders. No patient refused participation. The institutional ethics committee approved the study.

## 3. Questionnaires

### 3.1. The women completed two self-report instruments:

#### 1. The fatigue scale FACT-F (Functional Assessment of Cancer Therapy-Fatigue sub-scale) [26,27].

This validated 13-item scale which assesses fatigue, was specifically developed for use with cancer patients. It is now frequently used in clinical oncology medication trials. Items for inclusion in the scale were originally identified from semi-structured interviews with a small sample ( $n = 14$ ) of oncology patients and oncology experts ( $n = 5$ ) [26]. Responses to the items are on a 5-point scale (Table 3), ranging from ‘0’ (*not at all*) to ‘4’ (*very much*). Scores on items are unweighted and summed to give a single total score. In this study, items were scored so that a higher total score indicated more severe fatigue. (The questionnaire also includes two items,

which were reversed scored for consistency, ‘*I have energy*’ and ‘*I am able to do my usual activities*’). The maximum total score possible with this method is 52.

## 2. The 34-item Somatic and Psychological Health Report (SPHERE) [28,29].

This more general instrument assesses a wide range of somatic and psychological symptoms that are common in medical and psychiatric settings. Two six-item subscales are used [29] to identify cases of prolonged fatigue (‘SOMA-6’) or other common forms of psychological distress (i.e., depression and anxiety) (‘PSYCH-6’). The SOMA-6 subscale is a refinement of an original fatigue-screening tool (SOFA – Schedule of Fatigue and Anergia) developed using quality receiver operating characteristics [30]. The reliability and construct validity of the instrument in the identification of persisting fatigue syndromes have been well demonstrated in both cross-sectional [31,32] and longitudinal studies, as well as in twin studies [33,34]. Taken together, results of these studies support the argument that prolonged fatigue states can be measured independently of anxiety and depression. The second subscale, PSYCH-6 uses items that were derived from the 30-item General Health Questionnaire (GHQ-30) [35] and has been validated against Diagnostic and Statistical Manual Third Edition – Revised (DSM-III-R) and DSM-IV diagnoses of psychiatric disorder [29].

For each item on the questionnaire, the respondent is given a choice of three responses: ‘*some of the time or never*’, ‘*a good part of the time*’ or ‘*most of the time*’. These items are coded 0, 1, 2, giving a maximum total score of 12 on each subscale. Empirically derived ‘cut-off’ scores for both subscales permit categorical classification of patients into those with ‘fatigue’ only, those with ‘psychological distress’ only, or those in whom both symptom clusters predominate (score  $\geq 3$  for ‘SOMA-6’; score  $\geq 2$  for ‘PSYCH-6’). This classification system predicts disability ratings, rates of lifetime psychiatric diagnoses, as well as both patients’ and doctors’ report of reasons for presentation [29].

## 4. Statistical analyses

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows [36]. Demographic and clinical data was summarised using descriptive statistics. All scales were scored as described above. The algorithm [29] was applied to SPHERE sub-scale scores to identify diagnostic categories (‘fatigue’ or ‘psychological distress’). Relationships between the SPHERE classifications (‘fatigue only’ vs. ‘psychological distress only’ vs. ‘psychological distress and fatigue’ were explored using (Chi-square)  $\chi^2$  statistics.

Calculation of Cronbach’s alpha co-efficient was used to assess the reliability of the scales (FACT-F; SPHERE SOMA-6 subscale; SPHERE PSYCH-6 subscale).

Construct validity was examined by comparing total raw scores for each scale and sub-scale. Mean FACT-F scores for each SPHERE diagnostic category were examined using  $\chi^2$  statistics to compare groups.

Individual item scores were inter-correlated to identify relationships between the items.

## 5. Results

### 5.1. Patients

Questionnaires were completed by 109 women, median age 52 years (mean age 52.8 years range 36–77 years), during a routine clinic visit. The average time taken to complete both questionnaires was 10 min. All women had prior surgical treatment for early stage (non-metastatic) breast cancer, 55% of women had received mastectomy while 45% had undergone regional excision only. Most of the women had completed adjuvant treatment with chemotherapy and/or radiation 12.3 ( $\pm 14.6$ ) months previously (Table 1), with the remainder (11%) yet to complete adjuvant treatment. (No attempt was made to stratify women according to their treatment stage or type and details of the endocrine treatment given were not obtained at this time).

### 5.2. Diagnostic categories (as derived from responses on the SPHERE questionnaire)

Of the total sample of women, 37% ( $n = 40$ ) were categorised as ‘fatigue’ cases (SOMA-6), while 31% ( $n = 34$ ) gave responses indicative of significant ‘psychological distress’ (PSYCH-6) (Table 2). Overall, 20% ( $n = 22$ ) were designated cases with both ‘fatigue’ and ‘psychological distress’ (SOMA-6 and PSYCH-6), while 17% ( $n = 18$ ) were fatigued with no concurrent psychological distress. Eleven percent of women ( $n = 12$ ) reported psychological distress without fatigue symptoms. The remainder of the group ( $n = 57$ ; 52%) did not report significant levels of either symptom set. Overall those who reported fatigue were much more likely to also report psychological symptoms (22/40 vs 12/69,  $\chi^2 = 16.7$ ;  $df = 1$ ;  $P < 0.001$ ).

