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**Distress in significant others of patients with chronic fatigue syndrome: a systematic review of the literature**

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**Abstract**

**Purpose:** To systematically review existing empirical research assessing levels and correlates of distress in significant others of patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).

**Methods:** Systematic searches in CINAHL, Web of Science and PsycINFO were conducted in August 2014. The search was repeated in January 2015 to check for newly published articles. Studies published in English with quantitative, qualitative or mixed designs exploring distress, poor subjective health, poor mental health, reduced quality of life and wellbeing, and symptoms of depression and anxiety in significant others (>18 years) of children and adults with CFS/ME were included. Quality appraisal of included studies was carried out. Quantitative and qualitative studies were summarized separately.

**Results:** Six articles met eligibility criteria. Two quantitative studies with significant others of adult patients, and one quantitative and two mixed-method studies with significant others of child patients showed moderate to high levels of distress. One qualitative study (adult patients) found minimal evidence of distress and that acceptance of CFS/ME was related to better adjustment. In the quantitative and mixed-method studies, significant others who attributed some level of responsibility for symptoms to the patient, or who were female, or whose partners had poorer mental health, had higher levels of distress.

**Conclusions:** The small number of studies to date, the contrary evidence from a qualitative study, and the limited data available on levels of distress in significant others of patients with CFS/ME means that our conclusion that distress levels are elevated is provisional. We recommend that future qualitative studies focus on this particular topic. Further longitudinal studies exploring correlates of distress within the context of a predictive theoretical model would be helpful.

**Introduction**

Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a long-term condition in which the primary symptom of fatigue, plus other symptoms such as pain, sleep and mood disturbances (Fukuda et al., 1994; Sharpe et al., 1991), cannot be attributed to or explained by any other medical condition. It affects 0.2-0.4% of the UK population (Department of Health, 2002) and can be seriously disabling, often resulting in high health-care use and reduced capacity to work, with reports of increased sick leave, reduced working hours, and health-related unemployment (Collin et al., 2011). In addition to the economic and societal costs associated with CFS/ME, evidence suggests there is a substantial cost in relation to informal care provision (McCrone, Darbishire, Ridsdale, & Seed, 2003). Care provided by significant others, such as spouses or parents, has been estimated to take an average of 8 hours per week (Sabes-Figuera et al., 2010).

In the UK, NICE guidelines recommend diagnosing and managing CFS/ME in primary care services (NICE, 2007), but some GPs lack the confidence or specialist knowledge to do this (Bayliss et al., 2014; Chew-Graham, Dowrick, Wearden, Richardson, & Peters, 2010). It can take several months for other possible explanations for fatigue to be excluded, and if the diagnosis is delivered as one of exclusion rather than as a positive starting point for management, patients and their carers can feel that the legitimacy of the illness is undermined (Bayliss et al., 2014; Dickson, Knussen, & Flowers, 2007).

We know that carers of patients with other long-term conditions can suffer distress and other negative outcomes. For example, there is evidence that caring for people with dementia can have a deleterious impact on the mental and physical health of carers (Mittelman, 2005; Vitaliano et al., 2003). Studies of distress in carers of people with cancer (Hagedoorn et al., 2000; 2008) have shown moderately elevated levels of distress, mainly in female carers. Similarly, wives of multiple sclerosis patients report more burden than husbands (Knight, Devereux & Godfrey, 1997). It has been difficult to establish which factors predict burden, poorer mental health and lower quality of life in carers of patients with Parkinson’s disease (Greenwell et al., 2014).

Distress can be defined as negative affective states related to caring duties which can have an impact on carer’s life. However, in common with studies in other conditions, in this review we have taken a broad and inclusive approach to defining distress. We searched not only for studies measuring distress per se but also for studies with various negative outcomes potentially related to distress, such as poor subjective health, poor mental health, low overall quality of life and wellbeing, a feeling of being burdened, and symptoms of depression and anxiety, which can have a deleterious impact on one’s overall health and wellbeing.

