

**Significant others, patient outcomes and maintenance of symptoms in chronic
fatigue syndrome**

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List of Abbreviations

ANOVA: Analysis of Variance

CBRQ: Cognitive Behavioural Responses Questionnaire

CBT: Cognitive-Behavioural Therapy

CF: Chalder Fatigue Scale

CFI: Camberwell Family Interview

CFS: Chronic Fatigue Syndrome

CLRN: Clinical Research Network

CRD: Centre for Reviews and Dissemination

DRM: Day Reconstruction Methods

EE: Expressed Emotion

EMA: Ecological Momentary Assessment

EOI: Emotional Over-Involvement

ESM: Experience Sampling Methodology

ESMc: Computerised ESM

ESMp: Paper ESM

FRQ: Family Response Questionnaire

GET: Graded Exercise Therapy

HADS: Hospital Anxiety and Depression Scale

HEE-C: High-EE on the basis of Critical comments

HEE-EOI: High-EE on the basis of EOI

IPQ: Illness Perception Questionnaire

IPQ-R: Revised Illness Perception Questionnaire

IPQS-Relative: Illness Perception Questionnaire for Schizophrenia Relatives' version

LEE-C: Low-EE on the basis of Critical comments

LEE-EOI: Low-EE on the basis of EOI

ME: Myalgic Encephalomyelitis

MPI: Multidimensional Pain Inventory

MUS: Medically Unexplained Symptoms/ syndromes

NHS: National Health Service

NICE: National Institute for Health and Clinical Excellence

NOD: National Outcomes Database

PIS: Participant Information Sheet

SD: Standard Deviation

SF-36: Short Form (36) Health Survey

SO: Significant Other

SPSS: Statistical Package for the Social Sciences

SRM: Self-Regulation Model

VAS-F: Visual Analogue Scales for Fatigue

WSAS: Work and Social Adjustment Scale

Abstract

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Candidate: Rebecca Jane Band

A thesis submitted to the University of Manchester for the degree of Doctor of Philosophy in the Faculty of Medical and Human Sciences in September 2013

Thesis title: Significant others, patient outcomes and maintenance of symptoms in chronic fatigue syndrome

This thesis explored significant other responses to CFS/ME in association with patient illness outcomes and symptom maintenance utilising a multi-method approach; a systematic review, cross-sectional, longitudinal and momentary methods were included. The review identified empirical evidence for two potential interpersonal mechanisms. The evidence suggested that significant other beliefs and responses, dyadic relationship quality, and patient outcomes associated with each mechanism were different. Dyadic belief incongruence was also highlighted as important with respect to relationship quality. Thus, potential research questions and current methodological limitations were identified; the subsequent empirical papers presented attempted to address these. The first empirical study (Chapter 3) utilised the Expressed Emotion (EE) framework to investigate the impact of critical comments and EOI; no cross-sectional associations between EE and patient outcomes were observed. A longitudinal design was also employed to examine the predictive validity of EE. Longitudinally, high critical comments predicted higher fatigue severity; further analyses indicated that depression mediated this relationship. High EOI was also predictive of higher fatigue severity at follow-up. This was the first study to examine EE within a CFS/ME sample; the longitudinal impact of high-EE upon patient outcomes suggests that it is a potentially beneficial target for future interventions. Paper 2 (Chapter 4) sought to examine the factors that might contribute to significant other EE by examining significant other illness beliefs and dyadic belief incongruence. The results indicated that significant others rated as high-EE had stronger illness models, more negative beliefs about the consequences associated with the condition, and negative emotional representations. These findings identify those beliefs that may be particularly important for high-EE within the current patient group. Overall dyadic belief incongruence was not important for EE-rating; high-EE dyads reported similar illness beliefs, whilst low-EE significant others reported more optimistic beliefs about the condition. These findings suggest that optimistic beliefs about the condition may be better for both significant other and patient outcomes. The final empirical study (Chapter 5) examined the associations between significant other negative and solicitous responses and fluctuations in patient illness outcomes on a momentary basis. The impact of significant other responses was largely transitory; changes in patient outcomes did not extend past the current momentary assessment. Negative significant other responses were associated with momentary increases in symptom severity; patient distress partially mediated this relationship. Patient-perceived solicitous responses were associated with increased activity limitation, but reduced disability reported at the same momentary assessment. These results suggest that momentary reports capture more dynamic processes than observed in traditional cross-sectional analyses. Taken together, the findings presented within this thesis provide further evidence for the impact of significant other factors on patient outcomes. The evidence for the hypothesised mechanism associated with critical EE was consistent throughout studies. However, the evidence for the role of EOI currently requires further exploration. Finally, the results suggest that the development of significant other-focussed interventions may be beneficial for both patient and significant other outcomes.

Declaration

No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Alternative thesis format

The current thesis has been prepared in alternative format, and consists of 4 papers (1 systematic review and 3 empirical papers). The systematic review presented in Chapter 1 is currently under review at *Clinical Psychology: Science and Practice*. Paper 1 presented in Chapter 3 is currently under review at *Health Psychology*, Paper 2 is currently under review at *British Journal of Health Psychology*, and finally Paper 3 is currently under review at *Psychological Medicine*. To aid cross-referencing, all references are provided in the APA 6th style format throughout.

The design, conduct and write-up for each of these papers have been overseen by the project supervisors, Professors Alison Wearden and Christine Barrowclough. They are therefore listed as co-authors on each of those papers outlined above. In addition, the assistance of a software engineer was required in order to collect the data presented within Paper 3, a biostatistician also advised on the statistical analyses for this paper; they are both therefore also listed as co-authors for this paper.

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Context

Almost half a century ago, some of the first studies were published examining the psychosocial influences of normal family experiences on clinical outcomes for psychiatric patients (Brown & Rutter, 1966). The development of the Expressed Emotion (EE) construct for examining aspects of the patient-significant other relationship within families where one individual was experiencing schizophrenia (Brown, Birley, & Wing, 1972; Vaughn & Leff, 1976) prompted several decades of research within this patient population (Barrowclough & Hooley, 2003). Vaughn and Leff (1976) reported on an abbreviated version of the Camberwell Family Interview (CFI) following a replication of the Brown et al., (1972) study; EE ratings derived from this version of the CFI are still currently considered to be the ‘gold standard’ for examining the construct (Hooley & Parker, 2006). The key indices for determining EE ratings are significant other critical comments, hostility and emotional over-involvement (EOI); significant others who provide evidence for these subscales above certain thresholds are conceptualised as high-EE. The EE construct has proved to be a well-validated and robust predictor of poorer patient outcomes, typically relapse, in schizophrenia (Bebbington & Kuipers, 1994; Butzlaff & Hooley, 1998). More recently, the EE construct has usefully been applied to a range of other conditions, including physical health conditions, where outcomes of interest include factors other than illness relapse (Hooley, 2007; Wearden, Tarrier, Barrowclough, Zastowny, & Rahill, 2000). The evidence therefore suggests that EE is a general predictor, representing the role of family environmental factors in association with outcome, rather than a psychosocial process specific to psychoses (Butzlaff & Hooley, 1998).

In the last decade or so, an increasing amount of empirical attention has been paid to the influence of close interpersonal relationships in association with patient outcomes in chronic fatigue syndrome (CFS/ME). CFS/ME is a complex condition currently

lacking a clearly defined medical aetiology (Guise, McVittie, & McKinlay, 2010); principle symptoms such as fatigue, pain, or sleep disturbances (K. Fukuda et al., 1994) are known to fluctuate, with periods of better and worse functioning, as well as day to day variability (Afari & Buchwald, 2003; Prins, van der Meer, & Bleijenberg, 2006). The limited evidence to date indicates that the quality of the relationship experienced with the significant other may be important for patient outcomes in CFS/ME; significant other beliefs and responses towards patients have been identified as important for patient illness related outcomes (Brooks, Daglish, & Wearden, 2012; Heijmans, de Ridder, & Bensing, 1999; Romano, Jensen, Schmaling, Hops, & Buchwald, 2009; Schmaling, Smith, & Buchwald, 2000).

The first stage in the thesis was a systematic review of the literature examining significant other experiences of CFS/ME, and the association between significant other responses and patient illness outcomes. The conclusions arising from the synthesis provided the foundation on which the methodological design and hypotheses of the subsequent studies were formulated; the potential mechanisms through which significant other factors may impact on patient outcomes were identified. The empirically derived, well-validated EE construct was subsequently selected as an ideal methodological and theoretical framework to guide the thesis studies. The EE construct was considered to be ideal as it encompasses those significant other factors (such as, beliefs, behaviours, relationship quality) highlighted throughout the review. Therefore, the studies were designed as a series of empirical papers suitable for alternative thesis format submission.

The first empirical study (Paper 1) therefore employed an appropriately adapted version of the CFI to examine the association between significant other EE and patient outcomes. Guided by the previous cross-sectional CFS/ME literature identified within the review, the principal EE subscales of critical comments and EOI were investigated

separately, in addition to the conventional overall EE rating. A longitudinal aspect was included within the design of this study to examine the predictive validity of the EE construct across time. To our knowledge, this is the first study to report on EE within a CFS/ME sample.

Following this, an attempt was made to understand the factors that might contribute to the presence of EE within this population (Paper 2). This work focused upon significant other beliefs about the condition, comparing high- and low-EE significant others in order to understand which beliefs may differentiate between these groups. Furthermore, research has previously found a relationship between dyadic belief incongruence and ratings of dyadic relationship satisfaction; given that EE is thought to reflect various aspects of the patient-significant other relationship, belief incongruence was therefore also examined in the context of EE status.

The final empirical study (Paper 3) was included to investigate the impact of key significant other response styles, that is, negative and solicitous significant other responses, on fluctuations in patient symptom severity and disability in the course of daily life. The novel experience sampling methodology employed within this study allowed for analyses to examine whether changes in patient outcomes were triggered by significant other responses, and furthermore, to determine how enduring any effects were on a moment-to-moment basis.

