

## Subjective quality of life in patients with chronic fatigue syndrome

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Accepted in revised form 27 February 2004

### Abstract

The aim of this study was to (1) assess Subjective Quality of Life (SQOL) of patients with Chronic Fatigue Syndrome (CFS) using a generic concept and to compare the findings with those in groups with mental disorders and healthy subjects, and (2) investigate whether and, if so, to what extent socio-demographic and clinical variables predict SQOL in CFS patients. Seventy-three patients diagnosed with CFS were randomly selected and interviewed from two specialised clinics. CFS was diagnosed using the Oxford Criteria. SQOL was assessed on the Manchester Short Assessment of Quality of Life (MANSA) and Health-Related Quality of Life (HRQOL) on the Medical Outcome Study Short-Form 36 (MOS) SF-36. A battery of mood and symptom questionnaires, including the Symptom Checklist Questionnaire (SCL-90-R), was administered to assess various aspects of symptomatology as potential predictor variables. Multiple regression analyses were conducted to identify predictors of SQOL. Overall, SQOL was low in CFS patients and less favourable than in groups with mental disorders and healthy subjects. Satisfaction was particularly low with life as a whole, leisure activities and financial situation. Whilst SQOL was only moderately correlated with HRQOL, the SCL-90-R score, especially SCL-90-R Depression scale score, was the best predictor of SQOL explaining 35% of the variance. HRQOL and generic SQOL appear distinct despite some overlap. The findings underline that SQOL is significantly disrupted in CFS patients. Depressive symptoms are statistically the strongest 'predictor' of SQOL, although the direction of the relationship is not established. These data suggest that treatment of depression associated with CFS, regardless of causation, could help to improve SQOL in CFS patients.

**Key words:** Chronic fatigue syndrome, Health related quality of life, Quality of life, Subjective quality of life

### Introduction

Chronic fatigue syndrome (CFS) is a condition reported worldwide. As well as unexplained chronic fatigue, symptoms include pains in joints and muscles, headaches, sore throat, lymph node tenderness, cognitive difficulties, and sleep problems [1, 2]. CFS is commonly associated with anxiety and depression [3–5]. The functional impact of symptoms can be great and lead to

reduction in the patients' ability to carry out normal daily tasks [6, 7]. The syndrome usually follows a chronic and fluctuating course and aetiology remains essentially unknown. Only two treatments (cognitive behaviour therapy and graded exercise therapy) have shown promising efficacy to date, although symptomatic measures and other supportive measures are also used [8].

While only a few studies have specifically investigated the impact of CFS on patients' quality

of life (QOL) [6, 9–12], there has been research into related constructs, such as impairment of CFS patients, which can be interpreted similar to SQOL. Studies into SQOL used concepts of health related quality of life (HRQOL) or disease specific ones. One notable study [8] investigating disease specific QOL in a US convenience sample of people with CFS found a significant impact on health and functioning, social activities, relationships and economic status. The Quality of Life Index (QLI) was used to measure perceived QOL. The QLI differs from most other measures of QOL in its acknowledgement that people value things differently. Overall scores on the QLI were significantly lower in CFS than for other chronic illness groups. The authors concluded that QOL is ‘particularly and uniquely’ disrupted in CFS [8].

In an international multicentre study HRQOL was assessed in CFS patients in the US, UK, and Germany, using the Short-form General Health Survey (MOS) SF-36 [10]. Overall, HRQOL was poor in CFS patients from all three countries. In another study in the US, a sample of twins suffering from fatigue were compared with unaffected co-twins using the Short-form General Health Survey (SF-36) [11]. Substantial impairment was observed in fatigued twins across all levels of fatigue, while scores in the healthy twins were similar to scores in the general population.

Disease specific and health related concepts of QOL differ from generic ones. The latter use indicators that are overall applicable and usually combine objective and subjective criteria. The subjective indicators are regarded as central and are often based on ratings of satisfaction with life as a whole and different life domains. Generic concepts as assessed on standardised instruments are particularly useful when QOL is to be compared in different groups.

In the present study, a generic concept of QOL was applied to assess QOL in patients with CFS. Focussing on subjective QOL (SQOL), we addressed two questions: First, what are QOL scores in CFS patients, and how do they compare with results among patients with mental disorders and healthy subjects that were obtained by the same method? Second, to what extent do socio-demographic and clinical variables predict SQOL in patients with CFS?