While there is evidence of distress and other negative outcomes in significant others and carers of people suffering from other health conditions, little is known about the impact on carers of caring for people with CFS/ME (Missen, Hollingworth, Eaton & Crawley, 2012; Nacul et al., 2011). Based on observations from our previous research (Hannon et al., 2012), and anecdotally, carers describe finding the uncertain nature of the illness very difficult to deal with (Hannon et al., 2012), and we surmise that significant others caring for those with CFS/ME might be at particular risk of distress because of the uncertain nature of the condition. Understanding carer distress in the context of CFS/ME is important for several reasons. Firstly, it is important that carers do not suffer adverse consequences or even suffer mental or physical health problems themselves as a result of their caring duties. Secondly, levels of distress of significant others might influence their interactions with the patient, and thereby interact with or influence patients’ attempts to manage their symptoms (Band, Barrowclough, & Wearden, 2014). Finally, understanding factors associated with distress in carers would inform possible interventions for carers or family interventions for CFS/ME patients and carers. Results are also likely to be relevant to other long-term conditions such as cancer, Parkinson's disease, dementia, and depression. Developing constructive relationships with carers and considering their needs, are essential aspects of service provision for patients who receive care from significant others.

We have conducted a systematic review of the published empirical evidence on distress and potentially related outcomes in carers of people with CFS/ME. The review had two main aims: 1) to identify and report existing research describing distress and related outcomes in significant others of patients with CFS/ME; and 2) to identify and report existing research exploring factors associated with significant others’ levels of distress.

## **Method**

### **Search Strategy**

CINAHL, Web of Science and PsycINFO were searched in August 2014 in order to identify empirical research on the topic that met inclusion criteria. The search was repeated in January 2015 to check for newly published articles. Grey literature was also searched by all authors, and manual searches of reference lists of included articles were conducted. Experts in the field were also contacted for unpublished manuscripts.

Search terms were defined based on team discussions. A combination of 1) terms commonly used to describe CFS/ME; 2) terms commonly used to describe significant others; and 3) terms that could potentially suggest exploration of distress were used. See Table 1 for details on the search strategy.

[Insert Table 1 here]

**Inclusion Criteria**

 Three of the authors screened abstract and titles of a total of 3,333 articles identified in databases using the search strategy in Table 1. Only those articles that met the following inclusion criteria were included in the review: 1) they were original research articles; 2) the sample comprised significant others (e.g., parents, spouses, partners, close friends), or other people who were referred to as “carers,” “informal carers” or “significant others” in the studies, who provided informal (non-professional, unpaid) care for a patient(s) with CFS/ME (we did not further define caring duties or require a minimum number of hours caring); 3) patients with any diagnosis of CFS/ME (e.g., using recognised criteria, self-report, or authors' reports of the sample diagnosis); 4) the study assessed or inquired about levels of distress experienced by significant others; 5) significant others were adults (≥ 18 years) who cared for 6) either adults or children with CFS/ME. We only included articles assessing adult carers. Child carers face an additional set of difficulties from those faced by adult carers, and we reasoned that the inclusion of child carers would overly complicate our conclusions. We excluded studies that: 1) examined carers undertaking professional or volunteer caring duties; 2) were not published in English; and 3) recruited an obviously unrepresentative sample. See Figure 1 for a flowchart showing included and excluded articles.

[Insert Figure 1]

#### **Quality Assessment of Studies**

Full-text articles that met inclusion criteria were independently assessed by a team of two authors. Standardised data extraction forms were used to summarise methodological details, outcomes, and main findings. Studies were scored on their scientific quality using a published tool developed for assessing studies with different designs across several research areas (Sirriyeh, Lawton, Gardner, & Armitage, 2012). The tool consists of 16 items which can be scored from 0 to 3 (0 - not at all; 3 - complete), giving a total score ranging from 0-48. This tool allows for the assessment of studies depending on their sample size, participant recruitment strategies, presentation of rationale for method and analyses, and other methodological limitations. Non-applicable items can be excluded and a mean quality score can be computed by calculating the mean of all items. Thus, if a study is given a total score of 29, which is then divided by the number of applicable items on the scale (e.g., 14), this study would have a mean total score of 2.07. The total mean scores of the two raters are then compared and any differences are discussed to reach a consensus. In the present systematic review, quality assessment for each study was independently assessed by two authors and inconsistencies were discussed amongst all authors until consensus on the quality rating of the articles was reached.