Chapter 1: Literature Review

1.1 Overview

The aim of this section is to provide a summary of the relevant background literature concerning the role of significant other factors in CFS/ME. First, a brief description of chronic fatigue syndrome will be provided, in addition to a summary for the cognitive-behavioural model for the development and maintenance of CFS/ME. Following this, the rationale for investigating significant other factors will be addressed, and a systematic review of the relevant literature examining significant other experiences of CFS/ME, and the associations between significant other factors and patient outcomes will be presented. Finally, the aims of the thesis will be outlined.

1.2 Chronic Fatigue Syndrome (CFS/ME)

Chronic fatigue syndrome is a symptomatically defined condition, characterised by severe, unexplained fatigue (K. Fukuda, et al., 1994). In line with the widely used 1994 US Centres for Disease and Control case definition, patients must also present with at least four associated symptoms, these include malaise after exertion, muscular and joint pain, impaired cognitive functioning, sore throats, headaches, sore lymph nodes and unrefreshing sleep (K. Fukuda, et al., 1994). The reported prevalence of the condition has varied across settings; it is estimated that CFS/ME affects 0.2-0.4% of the adult population within the UK (Department of Health, 2002). Furthermore, the condition is associated with significant functional impairment (Komaroff et al., 1996) and high patient health-care use (McCrone, Darbishire, Ridsdale, & Seed, 2003). There has been debate over the extent to which chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) reflect the same condition (David & Wessely, 1993; Prins, et al., 2006), however, the condition is currently conceptualised as CFS/ME (NICE, 2007); this abbreviation will be used to refer to the condition throughout the thesis.

1.3 Theoretical models of chronic fatigue syndrome

CFS/ME cannot easily be conceptualised within a traditional biomedical model of disease; the encephalomyelitis implicated in the ME label is often not observed (Wojcik, Armstrong, & Kanaan, 2011), and other clearly defined medical aetiologies are currently lacking (Guise, et al., 2010). Multifactorial theoretical frameworks are therefore beneficial for examining the interactions of several distinct factors in understanding disturbance of function in the absence of a single underlying biological process (Surawy, Hackmann, Hawton, & Sharpe, 1995). Theoretical frameworks such as the Cognitive Activation Theory (Ursin & Eriksen, 2004) have attempted to incorporate the evidence for both physiological alterations and psychological factors; prolonged physiological activation of normal stress responses are proposed as the underlying mechanism for symptom experience in CFS/ME. Pre-morbid factors, cognitions and learning (i.e. conditioning) are also implicated within the integrative process (Wylle, Eriksen, & Malterud, 2009). Whilst this theoretical model of chronic fatigue syndrome offers potential future utility particularly for understanding the reciprocal interactions between psychological and physiological factors, there is currently limited evidence to support this (Deary, Chalder, & Sharpe, 2007). Consequently, much research has focused upon a cognitive-behavioural conceptualisation for CFS/ME; this theoretical framework has also been employed to guide the empirical studies presented within this thesis.

1.3.1 Cognitive Behavioural Models

Cognitive behavioural models of CFS/ME provide a theoretical explanatory framework for both the onset and maintenance of CFS/ME and its associated symptoms (Deary, et al., 2007; Surawy, et al., 1995; Wessely, Butler, Chalder, & David, 1991). Factors that may predispose and precipitate the onset of CFS/ME are separated from the factors that maintain symptoms once the disorder is established (Bleijenberg, Prins, & Bazelmans,

2003); the psychological responses which may mediate the pathway from the initial illness trigger to CFS/ME development are also defined (Moss-Morris, Spence, & Hou, 2011).

A number of factors have been identified as potential predisposing factors in CFS/ME, such as high levels of perfectionism and neuroticism; high standards including achievement orientation, high importance placed upon others' opinions with respect to high standards, and negative emotion suppression and avoidance appear to be commonly associated with CFS/ME (Fukuda et al., 2010; Hambrook et al., 2011; Surawy, et al., 1995). A pre-disposed individual may be exposed to a "critical incident" (Deary, et al., 2007), whereby precipitating factors such as high amounts of psychosocial stress or an acute illness such as a viral infection, compromises the individuals' ability to meet pre-morbid standards and expectations (Moss-Morris, 2005; Oldershaw et al., 2011). Consequently, patients become trapped in a vicious cycle where cognitive, behavioural, emotional and physiological factors interact to maintain and perpetuate the physical symptoms associated with the condition (Deary, et al., 2007; Surawy, et al., 1995). Initially, ongoing symptoms may arise as a result of doing too much, however, these symptoms are interpreted as a sign of ongoing physical illness; rest may be viewed as an appropriate response, in an attempt to control symptoms. Activity limitation may conflict with unmet dysfunctional expectations, and therefore bursts of activity, labelled all-or-nothing behaviours (Spence, Moss-Morris, & Chalder, 2005), punctuate these periods of rest. Typically, patients are unable to perform at their pre-morbid levels as a result of physiological de-conditioning; this exacerbates symptoms and reinforces the belief of a serious, incurable illness. Over time, patients become increasingly disabled and preoccupied with symptom experience (Surawy, et al., 1995).

Evidence for the cognitive-behavioural model has been derived from cross-sectional or retrospective research, and clinical evidence (Moss-Morris, 2005); further support has

been demonstrated through prospective studies following known trigger illnesses such as glandular fever (Moss-Morris & Spence, 2006; Moss-Morris, et al., 2011). Furthermore, interventions based upon cognitive models for CFS, such as Cognitive-Behavioural Therapy (CBT) or Graded Exercise Therapy (GET) have been shown to be efficacious in improving patient outcomes (Castell, Kazantzis, & Moss-Morris, 2011; Chambers, Bagnall, Hempel, & Forbes, 2006); the impact of these interventions appear to be at least partially as a result of changing cognitive processes, such as symptom focussing or beliefs about activity, rather than changes in objective outcomes, such as fitness levels (Deale, Chalder, & Wessely, 1998; Knoop, Prins, Moss-Morris, & Bleijenberg, 2010; Moss-Morris, Sharon, Tobin, & Baldi, 2005).

Although the evidence would seem to support an overarching cognitive-behavioural framework for understanding CFS/ME, further research is necessary in order to support the theoretical propositions outlined within the theory. Factors outlined within the model, such as social factors, are currently poorly defined; these may vary on an individual level, and as a result are important to develop and incorporate into the models. In addition, the assumption that those factors outlined within the theory interact and self-perpetuate to maintain the condition needs further empirical support (Deary, et al., 2007). Finally, cognitive behavioural models are limited to largely understanding the perpetuation and maintenance of the condition, whilst the onset of the condition is poorly understood within the theoretical framework (Surawy, et al., 1995).

1.4 The Rationale for Examining Significant Other Factors in CFS/ME

Social factors have been identified as potential perpetuating factors for medically unexplained symptoms or syndromes (MUS); with specific factors such as medical uncertainty and illness legitimacy outlined as particularly important (Deary, et al., 2007). The evidence suggests that with respect to CFS/ME, when faced with

delegitimizing interactions specifically in the context of the patient-significant other relationship, patients perceive poorer levels of coping and reduced social support (Dickson, Knussen, & Flowers, 2007). In addition, further research has highlighted that lack of social support and interactional difficulties may be associated with symptom perpetuation in CFS/ME (Fukuda, et al., 2010; Prins et al., 2004). Patient emotional factors such as compromised abilities to infer emotional states, negative emotion suppression, and avoidance of help-seeking behaviour have been highlighted as potential factors that may contribute to poorer social interactions and increased interpersonal problems in CFS/ME (Hambrook, et al., 2011; Oldershaw, et al., 2011). The evidence therefore points to potential specific interpersonal difficulties that may be experienced within CFS/ME, and furthermore, suggests that these may be associated with poorer illness outcomes.

In addition, medical uncertainty may be an important factor to consider with respect to the role of significant others in illness management. Interactions between patients and medical professionals can be difficult to negotiate (Bowen, Pheby, Charlett, & McNulty, 2005; Chew-Graham, Cahill, Dowrick, Wearden, & Peters, 2008; Guise, et al., 2010); it has been suggested that the role of significant others may therefore be highly influential in constructing patient narratives about the condition (Brooks, King, & Wearden, 2013; Cordingley, Wearden, Appleby, & Fisher, 2001). It has been noted previously that patient beliefs about chronic conditions may be influenced by social networks (Heijmans, et al., 1999). The course of CFS/ME is often associated with a reduction of wider social networks and an increasing reliance upon significant other relationships (Assefi, Coy, Uslan, Smith, & Buchwald, 2003; Duff, 2003; Melamed, 2003); recent evidence suggests that on average, significant others provide eight hours of informal care per week to patients (Sabes-Figuera et al., 2010). The limited evidence would therefore suggest that significant other responses to patients experiencing

CFS/ME are of importance with respect to symptom perpetuation and maintenance for a number of reasons.

1.5 Patient outcomes in association with Significant Other responses to CFS/ME: A systematic review of the literature

The overall aim of this thesis is to examine the impact that significant other responses to CFS/ME may have upon patient outcomes and symptom maintenance. Therefore, prior to study design and hypothesis formulation, a review of the literature examining significant other responses to CFS/ME, and the links between these responses and patient outcomes was conducted. The findings of this systematic review are presented in the following paper, which is currently under review for publication in *Clinical Psychology: Science and Practice*.

Patient outcomes in association with significant other responses to chronic fatigue syndrome: A systematic review of the literature.

Running head: Significant others and patient outcomes in CFS/ME

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1.5.1 Abstract

Evidence suggests that social processes may be important in symptom perpetuation in CFS/ME, but the specific role of close interpersonal relationships remains unclear. This paper reviewed studies investigating how significant others respond to the experience of CFS/ME in close relatives or friends, and the relationships between these significant other responses and patient outcomes. The review included 13 papers published between 1988 and 2012. Significant other beliefs that were incongruent with patient beliefs or those that attributed responsibility to the patient were associated with increased patient distress. Furthermore, solicitous and negative significant other responses were identified in association with increased symptom severity, disability and distress. Poor relationship quality, including increased conflict and reduced empathy and support, was associated with increased patient symptom experience. Good relationship quality was found to be associated with increased patient disability. The evidence points towards two potentially contrasting interpersonal mechanisms, each associated with different significant other beliefs, responses and overall relationship quality. Significant other difficulties and adjustment were also explored. The development of significant other focused interventions may be particularly beneficial for both significant other and patient outcomes. The review highlights the need for further research into interpersonal mechanisms in CFS/ME and current methodological issues are addressed.