$\chi^2$  statistics were used to assess the relationships between the SPHERE classifications of ‘PSYCH-6 & SOMA-6’, ‘PSYCH-6 only’ and ‘SOMA-6 only’. There were weaker (non-significant) relationships between ‘PSYCH-6 only’ and ‘PSYCH-6 & SOMA-6’ ( $\chi^2 = 3.41$ ,  $P > 0.05$ ) and ‘SOMA-6 only’ ( $\chi^2 = 2.67$ ,  $P > 0.10$ ) than between the two subscales measuring fatigue, ‘PSYCH-6 & SOMA-6’ and ‘SOMA-6 only’ ( $\chi^2 = 5.45$ ,  $P < 0.05$ ),

Table 2

Comparison of total FACT-F scores by SPHERE categories ( $n = 109$ )

Category (by SPHERE)	Number of patients (%)	Age (years)	Mean FACT-F score (range 0–52)	Mean <sup>a</sup> PSYCH-6 score (0–12)	Mean <sup>b</sup> SOMA-6 score (0–12)
No significant symptoms	57 (52)	52 (SD 9)	10.2 (CI 8.2–12.2)	0.15 (CI 0–0.25)	0.7 (CI 0.4–0.9)
Fatigue only (SOMA-6)	18 (17)	52 (SD 10)	18.8 (CI 13.6–24.0)	0.39 (CI 0.13–0.63)	4.8 (CI 4.0–5.6)
Psychological distress only (PSYCH-6)	12 (11)	51 (SD 7)	17.8 (CI 10.4–25.0)	3.8 (CI 2.7–4.8)	1.4 (CI 1.0–1.8)
Both fatigue and psychological distress (SOMA-6 + PSYCH-6)	22 (20)	57 (SD 10)	30.8 (CI 25.9–35.7)	7.0 (CI 5.9–8.0)	6.2 (CI 5.0–7.3)

SD, standard deviation.

CI, 95% Confidence Interval for mean score.

<sup>a</sup> PSYCH-6 Psychological symptoms subscale.<sup>b</sup> SOMA-6 Fatigue subscale.

providing support for the notion that ‘PSYCH-6 and ‘SOMA-6 subscales assess two different domains.

### 5.3. Comparison of questionnaires

Good internal consistency was demonstrated for both scales. Cronbach’s alpha coefficients were 0.94 for FACT-F and 0.82 for the fatigue (SOMA-6) subscale of the SPHERE, respectively. Total raw scores on both ‘fatigue’ questionnaires were significantly correlated ( $r = 0.72$ ,  $P < 0.001$ ). The mean FACT-F score was then calculated for each of the categories derived from the responses on the SPHERE subscales (SOMA-6 and PSYCH-6)

There was a significant difference ( $P < 0.001$ ) between the mean FACT-F scores for ‘non-cases’ on the fatigue subscale of the SPHERE (11.6; Standard deviation (SD) 9.4) in comparison to ‘fatigue’ cases (25.5; SD 12.2), demonstrating that both questionnaires distinguished between those women with minimal, and those with higher levels, of fatigue. The mean FACT-F score for women categorised as ‘fatigue only’ on the SPHERE (i.e., non-cases on the PSYCH-6 subscale) was 18.8 (SD 10.4). However, importantly there was no significant difference ( $P = 0.79$ ) in the mean FACT-F scores for those women categorised as cases of ‘psychological distress’ only (17.8; SD 11.5) using the PSYCH-6 score (Table 2) and those categorised as ‘fatigued’ only (i.e., with no significant psychological symptoms) (18.8; SD 10.4). Patients classified as cases of both ‘fatigue’ and ‘psychological distress’ had the highest mean FACT-F scores (30.9; SD 11.0).

### 5.4. Responses to individual items

The strongest correlation ( $P < 0.0001$ ) between individual items on the two questionnaires, was for the SPHERE item ‘prolonged tiredness after activity’, and FACT-F items ‘feel fatigued’ (0.649); ‘feel weak all over’ (0.658), ‘feel listless’ (0.671), ‘feel tired’ (0.643). Table 3 summarises the prevalence of responses to the individual items on both the SPHERE (fatigue and psychological subscales) and FACT-F questionnaires for the whole

sample ( $n = 109$ ). The most frequently scored items were those related to tiredness, while the most common and highly scored item on the psychological scale (PSYCH-6) was ‘feeling nervous or tense’. Overall, the range of responses scoring highly (i.e., ‘quite a bit/very much’) on the FACT-F ranged from 3.6% to 33.4%. The responses ranged from 22.0% to 48.6% for fatigue items scored similarly (‘a good part of time/most of time’) on the SOMA-6 subscale of the SPHERE. Items indicative of psychological distress on the SPHERE were affirmed by 18.4–29.3% of the women.