## **Results**

 Six studies met our inclusion criteria; the majority of results were irrelevant to the topic. Three of these relevant studies reported distress in significant others of adults with CFS/ME (Ax, Gregg, & Jones, 2002; Brooks, Daglish, & Wearden, 2013; Nacul et al., 2011) and three studies reported distress in significant others of children with CFS/ME (Gray et al., 2001; Missen et al., 2012; Rangel, Garralda, Jeffs, & Rose, 2005). Table 2 provides an overview of the relevant data extracted from each included study. Main results of the identified studies are summarised separately for adult and child patient groups.

[Insert Table 2]

### **Distress in Significant Others of Adult Patients**

Two cross-sectional quantitative studies suggested moderately high levels of distress in significant others (Brooks et al., 2013; Nacul et al., 2011). In Brooks and colleagues (2013), 13 (43%) out of 30 significant others reported caseness levels of distress (GHQ-28 mean score = 24.4; Goldberg & Williams, 1988), indicating poor psychological well-being. Similarly, Nacul and colleagues (2011) reported lower significant other mean scores on the SF-36v2 mental component scale (Ware et al., 2007) compared with healthy individuals of the same age (SO mean = 47.9; age norm mean = 50.9). In a qualitative study on illness beliefs and coping, Ax et al (2002) used semi-structured interviews to explore significant other experiences, beliefs, adjustment, acceptance of the illness, and the development of coping strategies over three stages: participants were requested to cast their minds back to the period before CFS diagnosis and the period shortly after the diagnosis, and also to speak about the past week (adjustment stage). Significant others’ retrospective recall of their experiences suggested that over time they accepted and adjusted to the illness relatively easily and that it had a generally low impact on their lives. In summary, these three studies show mixed outcomes. Ax et al (2002) reported limited distress in the context of acceptance of the patient’s illness, whereas Brooks et al (2013) and Nacul et al (2011) reported increased levels of distress in significant others.

Turning to factors associated with greater distress in significant others of adult patients, Brooks and colleagues (2013) explored the role of causal attributions for symptoms in predicting significant other self-reported distress. Significant others were more distressed when they attributed patients’ symptoms to factors that were both internal and personal to the patient; that is when they attributed some degree of responsibility for symptoms to patients. These associations were maintained when controlling for relationship satisfaction and depression in the patient. Nacul and colleagues (2011) reported that poorer mental health in patients and significant other’s female gender were associated with higher levels of distress. Ax et al’s (2002) qualitative analysis suggested that the level of acceptance of the illness, the impact of the illness on significant others’ life, and the quality of care provided by medical professionals were factors which might determine the level of distress experienced.

### **Distress in Significant Others of Child Patients**

In a mixed-methods study, Missen and colleagues (2012) assessed the level of distress in 40 mothers using self-report questionnaires and semi-structured interviews. Main measures of distress were obtained using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the General Health Questionnaire (GHQ-12; Goldberg, 1978). 28 out of 39 (72%) mothers scored above the cut-off point for the GHQ-12, indicating high levels of distress. 16 out of 38 (41%) and 5/39 (13%) mothers scored above the cut-off point for anxiety and depression on the HADS, respectively.

Using the longer version of the General Health Questionnaire (GHQ-28, Goldberg & Williams, 1988) Gray et al (2001) examined distress in significant others of children with CFS/ME, rheumatoid arthritis and mood disorders. The mean distress score of significant others in the CFS/ME group was found to be above the threshold score of 5 (GHQ-28 mean score = 6.2), and equivalent to the distress observed in significant others of children with mood disorders (GHQ-28 mean score = 7.0). A third study conducted by Rangel et al (2005) compared parents of 28 children diagnosed with CFS/ME with parents of children with juvenile rheumatoid arthritis or emotional disorders. Self-reports of distress using the GHQ-12 (Kellner, 1986), and burden using the Family Burden Questionnaire (FBQ; Pai & Kapur, 1981) were supplemented with a measure of Expressed Emotion from the CFI (Leff & Vaughan, 1985). Authors reported elevated scores on all measures of distress, and noted higher levels of emotional over involvement with the child, illness-related disruption of family interactions, and financial burden in CFS/ME families than in parents of children with arthritis. These three studies with child patient samples suggest consistently elevated levels of distress and distress-related variables.