Keywords:

Chronic fatigue syndrome; Significant others; Beliefs; Behaviours

1.5.2 Background

Patients diagnosed with chronic fatigue syndrome (also known as myalgic encephalomyelitis; CFS/ME) experience severe fatigue not accounted for by alternative medical diagnoses (K. Fukuda, et al., 1994). CFS/ME is associated with high levels of patient disability and healthcare use (McCrone, et al., 2003) and the worldwide prevalence is currently estimated to vary from approximately 0.2 to 2.6% within adult populations (Prins, et al., 2006). This article seeks to identify and review all empirical studies which have examined significant other responses to CFS/ME and the associations of these responses with patient outcomes.

Cognitive-behavioural models provide an explanatory framework for the development and maintenance of CFS/ME and distinguish between the predisposing, precipitating and perpetuating factors (Surawy, et al., 1995). These models propose that failure to recover from an initial illness trigger gives rise over time to a state of physiological dysregulation, involving muscular and cardiovascular deconditioning and disturbed sleep (Deary, et al., 2007). According to these models, severe fatigue and disability are maintained, at least in part, by behavioural and emotional responses to symptoms which are driven by patient beliefs about the condition and its management (Deary, et al., 2007; Moss-Morris, et al., 2005) with negative beliefs about the condition associated with poorer patient outcomes (Moss-Morris & Chalder, 2003). Patients who view symptoms as indicative of ongoing pathological damage in the body engage in higher levels of activity limitation (Deale, et al., 1998), which perpetuates deconditioning and consequently further reduces tolerance for activity (Schmaling, Fiedelak, Bader, & Buchwald, 2005). Long periods of rest may be interspersed with short bursts of exertion, referred to as all-or-nothing behaviour (Spence, et al., 2005); these behaviours are driven by symptom experience and by conscientious or perfectionistic attitudes, but exacerbate fatigue severity and increase symptom

preoccupation (Moss-Morris, 2005). Cognitive-behavioural therapy (CBT) and graded exercise therapy (GET) interventions, both of which seek to gradually increase activity while decoupling it from symptom experience, are effective in reducing fatigue and improving patient functioning (Castell, et al., 2011; Chambers, et al., 2006; P. White et al., 2011). Changes in activity regulation and symptom preoccupation have been identified as key mechanisms for improvement (Moss-Morris, et al., 2005; Wearden & Emsley, in press; Wiborg, Knoop, Stulemeijer, Prins, & Bleijenberg, 2010).

Social factors, such as others' beliefs about the legitimacy of the illness, have been outlined within these explanatory models as additional potential perpetuating factors, and the role of social support has been identified as an important factor to incorporate in understanding symptom maintenance (Deary, et al., 2007). There are a number of factors that provide the rationale for examining the role of significant other factors specifically in association with patient outcomes in CFS/ME. Perception of others' beliefs and opinions has been identified as being of central importance for CFS/ME patients (Surawy, et al., 1995), and indeed, patients report the role of significant other relationships in determining adjustment to the condition and feelings of wellbeing (Dickson, et al., 2007). Additionally, high disability associated with the condition may result in a reduction in opportunity for wider social contact (Assefi, et al., 2003; Duff, 2003) potentially amplifying any effect of interpersonal variables in close relationships with significant others.

Furthermore, research into other disorders has established the importance of interpersonal factors for both patient and significant other outcomes. A large literature has examined significant other factors in association with chronic pain. It has been suggested that chronic pain may be an appropriate comparison for CFS/ME, since both are characterized by chronic symptoms that are experienced privately and communicated socially (Schmaling, et al., 2000). Significant other behaviours have

been associated with patient responses to pain, such as patient acceptance or catastrophizing (Boothby, Thorn, Overduin, & Ward, 2004), as well as patient illness outcomes such as greater illness severity, disability and poorer psychological outcomes (Cano, Leong, Heller, & Lutz, 2009; Fillingim, Doleys, Edwards, & Lowery, 2003; Kerns, Southwick, Giller, Haythornthwaite, & et al., 1991; McCracken, 2005). Patient distress has also been shown to be associated with incongruence in illness beliefs between members of dyads (Cano, Johansen, & Geisser, 2004). Belief congruence within dyads has been shown to reduce negative significant other responses and significant other stress, as well as increase perceived support (Martire et al., 2006). Relationship quality has also been highlighted as an important aspect of the social context to consider when examining the association between patient and significant other factors (Taylor, Davis, & Zautra, 2013). This evidence therefore suggests that examining significant other factors in association with patient outcomes in CFS/ME may be beneficial to further advancing understanding the perpetuating role of interpersonal factors, and that significant other beliefs and responses to patients' symptoms and illness may be of particular interest.

1.5.2.1 Aims

The review will address two main objectives, first relating to significant other responses to the condition, and consequently the associations of those responses to patient outcomes such as symptom severity, physical functioning and psychological adaptation. The specific research questions of interest are as follows:

- How do significant others respond to the condition in a close relative or friend?
- What do significant others believe about the condition, how are these beliefs associated with their behavioural responses and patient outcomes?

- Are specific significant others' behavioural responses associated with worse patient outcomes?
- Are high levels of relationship satisfaction within the dyad associated with better patient outcomes?

The evidence for each of these research questions of interest will be presented in separate sections within the review. Each section will begin with a brief overview, followed by a detailed consideration of the relevant findings. After drawing together the evidence we will discuss the implications of these findings and pose questions arising for future research and clinical practice.

1.5.3 Method

1.5.3.1 Search Procedure

The following electronic databases were searched: psychINFO, Medline, EMBASE, CINAHL, Web of knowledge/science, PubMed and the Cochrane library. Further articles and unpublished manuscripts were sought by examining the reference lists of identified papers, in addition to seeking consultation with experts in the field. The search was completed in December 2012. The search strategy was devised in line with the Centre for Reviews and Dissemination (CRD) recommendations (Centre for Reviews and Dissemination, 2009). As this review is concerned with the interaction of significant other variables with patient outcomes, the search strategy followed a two-stage procedure whereby the initial search included specific CFS/ME population terms, and significant other population terms (see Table 1). Subsequently, significant other beliefs and response variable terms were combined with the patient and significant other population search terms.

Table 1: Review search terms, inclusion criteria and patient outcomes relevant for article selection

CFS/ME population terms:	
Chronic fatigue syndrome/ CFS/ Myalgic encephalomyelitis/ ME/ Chronic fatigue and immune dysfunction syndrome/ CFIDS/ Post viral fatigue syndrome	
Significant other population terms:	
Significant other/ carer/ caregiver/ partner/ spouse/ wife/ husband/ family member/ parent/ mother/ father/ daughter/ son/ child	
Significant other response variable terms:	
Illness representation/ cognitive representation/ common-sense model/ illness perception/ attribution/ solicitous/ distracting/ punishing/ facilitating/ belief/ emotion / expressed emotion/ EE/ criticism/ critical comments/ hostility/ warmth/ over-involvement/ overprotection	
Inclusion criteria:	
Adults (aged 16+) who had received a specialist clinician diagnosis of CFS/ME	
Assess significant other beliefs or responses to CFS/ME	
Assess significant other variables in association with patient outcomes	
Articles published in English	
Any significant other relationship	
Patient outcomes (with examples):	
Symptom severity	fatigue, pain, other CFS symptoms
Physical functioning	disability, physical activity, rest, functional abilities, daily activities
Psychological adjustment	depression, anxiety, distress, adjustment to illness
Relationship satisfaction	happiness, satisfaction, adjustment
Significant other predictor variables (with examples):	
Illness beliefs	causal attributions, illness perceptions
Behavioural responses	solicitous, distracting, punishing, facilitating
Affect	anxiety, depression, distress, anger, irritation
Expressed Emotion	emotional over involvement , criticism, hostility, warmth