## Methods

### *Sample*

Patients with CFS are often seen in outpatient hospital departments. A general practitioner whose differential diagnosis includes a psychiatric disorder may decide to send the patient to a clinic run by a psychiatrist; however, a prominent history of recurrent infections might determine referral to a clinic run by an immunologist or an infectious disease physician [13]. Because of this referral pattern, we approached a random sample of patients, with a diagnosis of CFS, attending CFS clinics in the Department of Immunology and the Department of Psychiatry at St Bartholomew’s Hospital, London.

Patients attending clinics were randomized using random number tables, so that between two and four patients were approached each week, a number chosen to give a manageable number of subjects for the study every week. Demographic characteristics, past medical history and current medical history were collected from medical notes and using a questionnaire designed specifically for the study.

Thirty-seven of 146 patients approached in the immunology clinic (response rate 25.3%) and 36 of 50 patients approached in the psychiatric clinic (response rate 72%) participated in the study. This resulted in a total response rate of 37.2% (73/196). Two members of the research team interviewed the patients to obtain informed consent and to ensure they met Oxford Criteria for CFS [2]. For convenience, patients from the immunology clinic were interviewed on the same day as a clinic attendance, whereas patients attending the psychiatric clinic were interviewed on a separate day. All 73 patients fulfilled criteria for CFS as defined by the Oxford criteria [2]. Excluded patients were unable to complete the questionnaires for reasons of either language or severe disability. Patients gave written informed consent after the study was fully explained to them.

There was a non-significant trend for more non-participants to be female (84%) compared to participants (75%). The mean age (SD) of the non-participants was 40 (9) years compared to 43 (10) in the participants (95% CI for difference = 0.5). The patients from the two clinics were closely

similar in their specific symptoms, disability, quality of life (QOL), and psychological distress [13]. Examining categorical symptoms on individual questionnaires used in the study also showed no significant difference between the clinics in the reporting of depression by patients, suggesting that research data from one type of chronic fatigue clinic can be generalized to others [13]. Because of the similarities between patients attending the two clinics, and despite differences in response rate between the two clinics, the sample from the psychiatry clinic and that from the immunology clinic were treated as one sample in the analyses for this study. The demographic and clinical characteristics of the sample are shown in Table 1.

### Measures

The degree of fatigue experienced by patients was assessed using the Chalder Fatigue Scale (CHFS) [14] and a visual analogue scale [15] measuring different aspects of fatigue. CHFS is an 11-item scale to assess the degree of physical and mental fatigue in the last month. The respondent rates each item on a categorical 0–4 point scale.

The Manchester Short Assessment of Quality of Life (MANSA) [16] was used to assess QOL. The MANSA is a brief instrument for obtaining a generic construct of QOL widely used in mental health service research. It is similar to, but much more concise than the Quality of Life Interview [17, 18] and Lancashire Quality of Life Profile (LQLP) [19]. All of these tools share the same concept and have very similar satisfaction questions including 1–7 rating scales with 1 being the unfavourable and 7 the favourable end of the scale. Apart from recording personal details and objective circumstances of life, the MANSA contains 16 questions of which four are termed objective and the rest are ratings of satisfaction with life as a whole and of satisfaction with the following life domains: leisure activities, financial situation, living situation, personal safety, social relations, mental health, and family relationship. As far as psychometric properties are concerned, results of the MANSA have been found to have high concordance with results of the much longer LQLP on which the MANSA was based. Correlations between subjective quality of life (SQOL) scores on MANSA and LQLP were all 0.83 or

**Table 1.** Demographic and clinical characteristics of the sample (n = 73)

	Percent (or mean $\pm$ SD)
Age (in years)	43.4 $\pm$ 9.5
Gender (female)	75
Ethnic group	
White	93
Other	7
Living with	
Family of origin	7
Partner	29
Partner and children	22
Children only	10
Friends/flatmates	1
Alone	31
Marital status	
Single	32
Married	31
Co-habiting	16
Separated	3
Divorced	18
Highest level of education	
GCSE/O'Levels	22
A'Levels	18
Degree	27
Higher degree	15
Diploma	8
Other	1
Not disclosed	9
Employment	
Unemployed	62
Employed	38
Onset of illness (mean duration in years)	7.1 $\pm$ 4.4
Length of outpatient treatment (in years)	3.0 $\pm$ 2.5

higher, Cronbach's  $\alpha$  for satisfaction ratings was 0.74, and association with psychopathology was in line with results for LQLP as reported in the literature [16].