Only one study with child patient samples assessed factors which may be associated with poorer significant other outcomes. Missen and colleagues (2012) explored such factors using a qualitative design and reported that lack of understanding from other relatives, marital tension, being concerned about their child’s distress, and the impact of the illness on siblings were potential contributors to carer distress.

### **Study Quality Assessment Scores**

There were only minor disagreements in quality rating scores between the researchers and consensus was generally good. The mean scores of the two raters for the articles were the same or very similar (mean differences ranged between .07 and .18; see Table 2). Included studies had moderate quality scores (mean scores ranging from 1.71 to 2.1). Sample sizes in half of the studies were relatively small (Ax et al., 2002; Gray et al., 2001; Rangel et al., 2005). Additional details about the recruitment and selection process in some studies would have been beneficial (Brooks et al., 2013; Missen et al., 2012; Rangel et al., 2005). Other methodological limitations identified were lack of detail on analytic strategies (Ax et al., 2002; Missen et al., 2012). However, when predictors of distress were explored, appropriate measures and analyses were used (Brooks et al., 2013; Nacul et al., 2011).

## **Discussion**

The main aim of the present review was to identify and describe findings in the existing literature relating to levels of psychological distress experienced by significant others of patients diagnosed with CFS/ME. This review included both quantitative and qualitative work. The quantitative studies identified were designed to assess distress directly, whereas in the one qualitative and one mixed method studies identified, distress was reported when it emerged as a relevant theme. Therefore, it may be helpful to discuss quantitative and qualitative findings separately.

Quantitative data suggests that an important proportion of significant others of adult patients reach caseness levels of distress (43% in the study by Brooks et al., 2013). It is difficult to say whether this is a higher than expected level, as no study defined expected levels of distress. However, we also found that significant others displayed higher levels of distress than various comparison groups (Gray et al., 2001; Rangel et al., 2005), and lower levels of functioning than population norms (Nacul et al., 2011) where these were available. Despite different measures being used across studies, the quantitative findings were consistent, and were particularly clear in the studies with significant others of child patients. This is consistent with previous findings that mothers who care for children with long term health conditions are at elevated risk of psychological distress (Hirst, 2005).

The qualitative arm of the Missen et al. (2012) study of mothers of children with CFS/ME suggested that a range of factors, some of which may be less relevant when caring for an adult patient, can impact on mothers’ psychological health. Mothers were worried not only about the health of the child with CFS/ME but also about the potential, varied, impact on any siblings. This study confirmed that lack of understanding from others is a particular problem for significant others of patients with CFS/ME. The qualitative study with significant others of adult patients reviewed here (Ax et al., 2002) produced quite different findings from the two quantitative studies with significant others of adults, in that participants described a situation in which, over time, they came to accept the condition. There are various possible reasons for this discrepancy. Firstly, carers (as they are termed) in the qualitative study were recruited via CFS/ME support groups, while Brooks et al. (2013) recruited patients from specialist NHS clinics while Nacul et al (2011) recruited patients who had been diagnosed by their GPs. It is therefore possible that the patient populations had different characteristics and different levels of illness severity; those who were in the Brooks et al. (2013) study had recently sought and/or started treatment, while those in Ax et al.’s (2002) study may themselves had accommodated to the condition. Furthermore, taking part in a study which elicited answers both from interviews and via questionnaires measures relating to symptoms, distress, beliefs, and mood disturbance (Brooks et al., 2013), may result in a different mind-set in respondents from when they are only being interviewed. The quantitative and qualitative studies had different research aims and therefore, while their findings can be considered together, they cannot easily be combined.