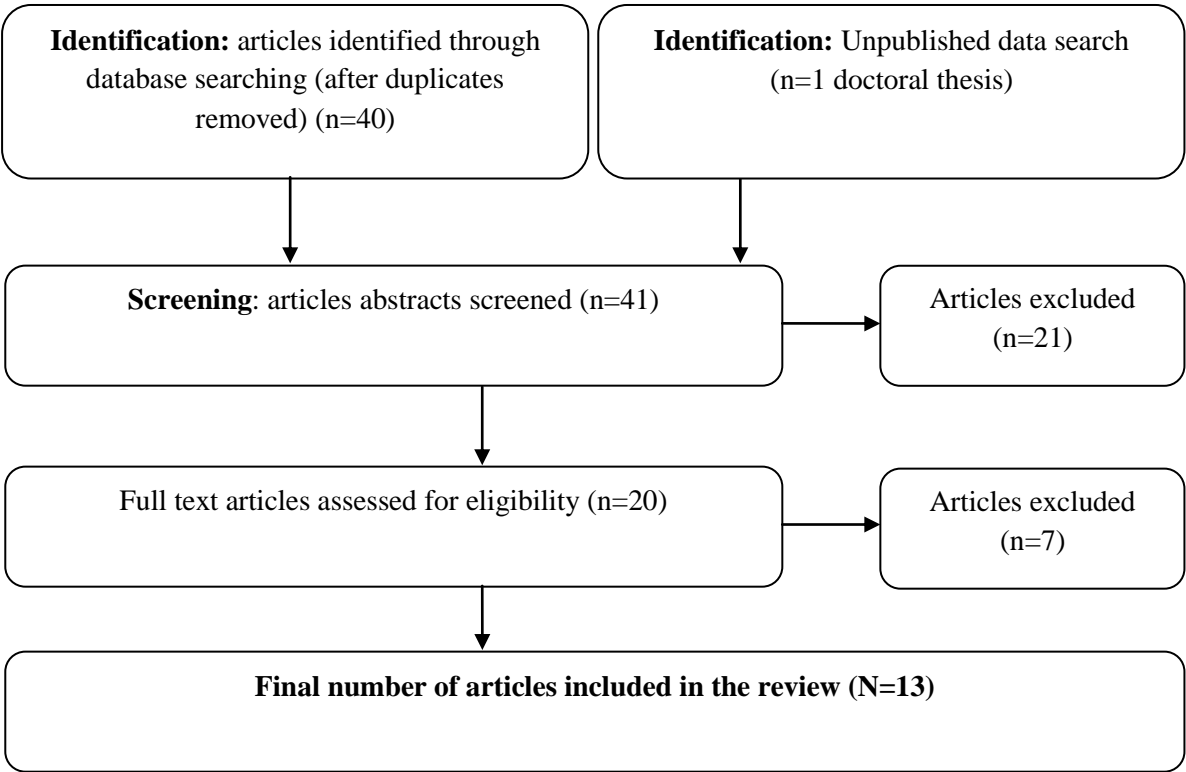
1.5.3.2 Article Selection

Patient inclusion criteria and outcome variables of interest were defined prior to the article search and selection (see Table 1). To be eligible for inclusion, articles had to include patients with a clinical diagnosis of CFS or ME. Studies also had to address at least one of the two review objectives; to examine significant other responses to CFS/ME, or to assess significant other factors in association with patient outcomes. Only articles published from 1988, the date when the first modern definition of CFS was published (Holmes et al., 1988), were sought and included.

The initial search produced a total of forty articles once duplications were removed, and one unpublished doctoral thesis. Twenty-one articles were excluded after screening the abstract for relevance to the review objectives, and the remaining full text articles were obtained and preliminary data extracted to assess against the inclusion and exclusion criteria. A further seven articles were excluded due to the patient population reported being below 16 years of age, and also due to an inability to distinguish CFS/ME from a general category of medically unexplained symptoms or syndromes (MUS). Five articles were identified that assessed significant other responses without assessment of patient outcomes, or did not report direct associations between significant other factors and patient outcomes. However, these articles were retained since they were relevant to the first review objective. Eight articles were identified that assessed patient outcomes in association with significant other predictor variables. This included the unpublished manuscript, which was accepted for publication in the period following the initial search (Brooks, et al., 2012), resulting in a total figure of 13 relevant published articles. Figure 1 demonstrates the number of studies included and excluded at each stage of the identification and screening process. To assess reliability, a second doctoral psychology student also selected articles to be included in the final synthesis. Of those full-text articles reviewed, consensus was reached on fifteen articles,

with initial disagreement on four articles. After discussion, it was agreed that these four articles did not meet the review inclusion criteria and the final thirteen articles agreed upon. In addition, a quality assessment was conducted for each of the selected articles; a tool developed for use with diverse methodological designs, including mixed methods, was selected as appropriate for use with the literature included in the synthesis (Sirriyeh, Lawton, Gardner, & Armitage, 2012).

Figure 1: Flowchart illustrating the stages of article selection and data extraction for the review.



1.5.3.3 Data Extraction and Synthesis

Table 2 provides an overview of the relevant data extracted from each included article, identifying both the significant other response variables and patient outcomes reported within each study, where applicable. The authors synthesized the major findings emerging from the data in line with the review objectives. This is summarized in the results section, and presented separately for each specific review question.

1.5.4 Results

1.5.4.1 Significant Other Responses to CFS/ME: Overview

Before attempting to establish how significant other responses to CFS/ME may impact upon patient outcomes, it is important to first consider how significant others react when faced with the illness in a close relative or friend. In total, the search identified seven relevant papers which examine significant other adjustment and coping (Ax, 1999; Ax, Gregg, & Jones, 2002), in addition to beliefs about the illness; significant other beliefs and responses; and the association between significant other beliefs and patient outcomes (Ax, et al., 2002; Brooks, et al., 2012; Heijmans, et al., 1999; Kelly, Soderlund, Albert, & McGarrahan, 1999; Richards, Chaplin, Starkey, & Turk, 2006; K. White, Lehman, Hemphill, Mandel, & Lehman, 2006). Significant others report difficulties associated with living with a patient with CFS/ME. Different stages of the illness give rise to varying levels of significant other adjustment, and the coping strategies employed by significant others appear to be influenced by a number of factors. The beliefs held by significant others have been found to be similar to those of patients in terms of beliefs about the factors responsible for the onset of the illness, and in relation to ongoing symptoms or illness events. Additionally, there is evidence linking significant other beliefs with their emotional and behavioural responses. The evidence linking significant other beliefs and responses to CFS/ME will be reviewed in the following sections, and the association between significant other beliefs and patient outcomes will be discussed subsequently.

1.5.4.2 Significant other adjustment to CFS/ME and coping strategies.

Significant others experience negative consequences as a result of the condition; over half report CFS/ME has had a negative impact upon their life and their relationship with the patient (Kelly, et al., 1999). Negative emotional outcomes resulting from the

development of relationship difficulties have been reported, such as experiencing guilt or embarrassment over not providing substantial levels of support (Ax, et al., 2002). Further practical limitations and obstacles within everyday and family life as a result of the CFS/ME are often raised, for example, disruption of family roles, financial difficulties and anger experienced as a result of the condition (Ax, et al., 2002; Kelly, et al., 1999). However, significant others retrospectively report that they manage these difficulties more effectively over time, alongside increasing adjustment to the condition. Initial optimism that the condition would improve gives way to acceptance, although doubts over the legitimacy of the condition are occasionally raised across the illness course (Ax, et al., 2002). However, in both of these studies diagnostic criteria to determine the presence of CFS/ME is either not employed or reported, therefore raising questions surrounding the representativeness of the findings to the wider CFS/ME population. This is further compounded by a lack of data reported on the significant other sample characteristics within the Kelly et al (1999) study; the quality assessment deemed this study to be one of the poorest quality studies included within the review.

Significant other coping appears to be influenced gender, and by the nature of the relationship with the patient. Within the theoretical framework outlined by Lazarus & Folkman (1987), it was proposed that coping arises in response to an individuals' perception or appraisal of the threat or stressor. Problem-focused coping may include cognitive or behavioural strategies which attempt to alter the source of the stress in the environment, such as making a plan, whilst emotion-focused coping includes attempts at regulating the emotional distress associated with the stressor, such as trying to forget about the situation (Susan Folkman & Lazarus, 1980). Overall, female significant others report engaging in higher levels of both distress reduction (emotion-focused) and stress reduction (problem-focused) coping strategies than their male counterparts (Ax, 1999). The patient-significant other relationship type also impacts upon significant

other coping strategies; parents report using more stress reduction coping strategies than spouses. Furthermore, significant gender differences in distress reduction strategies were revealed within married dyads. Husbands reported reduced levels of distress reduction techniques, resulting in greater disparity in coping strategies within the dyad compared to those partner dyads where the significant other was female (Ax, 1999). These significant other appraisals of their coping strategies are in line with wider reports of gender differences in coping; meta-analytical examination of responses to others' illness as a stressor revealed that men were more likely to report using withdrawal or avoidant strategies, perhaps as a result of perceiving these situations to be less controllable (Tamres, Janicki, & Helgeson, 2002). Furthermore, they were less likely to engage in all forms of coping strategies for any type of stressor, relative to women (Tamres, et al., 2002). Further research should not only describe, but attempt to identify factors that influence coping strategies. This is particularly relevant for male partners, as their levels of coping were highly correlated with patient coping strategies, and these dyads potentially make up a large proportion of the patient-significant other demographic. In addition, the impact of these various coping strategies on patient outcomes is currently unknown, and therefore, future research identifying effective significant other coping strategies would also be beneficial.

1.5.4.3 Significant other beliefs.

Understanding significant other beliefs is an important area of research for a number of reasons. Illness beliefs are proposed to determine an individual's reaction to an illness event, with the aim of regulating behavioural responses and guiding coping strategies (Leventhal, Meyer, & Nerenz, 1980). Therefore, significant other beliefs about CFS/ME are likely to guide their emotional and behavioural responses to the patient's condition. An additional consideration is the potential influence that significant other beliefs may have upon patient illness beliefs, particularly as patients' beliefs have been

identified as important for both symptom experience and informing illness management behaviours (Deale, et al., 1998; Moss-Morris & Chalder, 2003). Therefore, much of the empirical attention has been on establishing the beliefs that significant others hold about the condition, often in comparison to the patient. This research has focused predominantly upon either significant other beliefs about the initial illness onset or beliefs about symptoms and illness-related events. Beliefs surrounding the illness onset may be a pertinent issue for this patient group, particularly in relation to patient feelings of illness legitimacy. However, it is likely that beliefs about the condition and the meaning of symptoms may vary across the course of the condition, as patient and significant other adjustment changes over time. Attributions for ongoing symptom experiences may also be more relevant and informative for understanding illness related behaviours during the maintenance phase (J. Robbins & Kirmayer, 1991). As beliefs about the illness onset and ongoing illness events are proposed to have potentially different functional outcomes it is useful to distinguish between them when examining significant other beliefs.

1.5.4.3.1 Causal attributions for CFS/ME.

Consistent findings with respect to causal beliefs have been identified across studies; patients and significant others report a predominant preference for physical factors in explaining the illness onset, with factors such as infection or disordered immune systems being reported most often (Richards, et al., 2006). Many significant others also select a combination of causal factors (Kelly, et al., 1999), and interestingly, when significant others generated psychological explanations after open-ended questioning, stress, including family related stressors were also often implicated (Richards, et al., 2006). However, whilst the type of causal attributions held within dyads may appear to be highly concordant, the conviction with which significant others hold causal beliefs has been found to be reduced across all attribution types. Significant others endorsed

all casual factors (i.e. viral, external and internal) less strongly, relative to the patient (K. White, et al., 2006).