Different aspects of psychological distress as well as HRQOL were assessed as potential predictor variables on established scales. Specifically, the Medical Outcome Survey Short Form 36 ((MOS) SF-36) [20], Symptom Checklist-90-R (SCL-90-R) [21], Spielberger Trait Anxiety Scale [22], Beck Hopelessness Scale (BHS) [23], Health Anxieties Questionnaire (HAQ) [24], and Somatic Discomfort Questionnaire (SDQ) [25] were administered. For two of them, the (MOS) SF-36 and SCL-90-R, scores of sub-scales were com-

puted in addition to total scores. The (MOS) SF-36 is a self-report questionnaire to assess HRQOL based on physical functioning, social functioning, pain, mental health, role limitations due to physical problems, role limitations due to emotional problems, vitality and general health perception. The (MOS) SF-36 has been used to assess HRQOL in CFS patients [26, 27]. The Symptom Checklist-90-R (SCL-90-R) has 90 items of which 83 are grouped into nine primary symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The remaining seven items are used in the calculation of global scores.

#### *Comparison groups*

The MANSA scores of the study group were compared with corresponding findings among three other diagnostic groups from patient samples drawn in Germany. These were out-patients with schizophrenia who were assessed at 9 months after their first hospital admission; female in-patients with depression and female in-patients with alcoholism who were all interviewed in the second or third week of hospital treatment. A fourth comparison group consisted of healthy medical students. Details of these samples have been published elsewhere [28–31]. They were used as convenience samples for comparison since QOL data in those studies were obtained with directly comparable methods.

#### *Analysis/statistics*

In addition to descriptive statistics, correlation analyses between patients' MANSA sum scores and the various illness-related measures were conducted.

Using one way analysis of variance (ANOVA), the mean SQOL score of the study group ( $n = 73$ ) was compared with that of other patient groups comprising of first admission schizophrenia ( $n = 51$ ), alcoholic women ( $n = 70$ ), depressed women ( $n = 42$ ), and a sample of medical students ( $n = 207$ ).

Three regression analyses were performed to predict SQOL scores as the dependent variable.

Independent variables were socio-demographic and health/illness related characteristics. In model 1, only the socio-demographic characteristics were subjected to forward stepwise multiple linear regression (FSLR). In model 2, all the health/illness related variables were entered as predictors in a FSLR. In model 3, scores of individual subscales of the (MOS) SF-36 and the SCL-90-R were entered in the model instead of the total sum score of these measures.

## **Results**

### *Sum scores of various subjective measures*

Table 2 shows scores of the instruments used to assess QOL and health related variables in the study.

### *Comparison of SQOL in CFS patients with other groups*

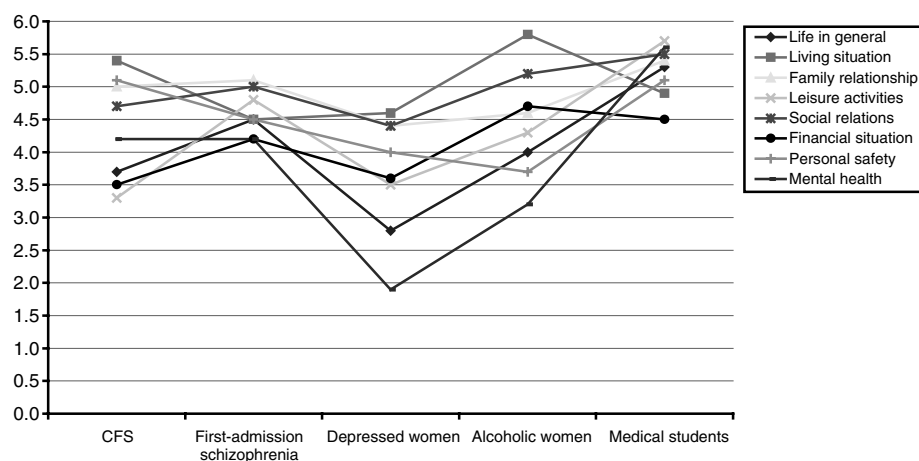
The mean SQOL score for the study group was 4.1 ( $SD = 0.8$ ) as compared to 4.6 ( $SD = 0.8$ ) in the first-admission schizophrenia group, 4.4 ( $SD = 0.9$ ) in alcoholic women, 3.5 ( $SD = 0.9$ ) in depressed women and 5.3 ( $SD = 0.7$ ) in medical students. Patients with CFS therefore had lower SQOL scores compared to all other groups except depressed women. However, when comparing the different samples on the various domains of QOL, CFS patients scored lowest only in the domains of satisfaction with their financial situation and satisfaction with leisure activities, and second lowest on satisfaction with life in general and with social activities. As indicated in Figure 1, all the comparisons across the five samples for each QOL domain were statistically significant.