 A strength of the present review is the fact that it includes a systematic and comprehensive search strategy; grey literature was searched and experts in the field were contacted for unpublished manuscripts but none were forthcoming. On the other hand, our study was limited by only being able to include articles published in English. A further strength is that the quality of available empirical data was assessed by multiple independent raters during data collection and analysis. Scores suggest that the limited existing data is of moderate quality. Our conclusions must be treated with caution given the scarcity of the literature. Lastly, there may be disadvantages of using a quality assessment tool scored from 0-3 as opposed to a dichotomous (yes/no) rating scale. One potential disadvantage is that a greater number of response options in the scale may increase the subjectivity of the ratings. In contrast, a dichotomous scale could have been rated on the absence or presence of key information, which would have provided fewer opportunities for bias. Furthermore, one of the included studies (Ax et al., 2002) used retrospective recall to explore changes in significant other experiences over time. This method has limitations as intervening experiences may affect recall of past experiences so the study design should be taken into account when interpreting the study’s findings.

 In order to move the field forward, future research should study significant other distress within the context of a theoretical approach to understanding it. An understanding of distress within the context of a theoretical model would provide an indication of potentially modifiable factors which could be addressed in interventions. It is of interest that two studies (Gray et al., 2001; Rangel et al., 2005) showed higher levels of distress in parents of children with CFS/ME than those with juvenile rheumatoid arthritis. It is possible that there are common factors which predispose children to CFS/ME and their parents to high levels of distress. However, we speculate that patterns of family functioning may be different in the two groups, and that part of this difference may be due to the perception that rheumatoid arthritis is a visible and relatively well understood condition, while CFS/ME is invisible and less well accepted. Parents of children with CFS/ME may therefore find themselves struggling to understand the condition as well as to explain it to others. If our suggestion is correct, interventions to reduce distress in carers might include elements of education about the condition, and role plays and practice in explaining it to others. Future research to identify the correlates of distress in parents of children with CFS/ME might therefore systematically measure parental knowledge and beliefs about the condition, and the social impacts of the illness. We know that causal attributions for symptoms are associated with distress in adult partners of adult patients (Brooks et al., 2013). Further exploration of significant others’ beliefs about the illness, as has been done in other conditions, using framework of the Common-Sense Model (e.g., Karademas, 2014), may prove worthwhile, and again might result in interventions that addressed misperceptions about the illness. Finally, a recent study with significant others of adult patients with CFS/ME has shown suggested that Expressed Emotion (Leff & Vaughn, 1985) may be an important determinant of patients’ response to treatment (Band, Barrowclough, & Wearden, 2014). Given the associations between Expressed Emotion and carer distress seen in many other physical health conditions (Wearden, Tarrier, Barrowclough, Zastowny & Rahill, 2000), the relationship between Expressed Emotion and distress in significant others may be fruitful topic for further research. Such research may inform interventions to reduce Expressed Emotion, similar to the skills training interventions which have been reported in families of patients with eating disorders (e.g., Sepulveda et al., 2009).

In conclusion, our review was the first to explore the level of distress experienced by significant others of people with CFS/ME, and to also look for potential factors which may be associated with significant other distress. We know that caring for patients with other long-term conditions, such as MS, dementia, cancer and Parkinson’s disease can be distressing. Our review suggests there is a gap in empirical research exploring distress in those caring for a patient with CFS/ME. The importance of considering carer needs overall quality of life has been acknowledged and documented in government and healthcare policies (Department of Health, 2014). The limited number of published, peer-reviewed articles to date on levels of distress in significant others of patients with CFS/ME, coupled with the contrary evidence from one of the qualitative studies included in our review, means that the conclusion that distress levels are elevated is provisional and needs further assessment. Further longitudinal studies exploring correlates of distress within the context of a predictive theoretical model would be helpful.

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**Declaration of Competing Interests**

None.

**Table 1**

Example of a complete advanced search strategy used on Web of Science.