Significant other beliefs about the condition would be expected to correlate with both emotional and behavioural responses to the condition. Significant others who attributed the onset of the condition to internal patient factors showed increased levels of unhelpful responses (K. White, et al., 2006), that is, behaviours such as encouraging patients to overcome the situation, giving advice, or acting in a forced cheerful way (Johnson, Hobfoll, & Zalcberg-Linetzy, 1993). However, no differences were found in the level of social support provided by significant others when comparing those with predominantly physical causal explanations to those with a dual physical-psychological explanation for CFS/ME (Kelly, et al., 1999). Methodological differences in the measurement of beliefs and responses may be, in part, responsible for the apparent inconsistencies arising between the studies outlined. Significant other causal beliefs were examined using rating scales (Kelly, et al., 1999; K. White, et al., 2006), but the way beliefs were classified and the number of items used to assess this varied between studies. For example, physical vs. psychological causes were rated on four items (Kelly, et al., 1999) compared to internal vs. external causal factors, rated by 11 items (K. White, et al., 2006), although direct comparison of these scales is not possible as the items within the Kelly et al (1999) study are not reported. Attributional beliefs may be elicited through various methodologies (such as rating scales, open-ended questions and spontaneous attributions), each with different associated benefits. Although fewer statements are likely to be obtained, spontaneous attributional statements offer the possibility of generating novel information as they are less determined by the researcher (Gudmundsdottir, Johnston, Johnston, & Foulkes, 2001). This methodology has increased validity for obtaining attributional statements (Barrowclough & Hooley, 2003) and may be the most useful for establishing the types of attributions that patients

and significant others make about the illness. However, in a study of attributional beliefs about myocardial infarction, Gudmundsdottir et al (2001) identified that the content of patient causal attributions was similar across all methodologies, resulting in similar findings for checklists, open-ended questions and spontaneous attributions.

1.5.4.3.2 Attributions for patient symptoms and illness events.

Significant others also demonstrate highly similar illness beliefs to those held by the patient (Heijmans, et al., 1999). Congruent attribution styles within dyads have also been identified when focusing upon the patient symptom experience (Butler, Chalder, & Wessely, 2001). In Butler et al's, investigation, both patients and significant others were asked to report on common physical symptoms, giving the likely cause for their own and their significant others' symptom experience. Potential attributions for those common symptoms can be ascribed to either physical (somatic) causes, which reflect beliefs that there is something wrong within the body, (e.g. 'there is something wrong with my muscles, nerves or brain'); psychological causes (e.g. 'I'm anxious or nervous'), or most commonly, environmental (normalized) attributions, such as 'I've exerted myself or drunk a lot of coffee' (J. Robbins & Kirmayer, 1991). CFS/ME patients tended to make somatic attributions for symptoms, including those they had never experienced, and for the symptom experience of others. Significant others demonstrated a typical normalizing attributional style for their own symptom experience, yet despite this, attributed patient symptoms to physical abnormalities most often, in line with patient beliefs (Butler, et al., 2001). The evidence would seem to confirm high concordance of dyadic beliefs about patient symptoms and illness events in CFS/ME.

Furthermore, significant other attributions for symptom events have been linked with significant other emotions and behavioural responses. Attributions obtained through

analysis of spontaneous significant other utterances demonstrated that significant others who attributed negative symptom changes and illness events to personal and internal patient factors were more distressed (Brooks, et al., 2012). Within the wider literature, these types of attributions have been consistently associated with increased levels of significant other criticism and hostility towards the patient (Barrowclough & Hooley, 2003), and indeed, in the Brooks et al study, were also associated with significant other rejecting-hostile responses on the Family Response Questionnaire (FRQ; Cordingley, et al., 2001). Additionally, beliefs that attributed high levels of patient controllability over symptoms and illness events were associated with higher levels of significant other encouragement to rest (Brooks, et al., 2012). This therefore implies that significant others believed that patients could control their symptoms by resting, which is in contrast to the principles of CBT or GET, as recommended by the UK National Institute for Health and Clinical Excellence (NICE) guidelines (NICE, 2007).

In addition to methodological considerations regarding the measurement of attributional beliefs, differences in measurement of significant other responses may also further explain inconsistencies within the literature. Significant associations between significant other beliefs and responses were only identified when examining specific significant other behavioural response styles (Brooks, et al., 2012; K. White, et al., 2006) rather than overall level of social support (Kelly, et al., 1999). Precise measurement of beliefs, behaviours and outcome variables may lead to a better understanding of the correlates of these interpersonal processes in CFS/ME and enable direct, specific comparisons between studies.

1.5.4.4 Significant other beliefs and patient outcomes.

The nature and content of significant other beliefs has been considered, yet the extent to which these impact upon long-term patient outcomes remains relatively under

researched in comparison to the wider literature. Only two published articles to date have examined the association between significant other beliefs and patient outcomes (Heijmans, et al., 1999; K. White, et al., 2006). Both identified that patient social and emotional functioning was poorer when associated with significant other causal beliefs that imply some degree of patient responsibility (or that minimize the role of physical causal factors) in the onset of the condition. Heijmans et al (1999) also considered how incongruent illness beliefs within the patient-significant other dyad may impact upon patient outcomes.

We know that both patients and significant others tend to make physical causal attributions for the onset of the condition (see section 1.2i). However, worse patient psychological wellbeing, specifically increased patient anxiety, depression and rumination, was associated with significant others holding stronger beliefs that the CFS/ME onset was due to internal patient factors, such as stress, depression or overwork (K. White, et al., 2006). Attributions made to external or viral factors did not however significantly relate to patient outcomes (K. White, et al., 2006). Similarly, significant other beliefs that minimized physical causes for the illness onset were also associated with poorer patient social functioning and vitality (Heijmans, et al., 1999). It is possible that significant others identify poorer psycho-social functioning in patients and therefore attribute the illness to these factors. However, the evidence suggests that attributing responsibility to the patient for any aspect of the condition is associated with increased distress for both patients and significant others (Brooks, et al., 2012; K. White, et al., 2006). These findings are in line with the wider literature, whereby those significant others who make patient-responsibility attributions and self-blaming attributions also report increased distress (Barrowclough & Hooley, 2003). Although the direction of causality cannot be established from cross-section examination of these

relationships, these associations are particularly relevant, given the controversial aetiology and fluctuating nature of the condition (Prins, et al., 2006).

Alternatively, poorer patient outcomes may arise as a result of discordance within the dyad. Significant other endorsement of internal or psychological causal factors would therefore not be in line with patient models of their illness (that is, arising as a result of physical or external factors). Dyadic belief incongruence has been identified as important for a number of patient and significant other factors within the wider literature (Cano, et al., 2004; Martire, et al., 2006). However, Heijmans et al (1999) examined dyadic illness representations using the Illness Perception Questionnaire (IPQ; Weinman, Petrie, Moss-Morris, & Horne, 1996) and identified that significant other beliefs in a shorter illness timeline, relative to the patient, were actually correlated with better patient functioning (activity, psychological adjustment and vitality). There are a number of issues to note whilst interpreting the results; dyadic beliefs were, in general, very similar across the sample and the direction of associations to outcomes is hard to interpret. Additionally, the timeline dimension showed low internal reliability; which raises questions about the extent that the items capture the timeline aspect sensitively. On the basis of these findings, systematic examination of significant other beliefs and dyadic belief incongruence in association with significant other responses would seem to be warranted, particularly with reference to patient outcomes.

1.5.4.5 Relationship Quality and Patient Outcomes: Overview

The most consistent evidence for the role of significant other variables in association with patient outcomes has been obtained by examining aspects of the dyadic relationship. Three papers specifically assessing relationship quality in association with patient outcomes were identified (Blazquez, Guillamo, Alegre, Ruiz, & Javierre, 2012; Goodwin, 1997, 2000), and a further two assessing relationship satisfaction in addition

to other significant other factors (Heijmans, et al., 1999; Schmalting, et al., 2000). Almost all of these papers have examined relationship quality in association with patient reported illness outcomes of symptom experience and indicators of disability. However, further preliminary evidence has indicated that relationship quality may potentially impact upon observable indicators of physical functioning in patients. Poorer patient outcomes have been associated with low relationship quality, although contrasting evidence has also implied that high relationship satisfaction is associated with increased disability, suggesting two potentially divergent interpersonal mechanisms. High relationship satisfaction has also been found to moderate the association between solicitous significant other responses and patient outcomes. In addition, level of support, empathy and conflict within the dyad have been highlighted as specific aspects of relationship quality that are important for patient outcomes.

1.5.4.5.1 Low relationship quality.

Persuasive evidence demonstrating the negative correlates of poor relationship quality has been obtained from a pair of studies examining the role of marital adjustment in CFS/ME (Goodwin, 1997, 2000). Several aspects of the marital relationship were examined from a patient, significant other, and dyadic point of view, in association with several patient outcomes. Increased symptom levels (total number of symptoms experienced and level of problematic symptoms) were found to be associated with lower overall relationship adjustment, as reported by the patient, significant other, and within the dyad (Goodwin, 1997). Similarly, this was replicated with increased symptom transition (i.e. pattern, frequency, duration of symptoms) as the main patient outcome variable (Goodwin, 2000). Goodwin (1997) identified that reports of marital adjustment were comparable for both patient and significant others and additionally, that patient outcomes were predicted by both patient and significant other relationship variables. However, several limitations with these studies must be noted. Firstly,

patients were recruited prior to the 1994 CDC criteria for CFS/ME (K. Fukuda, et al., 1994), and consequently patient eligibility for inclusion is determined by patient self-report of a practitioner diagnosis. In addition, the patient outcome measures utilised within these studies raise questions about the reliability of the findings reported. Both measures of ‘problem symptoms’ and ‘symptom transition’ are taken from unpublished doctoral data and therefore no previous psychometric data on these measures exist; the results must be considered in line with these limitations. It has been noted elsewhere that significant others who report low levels of relationship happiness also experience high levels of distress and increased reporting of ‘concern for self’ responses (Brooks, et al., 2012). This demonstrates the importance of relationship quality for both patient and significant other wellbeing. Furthermore, the association between low significant other relationship happiness and specific behavioural responses offers a potential explanation for the association between low relationship quality and increased symptom severity.