## 6. Discussion

Screening questionnaires [8] provide useful information in the clinical setting and have the potential to serve as an important guide for the management of fatigue in patients with cancer. This study was undertaken with the specific aim of examining the relative advantages of undertaking such assessment with two instruments, one a frequently used cancer-specific fatigue scale (FACT-F) and the other a generic tool (SPHERE) measuring both ‘fatigue’ and ‘psychological distress’. There was considerable concordance between total scores on each fatigue instrument (FACT-F and SOMA-6) with higher scores on each being indicative of greater fatigue.

Importantly, the results using the empirically derived SPHERE categorical diagnostic system [29] demonstrated that concurrent psychological symptoms are common in women who report fatigue and that greater fatigue is reported in women with concurrent psychological symptoms. Of key interest in this study, mean FACT-F total scores for the group of women categorised by the SPHERE as ‘fatigue only’ compared with the group identified as ‘psychological distress only’ were almost identical (18.8 and 17.8, respectively;  $P = 0.79$ ). Clearly, if psychological symptoms are not actively sought, clinicians may well begin a fruitless search for another medical explanation of these disabling symptoms of fatigue. The importance of identifying and treating affective disorders in women with breast cancer has been highlighted in recently published Danish

Table 3  
Prevalence of responses to individual items on the FACT-F and SPHERE questionnaires ( $n = 109$ )

FACT-F-(13 ITEMS) (coded – 0,1,2,3,4)	Mean score <sup>a</sup>	% Affirmed (scored 3 or 4) <sup>b</sup>	SPHERE SOMA-6 (fatigue) (coded – 0,1,2)	Mean score <sup>a</sup>	% Affirmed (scored 1 or 2) <sup>b</sup>	SPHERE-PSYCH-6 (Psychological distress) (coded – 0,1,2)	Mean score <sup>a</sup>	% Affirmed (scored 1 or 2) <sup>b</sup>
I feel tired	1.80	33.4	Prolonged tiredness after activity	0.53	48.6	Feeling nervous or tense	0.39	29.3
I have [no] energy	1.90	31.2	Needing to sleep longer	0.61	47.7	Feeling unhappy or depressed	0.33	25.7
I feel fatigued	1.75	30.2	Poor sleep	0.55	42.2	Everything getting on top of you	0.31	25.7
I am [not] able to do usual activities	1.52	24.8	Tired muscles after activity	0.43	34.0	Feeling constantly under strain	0.28	23.9
I feel listless	1.31	22.9	Poor concentration	0.29	22.9	Losing confidence	0.30	22.9
I have trouble starting things because I am tired	1.24	21.1	Muscle pain after activity	0.32	22.0	Being unable to overcome difficulties	0.22	18.4
I have trouble finishing things because I'm tired	1.28	20.2						
I have to limit my social activity because I am tired	1.23	20.2						
I need to sleep during the day	1.16	20.2						
I feel weak all over	1.05	18.4						
I am frustrated by being too tired to do the things I want to do	1.10	17.5						
I need help to do my usual activities	0.92	12.0						
I am too tired to eat	0.43	3.6						

<sup>a</sup> Mean score for individual item.

<sup>b</sup> Percent of women who endorse item as 'quite a bit' or 'very much' (FACT-F) or 'a good part of the time' or 'most of the time' (SPHERE).

studies which found that breast cancer patients with depression had a significantly higher risk of mortality (even after excluding unnatural causes of death such as accident and suicide) [37,38].

The FACT-F item-‘too tired to eat’ was infrequently endorsed by the women (3.6%). This item may not characterise the syndrome of fatigue in this population (i.e., those having had likely curative treatment), but may be of more importance in patients with advanced disease. Several FACT-F items (e.g., ‘have to limit my social activity’, ‘need help to do usual activities’) record the functional consequences of the fatigue state whereas comparable items are not included in the SPHERE. However, the various categories of disorder identified by the SPHERE have been linked with clear levels of disability in other studies. For example, cases of both fatigue and psychological disorder report 8.2 “days out of role in the last month” [29].

The SPHERE questionnaire provides distinct advantages in screening for fatigue and associated phenomena in cancer patients. This single instrument concurrently measures both fatigue and psychological distress, and the scoring system permits differentiation of both symptom states. It provides comparative data with a large Australian sample ( $n = 46000$ ) of general-practice patients [29], several international samples, other medical illnesses [39] and twin studies [33,34], where fatigue states have been described independent of conventional notions of anxiety and depression. As well as allowing for measurement of changes over time (comparison of total ‘raw’ scores), the empirically-derived case thresholds [29] permit prospective identification of patients in need of intervention, notably those with psychological distress.

Disabling fatigue is an important problem for women following treatment for breast cancer. In order to extract maximum benefit, fatigue assessments should use screening tools that incorporate measures of psychological distress, with the aim of identification of patients with fatigue needing further psychological evaluation. Additionally, instruments that are rapidly completed and easily scored provide an added advantage. Fatigue commonly co-occurs with psychological distress and may require a range of behavioural, psychological and/or pharmacological intervention strategies.

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