



Journal of Health and Medical Sciences

Thomas, Marie, and Smith, Andrew P. (2019), Measurements of Recovery and Predictors of Outcome in an Untreated Chronic Fatigue Syndrome Sample. In: *Journal of Health and Medical Sciences*, Vol.2, No.2, 167-178.

ISSN 2622-7258

DOI: 10.31014/aor.1994.02.02.33

The online version of this article can be found at:
<https://www.asianinstituteofresearch.org/>

Published by:
The Asian Institute of Research

The *Journal of Health and Medical Sciences* is an Open Access publication. It may be read, copied and distributed free of charge according to the conditions of the Creative Commons Attribution 4.0 International license.

The Asian Institute of Research *Journal of Health and Medical Sciences* is a peer-reviewed International Journal. The journal covers scholarly articles in the fields of Medicine and Public Health, including medicine, surgery, ophthalmology, gynecology and obstetrics, psychiatry, anesthesia, pediatrics, orthopedics, microbiology, pathology and laboratory medicine, medical education, research methodology, forensic medicine, medical ethics, community medicine, public health, community health, behavioral health, health policy, health service, health education, health economics, medical ethics, health protection, environmental health, and equity in health. As the journal is Open Access, it ensures high visibility and the increase of citations for all research articles published. The *Journal of Health and Medical Sciences* aims to facilitate scholarly work on recent theoretical and practical aspects of Health and Medical Sciences.



ASIAN INSTITUTE OF RESEARCH
Connecting Scholars Worldwide



Measurements of Recovery and Predictors of Outcome in an Untreated Chronic Fatigue Syndrome Sample

Marie Thomas¹, Andrew P. Smith²

¹ Reader in Psychology, College of Liberal Arts, Newton Park Campus, Bath Spa University

² Professor of Psychology, School of Psychology, Cardiff University, 63 Park Place, Cardiff, Cf10 3AS, UK

Abstract

The current study examined a large cohort of untreated Chronic Fatigue Syndrome patients at initial assessment and at specific time points over a three-year period. Methods used in previous studies to assess patient health, were validated and used to assess recovery and improvement. Possible predictors of outcome would then be identified by assessing improvements in health status at specific follow-up points. The illness was also assessed in terms of recovery and improvement by using health related and psychosocial measures together with the aetiology of the illness. These were further used to investigate possible mechanisms influencing or predicting recovery or improvement. Two-hundred and twenty-six patients completed wide ranging questionnaires at initial assessment and again six and eighteen months and three years later. A current state of health score was used to measure recovery over time and analyses conducted to investigate the relationship between this and other health related measures. Regression analyses were conducted to assess predictors of improvement and recovery. Spontaneous recovery rates in the untreated patient at three-year follow-up were low (6%). The data suggested, however, that illness length, symptom severity and health status have an important role in recovery. Although there was no evidence to suggest an association between illness onset type and subsequent recovery or psychopathology scores at initial assessment and recovery, regression analyses did indicate that levels of anxiety, cognitive difficulties and social support at initial assessment predict a positive outcome. The state of health measure was validated as a method of accurately assessed the health status of patients and was used as an indicator of improvement and recovery within this group. Spontaneous recovery in the patient group was associated with several factors measured at initial assessment. However, further studies are necessary to more fully identify the factors which affect recovery or improvement and to investigate the exact nature of the mechanisms involved. The present study shows that spontaneous recovery of CFS patients is rare. Treatment or management is essential, and the efficacy of different approaches must be assessed.

Keywords: Chronic Fatigue Syndrome, Improvement, Predictors of outcome, Recovery

1. Introduction

The fatigue experienced in Chronic Fatigue Syndrome (CFS) is not only of sufficient severity to cause substantial functional impairment but is accompanied by four or more co-existing symptoms including those of a cognitive or neuropsychiatric nature (Centre for Disease Control (CDC) criteria; Fukuda et al., 1994). The illness (by definition) must be of at least six months duration and can become very debilitating and persistent (Andersen, Permin & Albrecht, 2004).

In order to provide insight into the prevalence of CFS, Afari and Buchwald conducted an in-depth appraisal of the literature (Afari & Buchwald, 2003). Evidence from epidemiological studies suggested that, in large scale surveys, up to half the general population would report suffering fatigue-like symptoms (Chen, 1986; Pawlikowska et al., 1994) and 20% of this group would subsequently seek medical care (Bates et al., 1993; Cathebras, Robbins, Kirmayer & Hayton, 1992; David et al., 1990; Kroenke et al., 1988; McDonald, David, Pelosi & Mann, 1993). However, in the majority of these cases, the fatigue experienced could be explained by other mitigating circumstances. Therefore, the incidence of CFS in the general population, the review concluded, is relatively low. Similarly, Price et al. (1992) reported findings from a community-based survey suggesting that 7.4 per 100,000 of the population (0.0074%) fulfilled the CDC criteria for CFS. More recently, Ranjith's review of the literature also agreed that, although the symptom of fatigue is common, cases of medically unexplained fatigue that fulfil the CDC criteria are somewhat rare (Ranjith, 2005). The relatively low incidence of CFS should not, however, detract from the severe effect the illness has on the individual sufferer's quality of life. Decreased personal, occupational and social activities combine to instil a sense of frustration and hopelessness within the patient. In addition, financial concerns have been raised regarding the increased uptake of unemployment benefits and the drain on healthcare resources caused by the illness. Data collected as part of the CDC's surveillance study (Reyes et al., 1999) estimated that the cost in terms of lost productivity, per annum, for each CFS patient in the United States was \$20,000. In the light of this, continued research into the causes of and potential therapies for CFS are vital to alleviate this financial burden (Reynolds, Vernon, Bouchery & Reeves, 2004).