In addition to self-reported patient outcomes, a recent study demonstrated an empirical association between relationship quality and observable measures of patient functional capacity (Blazquez, et al., 2012). A number of patient cardio-respiratory responses, such as heart rate and oxygen intake during breathing, taken at rest and low activity, were examined in association with both patient and significant other reported relationship adjustment. These physiological responses have been investigated in a number of studies with CFS/ME patients, many showing a reduction in functional capacity relative to controls (Nijs et al., 2011). However, since these measures reflect patient aerobic capacity, they are thought to be important for a number of reasons; potentially highlighting underlying physiological mechanisms in CFS/ME, or alternatively, for informing knowledge on the physiological implications of reduced activity associated with CFS/ME (Cook, Nagelkirk, Poluri, Mores, & Natelson, 2006;

Nijs, et al., 2011). Blazquez et al (2012) identified that poorer dyadic adjustment was associated with poorer ventilatory efficiency at rest, although this association during activity was only observed for those patients who were high in anxiety. It has been noted previously that anxiety may impact upon performance during these experimental paradigms (Inbar et al., 2001), however it is conceivable that patient level of anxiety may also be highly correlated with relationship satisfaction. Tentative conclusions arising from the data note that poorer relationship adjustment appears to be associated with poorer patient cardio-respiratory responses. The findings would seem to suggest that the patient-significant other relationship may be interacting with psychobiological factors to impact upon health outcomes within this group although further evidence would be necessary to establish these relationships more clearly, and the implications for patient illness outcomes.

It is also worth noting that all of these studies (Blazquez, et al., 2012; Goodwin, 1997, 2000) have examined female patients only, confined to heterosexual relationships and mostly in married dyads. Whilst this may be applicable to a significant proportion of patients with CFS/ME, it will of course not be representative of all individuals with the condition, and therefore is limited to examining the role of relationship quality within this specific subgroup only.

1.5.4.5.2 High relationship quality.

In comparison with the bulk of the literature, high levels of relationship satisfaction have also been linked to poorer functional patient outcomes. High levels of patient reported relationship satisfaction have been found to be associated with high levels of patient disability (Schmalings, et al., 2000). Furthermore, relationship satisfaction was found to moderate the association between significant other solicitous responses and patient disability for highly satisfied relationships only; high relationship satisfaction

strengthened the association between solicitous responses and patient disability. In addition, relationship satisfaction also moderated the association between solicitous responses and fatigue severity for all patients; the impact of solicitous responses upon fatigue severity increased as relationship satisfaction increased within the dyad. Although these findings may seem counter-intuitive upon first inspection, it is possible that the significant other beliefs, emotions and responses associated with high relationship satisfaction are impacting on patient outcomes in a different way to those generated in dyads where relationship quality is low.

1.5.4.5.3 Specific aspects of relationship quality.

Goodwin (1997, 2000) identified that in addition to overall relationship adjustment; patient symptom reports (total number and problem symptoms) were associated with high levels of patient perceived conflict and reduced significant other empathy. Patient perception of symptom transition, that is, the extent to which the illness or symptoms are perceived to be in a state of change (Goodwin, 2000), was also associated with reduced levels of patient and significant other empathy, reduced significant other support and increased perceived conflict. These trends are mirrored in the Heijmans et al (1999) study; disagreement within the dyad relating to the role of biological factors in the onset of the condition was also associated with reduced patient relationship satisfaction (Heijmans, et al., 1999), which may reflect perception of low significant other support. Indeed, qualitative investigations of patient experiences of living with CFS/ME identified reoccurring themes surrounding the role of significant other empathy and support; when the legitimacy of CFS/ME was questioned by significant others, patients perceived reduced levels of support and empathy (Dickson, et al., 2007). Additionally, patient reports highlighted that significant other support would have engendered increased feelings of wellbeing and coping, however, lack of understanding

resulted in feelings of rejection and reduced confidence in communicating the illness to others (Dickson, et al., 2007).

Therefore, low relationship quality is associated with both poorer patient reported and observed outcomes (Blazquez, et al., 2012; Goodwin, 1997, 2000). Presently, the evidence seems to imply that low relationship quality is characterized by the perception of high conflict, in addition to low levels of support and empathy within the relationship. Increased ‘concern for self’ significant other responses are associated with low significant other relationship satisfaction, which is also associated with increased levels of distress (Brooks, et al., 2012). It is possible that these responses may arise as a result of distress, or alternatively, that having a partner who is concerned for themselves may negatively impact upon distress and relationship satisfaction within the dyad. High relationship satisfaction appears to be associated with different significant other responses; primarily those which are solicitous in nature (Schmaling, et al., 2000). It seems feasible to speculate that, given high levels of relationship satisfaction and solicitous responses; patients within these dyads may perceive high levels of support and empathy and lower levels of conflict, although further empirical research is required to establish if this is the case.

1.5.4.6 Significant Other Behavioural Responses and Patient Outcomes: Overview

Theoretically, it is proposed within the wider literature that behavioural responses may impact upon patient outcomes in a number of ways; significant others may inadvertently increase disability by responding with behaviours that reinforce patient dependent and ill behaviours, or may exacerbate illness behaviours via their own responses leading to an increase in patient distress (Kerns, Southwick, et al., 1991). Four relevant empirical papers were identified (Brooks, et al., 2012; Romano, et al., 2009; Schmaling, et al., 2000; K. White, et al., 2006), and the evidence examining

significant other behavioural responses in association to patient outcomes in CFS/ME largely supports these theoretical propositions. A number of significant other responses which may reflect a tendency to reinforce patient illness beliefs and behaviours have been identified across studies, and include behaviours such as engaging with the patient about the illness, encouraging the patient to rest, and doing tasks on the patients' behalf. These response styles have been associated poorer patient outcomes, primarily increased disability and worse levels of fatigue. Additionally, poorer psychological functioning, including higher levels of anxiety and depression, have also been associated with a different set of significant other responses, particularly those which may be classified or perceived as negative in nature. Both of these types of responses have been found to be predictive of patient illness behaviours. However, there is inconsistency between patient reports of responses and observed behavioural data, which would suggest that it is perhaps the patient interpretation of the response, rather than the response itself, which is impacting on patient outcomes.

1.5.4.6.1 Reinforcing (or solicitous) significant other responses.

Solicitous responses, for example, where the significant other assists or does tasks for the patient, were first examined within the chronic pain literature (Kerns, Turk, & Rudy, 1985), and modified for measurement within CFS/ME populations. Patients who perceived high levels of solicitous behaviour also reported higher levels of fatigue severity and bodily pain (Schmaling, et al., 2000), as well as worse levels of disability (Romano, et al., 2009). However, Romano and colleagues found no significant associations between solicitous responses and patient reported fatigue severity; a single item was used to assess level of fatigue severity at the time of responding (Romano, et al., 2009). Significant other responses using the MPI are measured with respect to how likely the significant other is to make the response in general, whilst fatigue was measured as a momentary variable within this study; this may therefore account for the

inconsistencies between studies. However, solicitous responses were found to predict not only higher levels of fatigue and disability but also patient reported illness behaviours, such as seeking help, or expressions of fatigue and pain (Romano, et al., 2009). In line with theoretical propositions, these significant other responses appear to be potentially reinforcing illness behaviours within this patient group, which may precede poorer patient outcomes.

Further evidence, using an alternative classification of significant other behavioural responses, has been obtained recently by Brooks et al., (2012). Increased patient disability was also found to be associated with high levels of significant other 'active engagement'; a response style which includes behaviours such as finding out about, and discussing the illness with the patient (Cordingley, et al., 2001). Although this may appear to be a fairly neutral, or even positive, response style, it is possible that by recognizing and assisting the patient to engage with the condition, patient negative illness beliefs and behaviours are reinforced. It has been suggested that solicitous-style responses may also indirectly impact upon patient outcomes as a result of reinforcing perceptions of being ill, or decreasing patient beliefs of self-efficacy (Itkowitz, Kerns, & Otis, 2003).

Finally, significantly increased levels of patient fatigue and disability across the sample were associated with significant others encouraging patients to engage in rest (Brooks, et al., 2012). Although these response styles are conceptualized differently, the extent to which significant others are encouraging patients to rest, either directly (i.e. 'encouragement to rest' responses), or indirectly, for example, by reducing the number of opportunities patients have to engage in everyday physical activities (for example, by increased solicitous responses), may result in reduction in overall activity levels. Patient beliefs about the role of activity have been shown to be important for activity limitation (Silver et al., 2002), and the adverse effects of excessive patient resting on

symptom maintenance in CFS/ME has been documented within the literature (Deale, et al., 1998). Since these response styles have been linked to poorer outcomes, particularly increased patient disability, reduced activity may mediate these response-outcome associations (Wearden & Emsley, in press). However, it is impossible to establish the direction of causation in cross-sectional studies, and therefore further empirical examination of these factors is required to establish if an increase in these response styles precedes increases in patient symptom severity and disability.

1.5.4.6.2 Negative significant other responses.

In comparison, negative responses (sometimes called punishing responses in the pain literature), which include behaviours such as expressing irritation, frustration or anger towards the patient or leaving the room, (Kerns, et al., 1985), have also been associated with patient outcomes in line with the hypothesized theoretical associations. Elevated levels of patient depression were associated with perceptions of negative responses from their significant other (Romano, et al., 2009). Negative responses were also significant predictors of both increased patient depression and patient illness behaviours (Romano, et al., 2009). Additionally, using an alternative classification of significant other responses, patient perceived ‘unhelpful’ responses were associated with elevated patient anxiety and depression (K. White, et al., 2006). The constituent behaviours for this subscale (SSBQ; Johnson, Hobfoll, & Zalcberg-Linetzy, 1993), such as trying to be cheerful despite the situation or offering the patient advice, seem to reflect a set of normalizing responses. These responses are different to the negative response classification (MPI) subscale, where behaviours such as expressing anger or frustration would be rated, yet these ‘unhelpful’ responses also provoke increased psychological distress within this population, and therefore are potentially being interpreted in a similar negative manner, possibly as demonstrating a lack empathy, or invalidation of the patient’s suffering by the significant other.