### *Correlations between SQOL and other health related measures*

Table 3 shows correlations between SQOL as measured by the MANSA and other health related measures. The strongest negative correlation was found with the SCL-90-R sumscore ( $r = -0.59$ ), while the strongest positive one was with the (MOS) SF-36 sumscore ( $r = +0.53$ ).

**Table 2.** Patients' scores on instruments of symptoms' experience, functional status and quality of life

Instruments	Mean $\pm$ SD
1. Chalder Fatigue Scale (CHFS)	9.0 $\pm$ 3.1
2. Spielberger Trait Anxiety Scale (STAI)	45.8 $\pm$ 5.0
3. Beck Hopelessness Scale (BHS)	6.6 $\pm$ 5.3
4. Fatigue Visual Analogue Scale (FVAS)	343.3 $\pm$ 41.9
5. Health Anxieties Questionnaire (HAQ)	37.8 $\pm$ 9.5
6. Somatic Discomfort Questionnaire (SDQ)	100.0 $\pm$ 21.8
7. Medical Outcomes Study Short form 36 ((MOS) SF-36)	295.3 $\pm$ 127.1
Bodily pain	38.1 $\pm$ 20.3
General health perception	30.2 $\pm$ 16.0
Limitations due to emotional problems	52.5 $\pm$ 45.1
Limitations due to physical problems	8.2 $\pm$ 20.4
Mental health	60.1 $\pm$ 20.0
Physical functioning	41.1 $\pm$ 21.3
Social functioning	42.6 $\pm$ 24.7
Vitality	22.4 $\pm$ 16.6
8. Symptom Checklist-90-R (SCL-90-R)	97.4 $\pm$ 48.5
Anxiety	10.9 $\pm$ 8.5
Depression	19.5 $\pm$ 10.4
Hostility	5.3 $\pm$ 4.7
Interpersonal sensitivity	8.3 $\pm$ 6.3
Obsessive-compulsive	19.5 $\pm$ 8.6
Paranoid ideation	3.8 $\pm$ 4.4
Phobic anxiety	5.1 $\pm$ 5.7
Somatization	20.5 $\pm$ 8.6
9. MANSA Quality of Life Scale	4.2 $\pm$ 0.8

**Figure 1.** Comparative analyses of domains of SQOL across samples of patients: CFS (n = 73); first-admission schizophrenia (n = 51); depressed women (n = 42); alcoholic women (n = 70); medical students (n = 207). The multiple comparisons between CFS patients' sample and the other samples on each domain of SQOL using one-way ANOVA were statistically significant at  $p < 0.0001$ .

### Multivariate prediction of SQOL

Table 4 summarises the results of all three regression analyses that were conducted to predict

SQOL in CFS patients on the basis of different sets of predictor variables.

In model 1, none of the socio-demographic variables was selected, suggesting that these vari-

**Table 3.** Correlations between SQOL and other health related measures

	Correlation coefficient
1. Chalder Fatigue Scale (CHFS)	-0.26
2. Spielberger Trait Anxiety Scale (STAI)	-0.24
3. Beck Hopelessness Scale (BHS)	-0.44
4. Fatigue Visual Analogue Scale (FVAS)	-0.30
5. Health Anxieties Questionnaire (HAQ)	-0.36
6. Somatic Discomfort Questionnaire (SDQ)	-0.48
7. Medical Outcomes Study Short form 36 ((MOS) SF-36)	+0.53
Bodily pain	+0.34
General health perception	+0.45
Limitations due to emotional problems	+0.40
Limitations due to physical problems	+0.22
Mental health	+0.57
Physical functioning	+0.23
Social functioning	+0.46
Vitality	+0.20
8. Symptom Checklist-90-R (SCL-90-R)	-0.59
Anxiety	-0.45
Depression	-0.60
Hostility	-0.49
Interpersonal sensitivity	-0.44
Obsessive-compulsive	-0.42
Paranoid ideation	-0.52
Phobic anxiety	-0.34
Psychoticism	-0.48
Somatization	-0.41