Before coherent treatment protocols were in place, research mainly concentrated on investigations into the long-term prognosis of CFS. These longitudinal studies also attempted to calculate recovery rates and identify possible predictors of positive outcome. However, when reviewing the literature, it became apparent that several different criteria had been used to define recovery in the patient group. For example, a patient in recovery (or remission) was described in one study as; (a) no longer suffering from fatigue, (b) experiencing less than four CFS related symptoms and, (c) a person whose health no longer interfered with normal activities (Reyes et al., 1999). When these criteria were applied, spontaneous recovery was calculated at 31.4% during the first five years of the illness (Reyes et al., 1999). Similarly, an assessment of 98 consecutive referrals to a specialised CFS clinic produced data suggesting that 41% of the sample were moderately to completely recovered two to three years post-baseline. Furthermore, 2.6% of these patients rated themselves as 'fully recovered' and 29.5% had returned to work (Russo et al., 1998). The issue of CFS and recovery was raised in a discussion by Cairns and Hotopf (2005) which highlighted inconsistencies in the literature. The review concluded that although improvement in patients at follow-up ranged from 8 to 63%, full recovery from the illness was actually quite rare.

CFS patients themselves are well aware that short periods of remission are common and can occur at any time during the illness. However, several studies have indicated that bouts of recovery are more likely in patients with short illness duration (Reyes et al., 1999; Nisenbaum, Jones, Jones & Reeves, 2000). Furthermore, there is evidence to suggest that several other factors may also influence recovery, including younger age (at onset), fewer physical symptoms, higher mental and general health scores and low levels of emotional distress at baseline (Russo et al., 1998). In addition, low levels of fatigue (at baseline), a sense of control over the symptoms associated with the illness and, the attribution of non-physical cause have also been linked with more favourable outcomes (Cairns & Hotopf, 2005).

Overall, when reviewing previous studies assessing recovery within this patient group it appeared that there were several crucial points that needed to be addressed. Firstly, the method used to define recovery should be as clear cut as possible. Each patient's perception of recovery will differ, that is, one patient's idea of recovery may not correspond to that of another. It might be more appropriate in illnesses such as CFS, therefore, to measure improvements within an individual sufferer's health rather than using a 'one size fits all' approach. This, in turn, would affect the choice of parameter(s) used to measure it. In the particular case of CFS these problems are further confounded by reports from sufferers of periods of remission throughout the illness. Ideally, therefore, several independent measures should be used to assess the validity of the recovery measure. In addition, the evaluation process must be capable of differentiating between true recovery and bouts of remission. The final point to consider is intervention. Longitudinal studies are, by definition, conducted over several years.

Although the studies reviewed were not part of any specific treatment protocols, it can not be assumed that the patients questioned did not attend some form of therapy during the intervening time period. Therefore, these data might not represent the true nature of the illness and this may be being reflected in high recovery rates.

Previous research had already highlighted several aspects of the disorder, such as psychopathology, ratings of well-being, psychosocial and demographic factors, which may affect outcome (Smith, Behan, Bell, Millar & Bakheit, 1993). CFS patients had been studied using a wide range of questionnaires and these data had indicated that there were possible confounding variables that affect the severity of CFS including psychosocial factors, support mechanisms, health measures and psychopathology (Smith, Pollock, Thomas, Llewelyn & Borysiewicz, 1996; Smith, Borysiewicz, Pollock, Thomas & Llewelyn, 1999). The severity of the illness was assessed by means of physical symptoms (Cohen & Hoberman, 1983; Smith et al., 1996), fatigue related symptoms (Ray, Weir, Stewart, Millar & Hyde, 1993), cognitive failures (Broadbent, Cooper, Fitzgerald & Parkes, 1982) and a 5-item health status measure (Smith et al., 1996). Psychosocial aspects of the disorder such as stress (Cohen, Kamarack & Mermelstein, 1983), social support (Henderson, Bryne & Duncan-Jones, 1981), self-esteem (Fleming & Watts, 1980) and the impact of inter-current life events (Cohen & Hoberman, 1983) were also assessed using several measuring instruments. Furthermore, measures of psychopathology (Beck, Ward, Mendelson, Mock & Erbaugh, 1961; Radloff, 1997; Spielberger, Gorsuch & Lushene, 1971), health related behaviours and illness history (Smith et al., 1996) were included in the study in an attempt to provide a more comprehensive picture of this complicated and debilitating illness.