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| **CFS/ME search terms:** | **TS**=(“chronic fatigue syndrome” OR CFS OR “myalgic encephalomyelitis” OR ME OR “chronic fatigue and immune dysfunction syndrome” OR CFIDS OR “post viral fatigue syndrome”)  |
| **Significant other/carer search terms:** | **AND TS**=(“significant other” OR carer OR caregiver OR partner OR spouse OR wife OR husband OR “family member” OR family OR parent OR mother OR father OR daughter OR son OR child OR dyad OR dyadic)  |
| **Distress search terms:** | **AND TS**=(depression OR anxiety OR distress OR burden OR wellbeing OR “quality of life” OR impact OR “emotional impact” OR strain OR “mental health” OR “physical health”). |

*Note:* TS = topic. Search was limited to articles in English language.

**Figure 1**

Flowchart of included and excluded studies.

**Records excluded:**

**N = 3,313**(CINAHL n = 336; Web of Science n = 2,039; PsychINFO n = 938)

**Contact with authors:**

 **N = 3** Brooks et al., 2013; Goodwin et al., 1997; Larun & Malterud, 2007)

**Manual searching:**

**N = 2** (Ax et al., 1999; Ferrari et al., 1997)

**Records identified through database searching and screened:**

**N = 3,333**

(CINHAL n = 342; Web of Science n = 2,047; PsychINFO n = 944)

**Records identified through contact with authors:**

**N = 3** (Brooks et al., 2013; Goodwin et al., 1997; Larun & Malterud, 2007)

**Records identified through manual searching of reference lists:**

**N = 2** (Ax et al., 1999; Ferrari et al., 1997)

## Identification and Screening

**Full-text articles excluded:**

**N without duplicates = 14**

 (CINAHL n = 5; Web of Science n = 11; PsychINFO n = 6)

n = 7 Other outcomes (dyadic adjustment, marital satisfaction, CFS predisposing factors, psychosocial correlates of CFS, similarity in symptoms between mothers and children) but not distress (Blazquez et al., 2012, 2013; Crawley et al., 2012; Goodwin et al., 2000; Janssens et al., 2009; Pelcovitz et al., 1995; van de Putte et al., 2006; Roche & Tucker, 2003)

n = 2 Not SO outcomes (Band et al., 2014; Romano et al., 2009)

n = 1 Patients did not have CFS diagnosis (Krishnan et al., 2013)

n = 1 SOs were not adults (Smith et al., 2010)

n = 1 Unrepresentative sample (Sidi-Ali-Mebarek, 2008)

n = 1 Case study on ampligen trial (Snell et al., 2001)

**Full-text articles assessed for eligibility:**

**N without duplicates = 20**
(CINAHL n = 7; Web of Science n = 13; PsychINFO n = 8)

## Eligibility

**Studies included in data synthesis:**

**N = 6**

(Ax et al., 2002; Brooks et al., 2012; Gray et al., 2001; Missen et al., 2012; Nacul et al., 2011; Rangel et al., 2005)