**Table 4.** Regression analyses predicting SQOL of patients diagnosed with chronic fatigue syndrome, using forward stepwise models

Models	Variable(s) selected	Standardised regression coefficients	Percent variance	Model F (df1, df2)
1. Age, sex, ethnicity, marital status, length of outpatient treatment	None	-	-	-
2. Total scores of: CHFS, STAI, BHS, FVAS, HAQ, SDQ, (MOS) SF-36; SCL-90-R	SCL-90-R	-0.59*	34%	37.11 (1.71)*
3. Total scores of: CHFS, STAI, BHS, FVAS, HAQ, SDQ, (MOS) SF-36 subscales, and SCL-90-R subscales	SCL-90-R: depression SCL-90-R: paranoid ideation (MOS) SF-36: mental health	-0.24** -0.24** +0.32***	35% 3% 5%	18.74 (3.69)*

\* $p < 0.0001$ ; \*\* $p < 0.05$ ; \*\*\* $p < 0.01$ .

ables have no predictive value for SQOL in this group of patients. In model 2, the SCL-90-R total score was found to be the only predictor of SQOL, explaining a considerable 34% of the total variance. In model 3, the SCL-90-R depression score was found to be the strongest predictor, explaining 35% of the variance, followed by the SCL-90-R paranoid ideation score (3% of the variance), and the (MOS) SF-36 mental health score (5% of the variance).

## Discussion

Whilst previous research on QOL in CFS patients focused on HRQOL, this study aimed to assess QOL using a generic concept. HRQOL and generic SQOL, as obtained on the MOS-SF36 and the MANSA, showed a statistically significant correlation, which however indicated less than 30% shared variance between the two constructs. This correlation might – to some extent – be seen as a

mutual concurrent validation of the two methods to assess QOL from different perspectives. Yet, it certainly suggests that HRQOL and generic SQOL are distinct concepts in CFS patients despite their considerable overlap. In further research in CFS patients, they may need to be assessed separately. Which one of the two should be taken as the more important indicator of QOL, will depend on the specific research question and the purpose of the given study.

CFS patients showed a remarkably low SQOL in this study. The mean satisfaction score with life as whole was below the neutral scale point four, which means that on average CFS patients were explicitly dissatisfied with their life as a whole, which is a rare finding in QOL research using similar methods. The low SQOL in CFS patients is illustrated by the comparison of the scores with other samples. CFS patients had lower mean SQOL scores not only than medical students, but also than first admission schizophrenia patients and female patients with alcoholism. The only group with a less favourable SQOL than the CFS group were female depressed patients. The groups used for comparison in this study were convenience samples, and also differed in various respects other than diagnosis from the group of CFS patients. Thus, the comparison is likely to be confounded by a number of factors which cannot be controlled for. It may nevertheless provide a background against which the findings of this study can be better interpreted than if looked at in isolation.

When comparing the different samples on satisfaction with different life domains, CFS patients were particularly dissatisfied with leisure activities. Fatigue symptoms and constraints on sustainable activity would hinder patients' ability to pursue leisure activities as intended and, hence, would particularly affect patients' satisfaction with this life domain. CFS patients were also dissatisfied with financial matters, which is highly likely to be a consequence of loss of income, as 62% of the sample were unemployed.

It is interesting to note that the patients expressed a relatively high degree of satisfaction with accommodation and their family. These two domains of life may be assumed to be less directly affected by CFS in most patients. The scores in these domains underline the plausibility of the SQOL findings in this patient group.

The CFS patient group did not show increased dissatisfaction with their mental health. This could be taken to suggest that they neither regard their disorder as a mental health problem, nor recognise that secondary mental health issues are particularly disruptive to their QOL. It is however likely that there was heterogeneity. Nevertheless, the subjective perception can be contrasted with our finding that a depression sub-scale score was the strongest association with SQOL (see below). It appears that dissatisfaction in this patient group focuses on life domains that are more or less directly affected by fatigue and on satisfaction with life as a whole.