With these measuring instruments in place, the aim of the current study was, in the first instance, to describe the characteristics of a large cohort of CFS sufferers at initial assessment and validate a measure for accurately measuring the health status of the individual patient. When validated, this measure was used to define and assess recovery and investigate possible predictors of outcome by comparing the health and psychosocial measures (at initial assessment) of patients who recovered over a three-year period to those who did not recover. These data also allowed us to monitor the natural progression of the untreated illness over time.

2. Method

2.1 Design

The study was longitudinal in nature, with assessments occurring at initial assessment (baseline), six and eighteen months and three years later.

2.2 Participants

Ethical approval for the study was granted by the relevant local Health Authority. Potential volunteers were informed that the research was being conducted as part of a long-term project investigating CFS and, that they would be asked to complete similar test batteries over a period of time as part of a research panel. Participation in the study was voluntary and all participants gave written, informed consent. Patient data were coded to ensure anonymity.

The research panel comprised consecutive GP referrals over a 7 year period to a specialised CFS outpatient clinic meeting the CDC criteria for Chronic Fatigue Syndrome. Patient volunteers were assessed at initial clinic visit (baseline), at six and eighteen months and again three years later. As there was no formal treatment available to these patients at that time, the data represents the untreated illness. However, a small number of participants were taking antidepressant therapy at baseline. Data from these patients were not included in the final analyses.

2.3 Materials and Method

The CFS volunteers completed wide ranging questionnaires developed to measure global ratings of well-being, sleep and psychopathology and established indicators of quality of life (Smith et al., 1996; Smith et al., 1999). Demographic data relating to the sample were collected, along with an illness history questionnaire and a 28-item symptom check-list. The resulting data were then used to examine associations between these measures and recovery or improvement.

2.3.1 Measurement of Recovery

Health status and severity were measured by a 'current state of health measure' (Smith et al., 1996). This 5-item scale categorised the patient's health as follows: (1) worse than at any stage of the illness; (2) bad; (3) bad with some recovery; (4) recovering with occasional relapses and (5) almost completely recovered. In order to test the validity of this measure to accurately describe health status at any given time, patients were categorised into two groups at baseline: those who were in poor health (scoring 'worse than any stage', 'bad' and 'bad with some recovery') and those who thought they were recovering (scoring 'recovering with occasional relapse' and 'almost completely recovered'). These baseline data were then compared to measures known to be associated with the illness, including: (a) positive and negative mood (Zevon & Tellegen, 1982); (b) depression (Beck et al., 1961; Radloff, 1997); (c) anxiety (Spielberger et al., 1971); (d) fatigue related symptoms (Ray et al., 1993); (e) physical symptoms (Cohen & Hoberman, 1983; Smith et al., 1996); (f) cognitive failures (Broadbent et al., 1982) and, (g) stress (Cohen et al., 1983).

Once validated, if measurable recovery was indicated at follow-up, we would then be able to identify factors at baseline that appear to be linked with recovery and, therefore, predict recovery later on. Improvement was also measured with the 5-item current state of health score by examining differences between the follow-up and baseline scores.

Recovery and improvement were then used as outcome measures. By comparing these data to other health related outcomes known to be associated with exacerbating and prolonging the illness we investigated possible predictors of outcome.

2.4 Procedures

The various measuring instruments were administered in the form of two questionnaire booklets. The first booklet concentrated on measures of a general nature, such as demographic and illness history data (Smith et al., 1996), cognitive failures, perceived stress and social support which could be completed by the patients at home in their own time. The second booklet required responses to subjective measures such as, anxiety, depression and fatigue related symptoms, which referred to the previous week.

Patients also responded verbally to a range of questions relating to illness beliefs, including type of onset (acute or gradual) and events which were thought to have preceded the illness. These data were recorded by research registrars at initial clinic visit.

2.5 Data Analysis

Continuous data were run through analysis of variance and categorical data from the study were run through Chi-Squared cross-tabulation analyses to describe the nature of the sample at initial assessment (baseline). Two-way contingency table analyses (Chi-Square) were carried out to investigate the relationship between: (a) the current state of health variable and other health measures and (b) the current state of health variable and psychosocial factors. Recovery and improvement were used as grouping variables in independent sample t-test analyses. Logistic regression analyses were conducted to assess predictors of improvement and/or recovery using the health and psychosocial measures. A further model was created which complied with findings discussed by Cairns and Hotopf (2005). That is to say, age, illness length, illness onset type, physical cause, total symptoms, fatigue, health status and emotional distress have all been previously indicated as predictors of outcome.

3. Results

In all, 307 CFS patients were recruited to the research panel. Patients taking antidepressant medication at baseline and for those whom antidepressant medication status was unknown (n=81) were excluded from the final analyses. 130 patients completed the baseline, six and eighteen months and three years later.

3.1 Patient Sample and Illness Characteristics

Table 1 describes the basic demographic data for the 226 patients at baseline which follows the profile one would expect in CFS. The majority of the patients fell into the 'bad with some recovery' category of the current

state of health variable (43%) and the mean total symptom score (calculated from the 28-item check list) was 15.84 (s.e.m=0.36). The mean illness length was approximately 5 years.

Table 1: Baseline Demographic and Illness History data for the original cohort of CFS patients and the final cohort who completed the study.