The limited evidence would appear to support the notion that patient interpretations of significant other responses have important implications for illness related outcomes and psychological distress, and the meaning attached to the response may be crucial to understanding the relationship between responses and outcomes in CFS/ME. Schmalting et al., (2000) raise this as a suggestion for interpreting these associations, and the dyadic observational data lends further support to the importance of patient perceptions, as the self-report trends were not replicated when observing dyadic interactions; observed negative responses were actually associated with reduced patient-reported disability (Romano, et al., 2009).

The empirical evidence reviewed demonstrates that specific significant other responses appear to be associated with patient outcomes, and, in line with the relationship quality data two general categories of responses are emerging in association with outcomes. Significant others who are highly supportive, but solicitous, may reinforce patient illness beliefs and behaviours associated with poorer outcomes. Yet, these solicitous behaviours may be perceived positively by the patients, as they are associated with high levels of relationship satisfaction. In contrast, negative significant other responses are associated with increased psychological distress. It is possible that the association between perceived negative significant other responses and poorer patient psychological adjustment may reflect a second interpersonal process, highly similar to that identified for low relationship satisfaction (that is, characterized by high conflict within the dyad, low significant other empathy and support; associated with poorer patient illness outcomes).

1.5.4.7 Limitations of the previous literature

As outlined throughout this synthesis, a number of methodological limitations are apparent with the current evidence base; these compromise the reliability and validity

of the findings of the body of literature. Firstly, the quality assessment determined there were a number of areas where studies were could have been improved. For example, none of the studies included reported consideration of statistical power in calculating the size of samples recruited; these vary between studies despite similar analyses being undertaken. These are important issues to consider when examining the potential for both Type I and Type II errors. Furthermore, the diagnostic criteria employed to determine patient eligibility is also a key issue with the current literature; 6 of the studies relied solely on patient reports of receiving a diagnosis from a medical professional. Given the problems that GPs report in confidently diagnosing and managing CFS/ME (Bowen, et al., 2005; Chew-Graham, et al., 2008), this is not recommended as an adequate indicator of CFS/ME caseness. Where possible, researchers should include patients who have been diagnosed by a specialist clinician and whom have met recognized diagnostic criteria, such as the CDC (K. Fukuda, et al., 1994) or Oxford criteria (Sharpe et al., 1991). However, it is worth noting that there may be additional difficulties associated with using different diagnostic criteria (Bagnall, Hempel, Chambers, & al., 2007). The CDC criteria are most often cited within the current sample of empirical papers and the literature more widely (Bagnall, et al., 2007); this requires that several physical symptoms must be present and reflects an assumption of an underlying immune dysfunction, whilst the Oxford criteria require mental fatigue as necessary for diagnosis (Cairns & Hotopf, 2005), suggesting that these may be also be heterogeneous groups. However, use of established criteria enables confidence in the assumption that participants are representative of the population, and allows for comparison with the wider literature.

Several references have been made throughout the synthesis to the properties of the measures used within the current body of literature. It is difficult to summarize the state of current knowledge given the wide variety of measurement techniques used to assess

the constructs of interest. This is relevant to both significant other factors (such as beliefs, behaviors), relationship quality, and patient outcomes; fatigue severity and depressive symptoms were not assessed by the same measure in any two studies included within the review. Only physical functioning was measured consistently across studies (using the SF-36 subscale). Where CFS/ME specific measures are available, it would be advantageous to use these, or those more widely reported within the literature, such as patient outcomes assessed by the National Outcomes Database (Crawley et al., 2013).

1.5.4.8 Summary

In summary, the review has identified a number of key findings. Significant others experience negative consequences following the development of CFS/ME in a close relative; however, these are managed more effectively over time with increasing adjustment to the condition (Ax, et al., 2002; Kelly, et al., 1999). Furthermore, coping strategies are associated with a number of factors such as relationship type and significant other gender (Ax, 1999). In general, significant others tend to hold similar beliefs to patients about the onset of the condition and indeed, ongoing symptom experience (Butler, et al., 2001; Heijmans, et al., 1999; Kelly, et al., 1999; Richards, et al., 2006). However, belief incongruence within the dyad can have negative consequences (Heijmans, et al., 1999). Additionally, significant other beliefs about the illness have been associated with their emotional and behavioural responses, and furthermore, those significant other beliefs that imply a degree of responsibility on the behalf of the patient are associated with worse social and emotional patient outcomes (Brooks, et al., 2012; Heijmans, et al., 1999; K. White, et al., 2006).

The remaining evidence suggests two potential interpersonal processes that are impacting upon patient outcomes. The first appears to be characterized by low

relationship satisfaction, negative (or delegitimizing) significant other responses, poorer patient psychological outcomes and high symptom severity. Increased patient symptom experience is associated with low relationship satisfaction, in addition to low support, lack of empathy and high conflict (Blazquez, et al., 2012; Goodwin, 1997, 2000). Low relationship happiness in significant others is also associated with significant other poorer psychological adjustment and increased concern for self responses (Brooks, et al., 2012). Significant other responses that are perceived negatively by the patient are also associated with higher levels of patient anxiety and depression (Romano, et al., 2009; K. White, et al., 2006). In contrast, a second set of significant other responses to CFS/ME appear to be characterized by solicitous responses which reinforce patient illness beliefs or behaviours (Brooks, et al., 2012; Schmalting, et al., 2000). These responses appear to be associated with increased levels of patient disability and fatigue, which are potentially mediated by reduced patient activity levels. However, these significant other responses to CFS/ME are also associated with high levels of patient relationship satisfaction (Schmalting, et al., 2000). Taken together, the review has identified the importance of two interpersonal processes in patient outcomes in CFS/ME.

1.5.5 Future Recommendations and Conclusions

Patient affective, cognitive and behavioural responses have been identified as important in CFS/ME symptom maintenance and perpetuation, in line with cognitive-behavioural models (Deary, et al., 2007; Surawy, et al., 1995). The evidence outlined within the review supports the proposition that interpersonal processes, and significant other factors in particular, are also important to consider with regards to symptom perpetuation in CFS/ME (Deary, et al., 2007). In particular, two interpersonal mechanisms have been identified, each with different cognitive and behavioural correlates and differential associations with relationship quality. Both of these proposed

mechanisms have been found to associate with poorer illness outcomes and patient distress.

This review aimed to address the evidence examining not only significant other responses to CFS/ME, but also the relationship that these responses may have upon patient outcomes. Significant others are thought to be important for informing patient understanding of the condition (Brooks, et al., 2013; Cordingley, et al., 2001); the evidence reviewed confirmed patients and significant others generally hold highly congruent beliefs about the illness (Butler, et al., 2001; Heijmans, et al., 1999; Kelly, et al., 1999; Richards, et al., 2006). Discordance within the dyad was identified as potentially unhelpful for patient psychological outcomes (Heijmans, et al., 1999; K. White, et al., 2006), mirroring the associations within the chronic pain literature, where incongruent illness perceptions have also been associated with negative responses and reduced perception of support (Martire, et al., 2006). Whilst these associations have not been examined directly, these aspects of relationship quality were highlighted as important for patient illness experiences (Goodwin, 1997, 2000), and furthermore, patients report significant other support and empathy as crucial for wellbeing and adjustment to the illness, experiencing a lack of these as delegitimizing (Dickson, et al., 2007). Future research could seek to examine these associations between dyadic belief incongruence and relationship factors, in line with the wider literature (Lobban, Barrowclough, & Jones, 2006; Martire, et al., 2006). An integrated, theory-driven approach to examining these significant other factors in a systematic way, would be beneficial to further clarify the role of these interpersonal processes in association with patient outcomes.

The evidence reviewed supports current UK National Institute for Health and Clinical Excellence (NICE) guidelines recommending that significant others should be involved in patient treatment programs where appropriate, and also be provided with the

information and support they require (NICE, 2007). In examining significant other responses to CFS/ME, some of the negative consequences associated with the experience of living with a close relative with CFS/ME have been explored (Ax, et al., 2002; Kelly, et al., 1999). In addition, aspects of the patient-significant other relationship have also been shown to be important for significant other wellbeing (Brooks, et al., 2012) in line with the wider literature suggesting that CFS/ME may impact upon the whole family (Donalek, 2009). Addressing significant other adjustment may be particularly important, especially since significant other coping strategies have been found to be associated directly with patient coping (Ax, 1999), and considering the evidence linking low dyadic relationship quality and poorer patient outcomes (Goodwin, 1997, 2000). The development of significant other-focused therapeutic interventions that take into account demographic factors such as gender and relationship type may facilitate alternative, helpful significant other coping strategies (Ax, 1999; Tamres, et al., 2002), particularly early in the illness course, where both patients and significant others experience difficulties understanding and adapting to the illness (Ax, et al., 2002; Brooks, et al., 2013). In addition, significant other psycho-education aimed at enhancing understanding of explanatory models may be particularly beneficial for ensuring that significant others well-intentioned responses to the condition are in line with current management strategies (Brooks, et al., 2013).