## Included

**Table 2**

Design, details and main findings of included studies.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Design** | **Patient group (N)** | **Type of significant other (SO) (N)** | **Measures of distress** | **Measures of factors associated with distress** | **Findings in terms of distress (descriptive)** | **Findings in terms of factors associated with distress** | **Quality rating score (with each rater’s mean score)** |
| Ax et al, 2002 | Qualitative (semi-structured interviews) | N/A | 17 SOs (mean age = 44y, 12 male, mean length of caring = 7 years). | Semi-structured interviews enquiring about three time-periods, 1)pre-diagnosis, 2) time of diagnosis 3) past week. | Several coping themes at the three stages of illness emerged: caring tasks and difficulties, meaning of diagnosis, beliefs about the origins of CFS, and acceptance. | Overall low level of distress, and acceptance of illness over time (as a resignation, rather than a positive experience). | Potential factors predicting distress were acceptance, impact in life, and quality of care by medical professionals. | 1.72 (Rater 1 = 1.81; Rater 2 = 1.63). |
| Brooks et al, 2012 | Quantitative (self-report questionnaires). | 30 adults (mean age = 41y; 22 female) who met CFS criteria from two hospitals. | 30 SOs (mean age = 48y, 20 female). | CFI for causal attributions, GHQ-28 for distress, FRQ for behavioural responses. | Semi-structured interviews coded for attributions using the LACS, and the FRQ. | Mean SO GHQ-28 score = 24.43. 43% of the sample was in the caseness range (>24). | Internal and personal attributions about patient’s problems. | 1.97 (Rater 1 = 2.0; Rater 2 = 1.93). |
| Gray et al, 2001 | Quantitative (self-report questionnaires). | 15 adolescents who met the CFS criteria (mean age = 14.7y), 15 with rheumatoid arthritis (mean age = 12.7y), 15 with mood disorders (mean age = 14.3y). | N/A | GHQ-28  | GHQ-28 scores | For SO of CFS sufferers (mean GHQ-28 = 6.2), for mood disorders (GHQ-28 = 7.0). This was significantly more (*χ* 2 = 12.01, *p* = .002) symptomatic than the arthritis group (GHQ-28 = 1.5).  | N/A | 1.71(Rater 1 = 1.71; Rater 2 = 1.71). |
| Missen et al, 2012 | Mixed design (self-report questionnaires, semi-structured interviews). | 39 children (mean age = 13.3y; 26 female). | 40 mothers recruited from Specialist Paediatric CFS/ME Service. | HADS for anxiety and depression (cut off >10), GHQ-12 to assess general health. Semi-structured interviews with 8 mothers. | Themes from qualitative study: financial effects, parental mental health (sub-themes: lack of understanding from others, marital tension, concern about child’s distress, concern about the impact on siblings, maternal emotional distress. | 72% of the mothers scored above the cut-off for the GHQ -12 compared with 20% in the healthy population, suggesting possible mental health problem. | Lack of understanding from others, marital tension, concern about child’s distress and the impact on siblings, and emotional distress causing physical symptoms were factors contributing to poor parental health. | 1.85 (Rater 1 = 1.80; Rater 2 = 1.90). |
| Nacul et al, 2011 | Quantitative (self-report questionnaires). | 170 patients (age range: 18-65y; 133 female) recruited from 29 GP practices with confirmed diagnosis. | 43 SOs (25 male). | SF-36v2 for SO physical and mental. | SF-36 scores. | Emotional burden felt by SOs. Quality of life and functional status of CFS carers were lower than healthy individuals of the same age group. No cut-offs for level of distress. | Gender, patient scores on SF-36 (i.e., lower mental health in patient). | 1.86 (Rater 1 = 1.86; Rater 2 = 1.86). |
| Rangel et al, 2005 | Mixed methods (questionnaires, interviews). | 28 children and adolescents (mean age = 15y; age range: 11-18y, 22 female) with CFS who met criteria for CFS. Recruited from specialist paediatric/ psychiatric clinics. | 28 SOs. | Illness impairment data from semi-structured interviews. GHQ-12 for parental mental illness, IAS for parental attitudes toward illness, CFI for parent’s expressed emotion towards the child, FBQ for family burden. | N/A | An excess of CFS-like problems, more parental mental distress (GHQ-12 caseness = 12 (52%), emotional over involvement with the child (CFI mean score = 47.46), and illness-related disruption of family interactions in CFS families (FBQ mean scores: financial burden = 35.56, disruption of family leisure = 42.48, disruption of family interactions = 46.48, effect on health of others = 42.61). | N/A | 2.1 (Rater 1 = 2.1; Rater 2 = 2.1). |

*Note:* CDC – Centre for Disease Control; CFI - Camberwell Family Interview; ECD – Epidemiological Case Definition; FBQ – Family Burden Questionnaire; FRQ – Free Response Questions; GHQ – General Health Questionnaire; GP – General Practitioner; HADS – Hospital Anxiety and Depression Scale; IAS - Illness Attitude Scale; LACS – Leeds Attributional Coding System; SF-36 – Short Form Health Survey