Baseline Measures		Original Cohort (n=226)	Final Cohort (n=130)
Gender:	Male	31%	34%
	Female	69%	66%
Mean Age:		41.7 (0.80)	45.05 (1.15)
Marital Status:	Single	21%	10%
	Married	65%	75%
	Divorced/ Separated	10%	9%
	Widowed	3%	5%
Educational Status:	No Formal Schooling	0	0
	Primary Education only	0	0
	Secondary Education	29%	30%
	O Levels	33%	31%
	A Levels	9%	9%
	At least 1yr at University	7%	8%
	BSc or BA	16%	17%
	MSc or MA	2%	2%
	PhD, MD, etc	3%	2%
Illness Duration (months):		62.13 (3.84)	65.49 (5.83)
Current State of Health:	Worse than at any stage	8%	6%
	Bad	20%	15%
	Bad with some recovery	43%	43%
	Recovering with relapses	38%	36%
	Almost completely recovered	0.9%	0
Total Symptom Score (maximum = 28):		15.84 (0.36)	16.32 (0.59)

In addition, the majority of patients (68%) had their condition diagnosed by their GP and 34% of the sample was in employment at the time of initial assessment. 49% were unemployed and 16% were on sick leave. These groups represented 76% of the total sample (the rest of the sample being either retired or home-makers). Of the patients who were working, 21% believed that their job security was threatened by the illness. Respondents who reported trying alternative therapies to alleviate their symptoms spent on average £235 doing so. Less than half of these patients believed that they had received value for money by taking the alternative therapy route.

3.2 Health Measures

Re-examining the sample in terms of type of illness onset (that is, acute or gradual onset) provided no significant differences with regard the demographic nature, illness history or total symptom scores of the sample.

The majority of patients (84%) believed that a specific event had proceeded, and therefore, may be attributed to their illness. The majority of these (42%) suggested that influenza was the causal agent. We found no evidence to suggest that there might be a link between type of onset (acute or gradual) and the patient's belief that a virus had caused the illness. Table 2 goes on to describe the 28-item symptom check-list for the group at baseline in detail.

Table 2: The Symptom Checklist Scores for the patient group at baseline. Scores are ranked most to least prevalent.

Symptom	%	Symptom	%
Lack of concentration	91	Sensitivity to light	53
Muscle pain (back, arms or legs)	89	Sore throat	52
Excessive fatigue	87	Wind	49
Physical weakness	81	Insomnia	47
		Nausea	46

Legs feeling heavy	80	Shivering	45
Fever	77	Glands swollen	45
Loss of memory	76	Racing heart	44
Headache	70	Chest pain	44
Aching joints	69	Indigestion	41
Sensitivity to noise	59	Panic attacks	40
Bloated stomach	55	Depression	37
Sweating	54	Allergies	35
Sore eyes	53	Earache	33

These data indicate that muscle pain, lack of concentration and excessive fatigue were the highest rated symptoms in the patient group.

3.3 Comparability of the Follow-up Sample

Chi-squared cross-tabulation and analysis of variance were used to compare the baseline demographic and illness history data from members of the original CFS cohort assessed at baseline (n=226) to those completing all follow-up sessions (n=130). Table 1 indicates that the original cohort assessed at baseline have comparable data at baseline, in terms of gender, age, marital and educational status to those completing all assessment session. In addition, there were no significant differences between the two samples in respect to length of illness, health status and total symptom scores at initial assessment (baseline).

3.4 Validation of the Health Status Measure

The following table presents data in relation to the patient's current state of health at baseline. Patients in the 'recovering' group had fewer symptoms at baseline than those in the 'not recovering' group. Table 3 indicates further associations between the current state of health measure and physical and mental health variables.

Table 3: The relationship between Current State of Health at baseline and Health Outcomes. 'Recovering with occasional relapses' and 'Almost completely recovered' represent the 'Recovering' group, the remaining values represent the 'not recovering' group. Values are the group means with s.e.m in parenthesis.

	Baseline Current State of Health		P value
	Not Recovering	Recovering	
<i>Baseline Measures:</i>			
Positive Mood	25.02 (0.74)	29.44 (1.19)	0.002
Negative Mood	24.66 (0.92)	20.28 (1.21)	0.009
CES_depression	42.21 (0.82)	37.78 (1.25)	0.004
State Anxiety	41.20 (0.83)	37.25 (1.14)	0.009
PFRS			
<i>Emotional Distress</i>	49.04 (1.73)	42.36 (2.50)	0.036
<i>Fatigue</i>	67.22 (1.05)	53.95 (2.07)	0.000
<i>Cognitive Difficulties</i>	49.33 (1.21)	41.47 (1.95)	0.001
<i>Somatic Symptoms</i>	57.56 (1.56)	44.97 (2.17)	0.000
BDI	16.20 (0.66)	12.28 (0.82)	0.001
Cohen-Hoberman Inventory of Physical Symptoms	27.02 (0.60)	20.36 (0.92)	0.000
<i>Six Month Follow-up Measures:</i>			
PFRS			
<i>Fatigue</i>	62.42 (1.59)	54.39 (2.55)	0.007
<i>Somatic Symptoms</i>	55.39 (2.17)	45.82 (2.60)	0.011
Inventory of Physical Symptoms	25.18 (0.82)	20.21 (1.23)	0.001
<i>Three Year Follow-up Measures:</i>			
PFRS			
<i>Fatigue</i>	61.43 (2.02)	52.54 (2.92)	0.012
Inventory of Physical Symptoms	23.92 (1.13)	20.02 (1.34)	0.031

The data here provides clear-cut differences between the 'recovering' and 'not recovering' groups in terms of both emotional and health related scores at baseline. As these health-related measures are often associated with the severity of the illness (Russo et al., 1998; Smith et al., 1993) the 'current state of health' variable also appears to accurately assess the true severity of the illness for each patient.