Whilst sociodemographic variables had no predictive value for SQOL, SCL-90-R score, especially the SCL-90-R depression score, was found to be the major predictor of SQOL. In a multivariate analysis other symptoms, i.e. paranoid ideation, and the mental health sub-scale of the (MOS) SF-36 also contributed to the predictive equation. Other constructs including scores on anxiety scales and the Beck Hopelessness Scale, which can be seen as related to depression, did not. One may conclude that out of all variables tested as predictors for SQOL in this study self-rated depression is clearly the most important one. This association is not specific for CFS patients. The literature suggests that depressive symptoms are a significant predictor of low SQOL in depressive samples and groups with other mental disorders such as schizophrenia [32], as well as in the general population. Dissatisfaction and depressive symptoms have been found to be correlated in various cross-sectional surveys, and to co-vary over time in several longitudinal studies [32]. This association does not indicate the direction of any causal relationship. Depressive symptoms may impact on patients' satisfaction ratings, and – vice versa – low satisfaction with life may lead to depressed mood. Both, ratings of depressive symptoms and dissatisfaction with life might be influenced by the same underlying cognitive processes determining negative views of oneself and one's life.

In previous studies the shared variance between psychopathology scores, including depressive symptoms, and SQOL rarely exceeded 30% [33]. In this study of CFS patients, depressive symptoms explained 35% of the variance of SQOL. The association between depressive symptoms and

SQOL might therefore be closer in CFS patients than in other groups. Yet, it must be noted that the greater part of the variance of SQOL still remains unexplained by the variables studied here, so SQOL cannot be considered to be a mere epiphenomenon of depressive symptoms.

The present study has several methodological limitations. We aimed to recruit representative samples from the two clinics involved and approached a randomly selected patient group. Yet, a number of patients had to be excluded or did not consent to participate which may have introduced a selection bias. Also, the data was collected in tertiary care, i.e. specialised referral clinics for CFS patients, and the results may not be generalizable to patients in primary care or other settings. As patients with severe forms of CFS are more likely to be diagnosed in primary and secondary care and, subsequently, referred to a specialised clinic, patients in other settings might be less severely affected by their disorder and have a more favourable SQOL. Also, this was a cross-sectional investigation. Given that symptoms of CFS may vary considerably over time, this study may not adequately reflect the fluctuating nature of the illness and its impact, and consequently of relevant QOL measures.

## Conclusion

Standardised instruments that assess SQOL using a generic concept of QOL yield results in CFS patients that are distinct from – although overlapping with – HRQOL. Patients in specialised CFS clinics appear to have a low SQOL as compared with groups with mental disorders and medical students. They express particularly low levels of satisfaction with life as a whole, leisure activities and finances, whilst their satisfaction with other life domains that are less directly affected by fatigue symptoms is more positive. Whatever the nature or aetiology of CFS, this study demonstrates that CFS can have a disruptive impact on patients' SQOL, a result that is in line with other research findings in CFS patients that were obtained using different concepts and methods.

Although the CFS patient group did not show increased dissatisfaction with their mental health, depressive symptoms were identified as the stron-

gest predictor of patients' SQOL. Thus, depressive symptoms are a relevant factor in the subjective experience of CFS patients. They thus could be the target of specific interventions to improve patients' SQOL, regardless of whether they are primary, secondary or simply co-morbidities. It is however important to note that several specific pharmacological treatments for depression appear to be ineffective for groups of patients with CFS in whom depression has been excluded [8].

Longitudinal and experimental studies are needed to establish whether – and, if so, in what way – pharmacological, psychological and social interventions to reduce depression can have a positive impact on patients' SQOL. Such evidence does not exist for the time being, beyond the use of certain antidepressant drugs in non-depressed CFS patients. For clinical practice in the meantime, one may still conclude from this study that it is useful for the patients' SQOL to diagnose and treat depressive features in CFS patients, in order to ameliorate the severe disruption of SQOL that has been identified.

Since both cognitive behaviour therapy and graded exercise therapy can relieve both depression and CFS, it could be argued that these two treatments seem well suited as treatments for both the disability itself and a factor that reduces QOL. However, the focus, nature and extent of cognitive behaviour therapy applied would need to address both domains (depression and CFS itself). In further research on SQOL in CFS patients, mood should be systematically assessed as an important factor for explaining variance, whilst other, as yet unidentified, variables should also be sought.

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