3.5 Health Measures and Recovery

The topic of recovery over time was examined using the current state of health variable. People responding 'almost completely recovered' to this scale represented recovery. The results suggest that very few patients will completely recover over time without treatment. Levels of spontaneous recovery were only 2% at 6 months and rose to 6% at 18 months and 3 years.

As the number of patients who completely recover over time was low, recovery was redefined as patients who were 'recovering with occasional relapses' and those who had 'almost completely recovered'.

When considering illness onset type, there was no evidence to suggest that an association existed with recovery either in terms of state of health measures or total symptom scores. Similarly, there was no indication from the data that an association between the belief that physical or non-physical event caused the illness and recovery exists. When considering illness length at baseline, there were no significant differences associated with current state of health (recovering/not recovering) or total symptom scores except with respect to recovery at three year follow-up. To investigate this further, illness length was further split into quartiles and cross-tabulated with the recovering/not recovering variable. Although there was no association between illness length and recovery at baseline, 6 and 18 months, there was an association between the lowest quartile history length group and the likelihood of recovery at three-year follow-up ($df=3$, $p<0.032$).

3.6 Employment Status and Recovery

Table 4 describes the employment status of the patient sample at baseline. When comparing the three employment status groups there was an association between recovery and employment status at baseline, eighteen month and three-year follow-up. Patients in the employed group were significantly more likely to recover over time than those that were unemployed or on sick leave at baseline.

Table 4: The relationship between employment status at baseline and recovery at baseline, 18-months and 3 year follow-up. 'Recovering with occasional relapses' and 'Almost completely recovered' represent the 'Recovering' group, the remaining values represent the 'not recovering' group.

	EMPLOYMENT STATUS AT BASELINE			P value
	Employed	Unemployed	On sick leave	
<i>Baseline:</i>				
Not Recovering	31	43	17	n/s
Recovering	52	43	14	
<i>Six Month Follow-up:</i>				
Not Recovering	27	35	17	n/s
Recovering	56	47	18	
<i>Eighteen Month Follow-up:</i>				
Not Recovering	19	54	21	0.000
Recovering	60	36	10	
<i>Three Year Follow-up:</i>				
Not Recovering	20	46	13	0.035
Recovering	67	40	14	

3.7 Symptoms and Recovery

The association between recovery at initial assessment (baseline) and two other health related measures namely, total symptom and fatigue scores were then examined at baseline, six month, eighteen month and three year follow-up. Patients in the 'recovering' group at baseline reported significantly lower total symptom scores at baseline (recovering=13.71 (sem=0.69), not recovering=16.71 (sem=0.41), $p<0.000$), 6 months (recovering=12.89 (sem=0.93), not recovering=15.82 (sem=0.56), $p<0.006$) and 18 months (recovering=12.72 (sem=0.86), not recovering=15.54 (sem=0.54), $p<0.006$).

Fatigue in this cohort of patients was assessed using the Profile of Fatigue Related Syndromes questionnaire (PFRS). When splitting these scores into quartile ranges, there was an association between fatigue levels at baseline and rates of recovery. Patients who recorded low levels of fatigue at baseline were significantly more

likely to be in the 'recovering' group than those with high fatigue scores. This association occurred at baseline (recovering=55%, $p<0.000$), 6 months (recovering=67%, $p<0.000$), 18 months (recovering=56%, $p<0.001$).

3.8 Psychopathology and Recovery

In terms of psychopathology, there was an association between low depression scores at baseline (BDI) and recovery at baseline (recovering=67.2%; not recovering=47.5%, $df=1$, $p<0.006$). This trend was repeated at six-month follow-up (recovering=70.7%; not recovering=44.6%, $df=1$, $p<0.001$). This suggests that patients with lower depression scores at baseline were more likely to be in the recovering group. The trend, however, did not continue at the three-year follow-up point. There was no association between anxiety scores at baseline and subsequent recovery.

3.9 Psychosocial Measures and Recovery

The psychosocial measures administered in the current study included those assessing illness coping strategies, levels of perceived stress and daily hassles and levels of social support. Previous studies had already highlighted the differences between the psychosocial data from the CFS population when compared to a group of healthy controls [Thomas & Smith, submitted].

There were, however, no associations between baseline psychosocial measures and recovery at baseline, six months, eighteen months and three-year follow-up.

3.10 Health Measures and Improvement

Improvement was again calculated using the current state of health score. Patient responses at baseline were subtracted from subsequent follow-up measures to calculate whether their health status was 'improving' or 'not improving' at that time point. It is clear that when measuring recovery in terms of improvement, the percentages become much greater. Improvement is rated at 25% at 6 month follow-up rising to 29% at 18 months and 3 years.

This measure was then run through a similar analysis process to the 'recovering'/'not recovering' variables. However, these data did not show the clear-cut differences between observed when using the recovery variable.

3.11 Psychosocial Measures and Improvement

There no associations between improvement and these baseline scores. One exception being positive life events at baseline: patients in the highest quartile of positive life events were significantly less likely to be in the improved group at 3 year follow-up (improved=9%; not improved=29%, $df=2$, $p<0.029$). This implies that patients with the higher positive life events at baseline are least likely to improve three years later. As we can offer no explanation as to why this should be the case, it is considered that this finding represents chance effect.

3.12 Illness Characteristics and Health Measures as Predictors of Outcome

Logistic regression analyses were used to examine the relationship between baseline questionnaire data and improvement at three-year follow-up. Improvement was chosen as the dependant variable due to the low numbers of patients in the study who could be classified as recovered at the follow-up point (that is, only 6% of the sample). Two models were created, the baseline predictor variables being; (a) the aetiology of the illness (illness onset type, length of illness, viral cause and health status at onset) and, (b) health measures (fatigue, emotional distress, somatic symptoms, cognitive difficulties, cognitive failures, total symptoms, physical symptoms, anxiety and depression). There was no evidence to suggest that any of the health measures recorded at initial assessment were predictors of outcome. However, in terms of the aetiology of CFS, the current state of health measure was indicated as a predictor of outcome. Patients who reported better health status at initial assessment were significantly more likely to show improvement at the three-year follow-up point (OR=4.924, $df=1$, CI=1.453 – 16.688). 91 cases were used in the analysis and 70% of the sample was correctly classified by the prediction variables. Illness onset type, illness length and viral cause were not indicted as predictors of outcome.

3.13 Psychosocial Measures as Predictors of Outcome

There was no indication that any of the psychosocial factors measures at baseline could be described as predictors of improvement at three-year follow-up.

3.14 Further Regression Analyses

Further logistical regression analyses were conducted to test whether certain factors discussed in the literature namely, age, illness length, illness onset type, viral cause, total symptom scores, fatigue scores, emotional distress scores and health status scores are predictors of outcome in CFS. Again, only the current state of health of the patient at initial assessment (baseline) was indicated as a predictor of outcome at three-year follow-up (OR=9.618, df=1, CI=2.094 – 44.175). 89 cases were used in the analysis 75% of the sample were correctly classified by the prediction variables.

4. Discussion

The aims of the current study included the description of the demographic and illness characteristics of a large group of Chronic Fatigue Syndrome (CFS) patients at initial assessment, the validation of a measure (developed in previous studies) which could accurately evaluate health status and, therefore, recovery in the condition, and to identify factors which influence and predict positive outcome.

The patients recruited onto the volunteer panel were consecutive GP referrals to a dedicated research clinic and were categorised by the Centre for Disease Control case definition for CFS (Fukuda et al., 1994). The demographic data of the sample follows a similar profile to patients described by others (Fukuda et al., 1997) and, therefore, the group comprises predominantly married females in their forties. There has, in the past, been some debate as to whether an association between social classification and increased cases of Chronic Fatigue Syndrome exists (Fukuda et al., 1997; Dowsett, Ramsay, McCartney & Bell, 1990; Hinds & McClusky, 1993; Ho-Yen & McNamara, 1991). Data from the current research indicates that the majority of the sufferers recruited to the study were grouped in the professional or semi-professional social categories confirming that patients with this illness are more likely to be members of a specific social grouping.

The persistent and debilitating nature of the illness, demonstrated by a mean history length of five years and the number of symptoms present (16 of a possible 28), is apparent. For example, in the case of total symptoms, one would expect scores of 3 from a group of healthy controls (Thomas & Smith, 2009). The findings reported in the current study, therefore, indicate the wide range of symptoms associated with this illness. Furthermore, symptoms such as lack of concentration, muscle pain, excessive fatigue, physical weakness and legs feeling heavy were reported in over 80% of the cases. The length and severity of the illness is also reflected in the high numbers of patients who were either unemployed or on sick leave at initial assessment (baseline).

The health status of the patient group was assessed by the 5-item current state of health variable (Smith et al., 1996). Applying this measure at initial assessment (baseline) revealed data indicating that the health status for the cohort was poor; the majority of the group (41%) rating their health as 'bad with some recovery'. Further analyses also suggests that the health status variable correlates negatively with other measures such as total symptom scores, that is, lower scores on the current state of health measure are accompanied by increased total symptom scores.

Considering that the patients described in the current study represented different stages of the illness in terms of severity and illness length, one might presuppose a link between the current state of health variable and the length of illness measure. That is to say, either patients with longer illness length could be categorised as having greater illness severity or conversely, after a certain length of time, the patient begins to recover. This, however, does not appear to be the case. Cross-tabulation analyses reveals data indicating that illness length (represented by quartile ranges) is equally spread over the 5-items of the health status measure.

The current state of health measure was also used to assess recovery. Spontaneous recovery rates for the group are low at only 2% at six-month follow-up. Furthermore, these rates did not improve a great deal eighteen months or three years later (6%). The recovery rates reported here are much lower than those seen in previous studies (Reyes et al., 1999) but are in-keeping with results from a recent review by Cairns & Hotopf (2005) and a patient survey conducted by Thomas & Smith (2005), which indicate that the occurrence of spontaneous recovery from CFS is, in fact, relatively rare. When changes (or improvement) in health status rather than

recovery were measured, 25% of the sample reported an improvement at six months follow-up. These levels of improvement rose to 29% at eighteen months and remained constant at three years. As both recovery and improvement are calculated from the same 5-item scale, the problems one might encounter when interpreting subjective data are highlighted. Data from the improving/ not improving grouping did not provide the associations between state of health and improvement in other health-related measures that one sees in the recovery/ not recovering grouping. However, these data do indicate that both recovery and improvement peak at the 18 month follow-up point in the untreated patient.

Data linking state of health at baseline (recovering or not recovering) with other health-related measures at baseline, such as fatigue and depression, suggests that this measure can be used to accurately assess an individual patients' health at any given point. In addition, these data also demonstrate that illness status at baseline affects outcome i.e. better health status at baseline is associated with positive outcome at follow-up.

There is also evidence to suggest that total symptom scores and shorter illness lengths, again at baseline, are associated with more favourable outcomes. Overall, these data re-enforce the well held belief that diagnosing CFS effectively and setting coping and/or management strategies in place swiftly are vital to prevent the entrenchment of negative illness perceptions in patients and help facilitate positive outcome.

There is no suggestion from these data that physical cause attribution is associated with outcome. Similarly, there is no evidence to suggest that type of illness onset (acute or gradual) affects prognosis (although the type and frequency of symptoms reported by patients with acute or gradual illness onset do differ). Furthermore, there is no evidence from these data to suggest that co-morbid anxiety or depression at baseline is associated with recovery in the longer term. Physical cause, illness onset type and co-existing psychopathology have all been cited as possible factors affecting recovery in this patient group (Cairns & Hotopf, 2005; Russo et al., 1998). The data from the current study indicates that these associations may not exist.

Of interest, however, is evidence linking employment status at baseline and subsequent recovery. The suggestion being that patients in employment at baseline are more likely to be in the recovered group at baseline, eighteen months and three years later. These data can be interpreted in two ways, (a) employment brings with it a sense of belonging and maintains levels of social support which prevents feelings of isolation which may in turn exacerbate the illness, or (b) patients in employment may be able to continue working because they have better health scores and these data may simply be reflecting illness severity.

Logistical regression analyses were used to highlight possible mechanisms for predicting positive outcome in terms of improvement. It had already been suggested that a wide range of psychosocial, psychopathological and health related factors are associated with prolonging CFS (Surawy, Hackman, Hawton & Sharpe, 1995). We aimed to examine the role of these factors by means of improvement in the condition. These data suggests that, despite the findings reported in previous research, only one measure, namely the current state of health variable could accurately predict positive outcome. When the analyses were re-run using the factors indicated to be predictors of outcome in previous research, again only the current state of health variable is indicated as a predictor of outcome. These data should be regarded with caution due to the large confidence intervals involved; however, the heterogeneity of CFS may explain the large differences observed. Although these data are interesting, the health status of the patient at initial assessment only exerts (at most) an 18% effect over improvement. There are, therefore, other factors, which we have not yet considered, exerting a greater effect on recovery.

5. Conclusion

Overall, the current longitudinal study has provided data indicating that prognosis for the untreated CFS patient is poor. Associations between the state of health measure and other physical and mental health variables have been verified using a large group of patients. The validation of a simple 5-item measure by other standardised measures leads us to believe that this score can be used to accurately rate patient illness severity. We have also shown that this measure can predict and assess recovery. Positive outcome measures are indicated in cases where illness length is short and when the number and severity of symptoms are low. We have confirmed the

widely held belief among healthcare professionals that offering care to this patient group before the illness is allowed to become entrenched is of major importance if therapy is to be successful. The measures described here can now be used to evaluate the efficacy of treatments in future studies. Further research is necessary, however, to identify the, as yet, unidentified factors which can accurately predict positive outcome in this illness.

Acknowledgements

The authors would like to express their thanks to Professor Sir LK Borysiewicz and Dr MB Llewelyn for allowing access to their clinics. This research was funded by the Linbury Trust and the Gatsby Foundation.

References

- Afari N, Buchwald D. Chronic fatigue syndrome: a review. *American Journal of Psychiatry* 2003; 160: 221-36.
- Andersen MM, Permin IH, Albrecht F. Illness and disability in Danish chronic fatigue syndrome patients at diagnosis and 5-year follow up. *Journal of Psychosomatic Research* 2004; 56: 217-29.
- Bates D, Schmitt W, Lee J, et al. Prevalence of fatigue and chronic fatigue syndrome in primary care practice. *Archives of International Medicine* 1993; 153: 2759-2765.
- Cairns R, Hotopf M. A systematic review describing the prognosis of Chronic Fatigue Syndrome. *Occupational Medicine* 2005; 55: 20-31.
- Cathebras PJ, Robbins JM, Kirmayer LJ, Hayton BC. Fatigue in primary care: prevalence, psychiatric comorbidity, illness behaviour and outcome. *Journal of General International Medicine* 1992; 7: 276-286.
- Chen M. The epidemiology of self-perceived fatigue among adults. *Preventative Medicine* 1986; 15: 74-81.
- David A, Pelosi A, McDonald E, et al. Tired, weak or in need of rest: a profile of fatigue among general practice attenders. *British Medical Journal* 1990; 301: 1199-1202.
- Dowsett EG, Ramsay AM, McCartney RA, Bell EJ. ME – a persistent enteroviral infection? *Postgraduate Medical Journal* 1990; 66: 526-530.
- Fleming JS, Watts WA. The dimensionality of self esteem: Some results from a college sample. *Journal of Personality and Social Psychology* 1980; 39: 921-929.
- Fukuda K, Dobbins JG, Wilson LJ, Dunn RA, et al. An epidemiologic study of fatigue with relevance to the Chronic Fatigue Syndrome. *Journal of Psychiatric Research* 1997; 31: 19-29.
- Fukuda K, Straus S, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. International Chronic Fatigue Syndrome Study Group. The Chronic Fatigue Syndrome: a comprehensive approach to its definition and study. *Annals of Internal Medicine* 1994; 121: 953-959.
- Henderson S, Bryne DG, Duncan-Jones P. *Neurosis and the Social Environment*. Sydney, Australia. Academic Press 1981.
- Hinds, McClusky, A retrospective study of CFS. *Proceedings from the Royal College of Physicians (Edinburgh)* 1993; 23: 10-14.
- Ho-Yen DO, McNamara I. General Practitioners' experience of CFS. *British Journal of General Practice* 1991; 41: 324-334.
- Kroenke K, Wood DR, Mangelsdorff AD, et al. Chronic fatigue in primary care: prevalence, patient characteristics and outcome. *Journal of the American Medical Association* 1988; 260: 929-34.
- McDonald E, David AS, Pelosi AJ, Mann AH. Chronic fatigue in primary care attenders. *Psychological Medicine* 1993; 23:987-98.
- Nisenbaum R, Jones AB, Jones JF, Reeves WC. Longitudinal analysis of symptoms reported by patients with CFS. *Annals of Epidemiology* 2000; 10: 458.
- Pawlikowska T, Chalder T, Hirsch SR, Wallace P, et al. Population based study of fatigue and psychological distress. *British Medical Journal* 1994; 308: 763-766.
- Price RK, North CS, Wessely S, Fraser VJ. Estimating the prevalence of CFS and associated symptoms in the community. *Public Health Report* 1992; 107: 514-522.
- Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measure* 1977; 1: 385-401.
- Ranjith G. Epidemiology of Chronic Fatigue Syndrome. *Occupational Medicine* 2005; 55: 13-19.
- Ray C, Weir WRC, Stewart D, Millar P, Hyde G. Ways of coping with CFS: Development of an illness management questionnaire. *Social Science and Medicine* 1993; 37: 385-391.
- Reyes M, Dobbins JG, Nisenbaum R, Subedar NS, et al. CFS progression and self-defined recovery: Evidence from the CDC surveillance system. *Journal of Chronic Fatigue Syndrome* 1999; 5: 17-27.
- Reynolds KJ, Vernon SD, Bouchery E, Reeves WC. The economic impact of Chronic Fatigue Syndrome. *Cost Effectiveness and Resource Allocation* 2004; 2. <http://www.resource-allocation.com>
- Russo J, Katon W, Clark M, Kith P, Sintay M, Buchwald D. Longitudinal changes associated with improvements in CFS patients. *Journal of Psychosomatic Research* 1998; 45: 67-76.

- Smith AP, Behan PO, Bell W, Millar K, Bakheit M. Behavioural problems associated with CFS. *British Journal of Psychology* 1993; 84: 411-423.
- Smith AP, Borysiewicz L, Pollock J, Thomas M, Llewelyn, M. Acute fatigue in CFS patients. *Psychological Medicine* 1999; 29: 283-290.
- Smith A, Pollock J, Thomas M, Llewelyn M, Borysiewicz L. The relationship between subjective ratings of sleep and mental functioning in healthy subjects and patients with chronic fatigue syndrome. *Human Psychopharmacology* 1996; 11: 161-167.
- Spielberger C, Gorsuch R, Lushene RE. *STAI Manual for the State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press 1971.
- Surawy C, Hackman A, Hawton K, Sharpe M. CFS: A cognitive approach. *Behavioural Research Therapy* 1995; 33: 535-544.
- Thomas M, Smith A. Primary healthcare provision and Chronic Fatigue Syndrome: a survey of patients' and General Practitioners' beliefs. *BMC Family Practice* 2005; 6: 49.
- Thomas M, Smith A. An investigation into the cognitive deficits associated with chronic fatigue syndrome. *The Open Neurology Journal* 2009; 3: 13-23.
- Zevon MA, Tellegen A. The structure of mood change: An idiographic/nomothetic analysis. *Journal of Personality and Social Psychology* 1982; 43: 111-122.