The findings outlined in this review need to be considered alongside the various methodological issues that have been raised. In particular, significant other factors (i.e. beliefs, behavioural responses) and patient outcomes (i.e. symptom severity) have been measured in different ways across studies, making direct comparisons and firm conclusions difficult to draw from the limited evidence available. Widely used patient outcome measures, such as those listed in the UK CFS/ME national outcomes database (Collin et al., 2011) may be particularly useful to include in future studies, in addition

to CFS/ME specific significant other measures where possible, such as the Family Response Questionnaire (FRQ; Cordingley, et al., 2001). Other validated measures such as the IPQ (Moss-Morris et al., 2002; Weinman, et al., 1996) or MPI (Kerns, et al., 1985) enable comparisons with the wider literature and other patient groups. An additional limitation is the cross-sectional, largely correlational nature of those studies reviewed. It is recommended that the longitudinal relationships between these significant other factors and patient outcomes are explored in future studies. Additionally, alternative methodologies such as experience sampling methodology (ESM; Csikszentmihalyi & Larson, 1987) or ecological momentary assessment (EMA; Stone & Shiffman, 1994) may be particularly suited to examining the potential fluctuations in symptom experience within CFS/ME. These methodologies offer advantages over traditional self-report techniques, allowing for the assessment of temporal relationships between variables within the flow of daily life (Palmier-Claus et al., 2011). Additionally, more systematic inclusion of significant other reports of these variables in future research would reduce potential common method variance arising from patient reports of both significant other factors and illness related outcomes, which must be considered as a potential confound within the current literature.

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Table 2: Summary of studies examining significant other responses to CFS/ME and the association to patient outcomes

Study	Demographics							Study assessment			Key results	Study quality	
	Patient			Significant other			SO type (%)		SO variables (measure)	Patient outcomes (measure)			
	N and CFS definition	% Female	Age (mean)	N	% Male	Age (mean)	Partner	Parent					
Ax (1999)	155 medical professional diagnosis of CFS/ME/PVF	with	76.8	40.4	94	50.5	48.45	62	32	Coping strategies ¹ (WCQ)	-	SO coping strategies influenced by gender; females reported higher levels of problem and emotion focused coping strategies, relationship type (parent or partner) was also important.	.71
Ax et al., (2002)		n/a			17	71	44	71	6	Coping ² Illness adjustment ²	-	Difficulties are highlighted, but become more manageable over time with increased adjustment.	.69
Blazquez et al., (2012)	40 CDC criteria		100	41	40	100	44.6	100		Relationship adjustment ¹ (32 item DAS)	Cardio-respiratory responses ³	Dyadic relationship adjustment variables were associated with patient indicators of functional capacity (i.e. cardio-respiratory responses) at resting and low intensity activity levels.	.50
Brooks et al., (2012)	30 CDC criteria		73.3	41	30	40	48	60	33.3	Attributional beliefs ² (LACS) Response styles ¹ (FRQ) Distress ¹ (GHQ) Relationship	Fatigue severity ¹ (CF) Disability (physical functioning) ¹ (SF-36)	Increased SO distress and negative responses associated with attributing illness events to personal & internal patient factors. Encouragement to rest responses associated	.65

									satisfaction ¹ (6-point VAS)			with SO controllability attributions and poorer patient outcomes.	
Butler et al., (1999)	50 criteria	Oxford	56	39	44	50	39.6	100	Attributional beliefs ¹ (Modified-SIQ)	-		SO's made predominantly normalising attributions for their own symptoms but somatic attributions for patient symptoms, in line with patient beliefs.	.67
Goodwin (1997)	131 medical professional diagnosis of CFS	with	100	42.9	131	100	45	100	Marital adjustment: Empathy ¹ (DPT) Support & Conflict (IPRI)	Number of symptoms ¹ Problem symptoms ¹ (DCFSSS)		Increased problem symptoms associated with reduced marital adjustment and high conflict. Higher number of symptoms associated with lower SO empathy.	.48
Goodwin (2000)	131 medical professional diagnosis of CFS	with	100	42.9	131	100	45	100	Marital adjustment: Empathy ¹ (DPT) Support & Conflict (IPRI)	Symptom transition ¹ (DPSTS)		Increased patient symptom transition was associated with high conflict, reduced marital adjustment, and reduced SO support and empathy.	.45
Heijmans et al., (1999)	49 with medical professional diagnosis of CFS		92	40.4	49	-	42.7	100	Illness representations ¹ (IPQ)	Disability ¹ (SF-36)		Dyadic differences in timeline beliefs; shorter SO timeline beliefs associated with better patient functioning. Poorer outcomes associated with reduced SO biological causal beliefs.	.52
Kelly et al., (1999)	41 (diagnostic criteria not reported)		83	46	25	-	-		Illness beliefs ¹ Impact of CFS/ME ¹ Social support ¹ (ISSB)	Depression ¹ (BDI; POMS) Stress ¹ (PSS)		High prevalence of negative consequences for SO's. No difference in level of support reported according to SO causal beliefs. No differences in patient outcomes for those with/without support.	.48

Richards et al., (2006)	21 criteria	Oxford	63	17*	21	-	-	100	Illness beliefs ²	-	Highly similar patient and SO beliefs about onset; preference for physical causes with some psychosocial causes identified.	.55	
Romano et al., (2009)	111 CDC 6 met criteria for Idiopathic CF		93	44.4	94	63	46.2	75	3	Response styles (patient reported) ¹ (MPI) Relationship satisfaction ¹ (7-item DAS) Perceived illness behaviours ¹ (PBC) Observed responses ⁴	Fatigue severity ¹ (1 item MAF) Disability (physical functioning) ¹ (SF-36) Pain intensity ¹ (11-point VAS) Depression ¹ (CES-D) Observed illness behaviours ⁴	Sollicitous responses associated poorer physical functioning. Negative responses associated with increased patient depression. Observational data did not replicate self-reported associations; observed negative responses were associated with decreased patient illness behaviours and better physical functioning.	.67
Schmaling et al., (2000)	119 criteria	CDC	76	39.0		n/a		100		Response styles (patient reported) ¹ (MPI)	Fatigue severity ¹ (16 item MAF) Disability (physical functioning) ¹ (SF36)	Sollicitous responses associated with greater fatigue and bodily pain; moderated by relationship satisfaction. High relationship satisfaction associated with increased disability.	.62
White et al., (2006)	105 medical professional diagnosis and CDC criteria	with	88	47	87	-	50	60		Attributional beliefs ¹ Response styles (SO reported) ¹ (SSBQ)	Psychological adjustment ¹ (BSI)	SO causal beliefs for internal patient factors associated with poorer psychological outcomes and more unhelpful SO responses. Unhelpful SO responses associated with increased anxiety and depression.	.53

Note.

Dashes indicate where information was not reported.

SO denotes significant other.

* denotes median value.

SO variable and patient outcome assessment: ¹ Indicates measured by questionnaire measure; ² Indicates measured by interview; ³ Indicates measured by patient physical task; ⁴ Indicates measured by dyadic observational task.

Acronyms for questionnaire measures used: **SO responses:** FRQ – Family response questionnaire (Cordingley, et al., 2001); ISSB – Inventory of socially supportive behaviours (Barrera, Sandler, & Ramsay, 1981); MPI – Multidimensional pain inventory (Kerns, et al., 1985); SSBQ – Social support behaviour questionnaire (Johnson, et al., 1993); WCQ – Ways of coping questionnaire (S. Folkman & Lazarus, 1988). **SO illness beliefs:** IPQ – Illness perception questionnaire (Weinman, et al., 1996); LACS – Leeds Attributional Coding System (Stratton, Munton, Hanks, Heard, & Davidson, 1988); SIQ – Symptom interpretation questionnaire (Sensky, MacLeod, & Rigby, 1996). **Relationship quality:** DAS – Dyadic adjustment Scale (Spanier, 1976); DPT – Dyadic perspective taking questionnaire (Long, 1990); IPRI – Interpersonal relationship inventory (Tilden, Nelson, & May, 1990) **Patient outcomes:** BDI – Beck Depression Inventory (Beck & Steer, 1989); CES-D – Centre for Epidemiological studies depression scale (Radloff, 1977); CF – Chalder fatigue scale (Chalder, Berelowitz, Pawlikowska, Watts, & et al., 1993); DCFSSS – De Groot Chronic Fatigue syndrome symptom scale (De Groot, 1989); DPSTS – De Groot perceived symptom transition scale (De Groot, 1989); MAS – Multidimensional assessment of fatigue (Belza, Henke, Yelin, Epstein, & Gilliss, 1993); PBC – Pain behaviour checklist (Kerns et al., 1991); POMS – Profile of mood states (McNair, Lorr, & Droppleman, 1992); PSS – Perceived stress scale (Cohen, Kamarck, & Mermelstein, 1983); SF-36 - The Short Form (36) Health Survey (SF-36; Ware & Sherbourne, 1992); VAS – Visual analogue scale.

1.6 Summary and thesis aims

The literature outlined within this chapter has provided the rationale for examining significant other factors in association with patient outcomes in CFS/ME. The findings arising from the systematic review noted that significant other beliefs about the condition and behaviours towards the patient might be of particular interest, in addition to overall relationship quality; it was speculated that two potential interpersonal mechanisms existed, each with different associated factors. Firstly, negative significant other responses and low relationship satisfaction appear to be associated with poorer patient psychological outcomes and increased symptom severity, whilst in contrast, solicitous significant other responses and high relationship satisfaction appear to be associated with increased levels of patient disability and fatigue. Furthermore, several methodological limitations with the current literature were highlighted, including the predominance of cross-sectional research lacking a clear theoretical framework to guide empirical lines of enquiry. In addition, measurement issues with the previous literature make comparisons to the wider literature difficult. Therefore, the Expressed Emotion (EE) framework was selected in an attempt to address those research questions posed, and overcome some of the methodological issues highlighted. The individual aims of each empirical study will be outlined below:

- The first empirical study will examine patient outcomes in association with significant other EE. In line with the hypothesised mechanisms, patient outcomes will be examined separately in association with high critical comments and high EOI. Furthermore, the inclusion of a longitudinal design will help to identify if EE can predict patient outcomes over time.
- The second empirical study will focus on significant other beliefs about CFS/ME in association with significant other EE status. This will help identify those beliefs that

may be important for the presence of high-EE. In addition, building upon the previous research, this study will also examine dyadic belief incongruence in the context of EE status.

- Finally, the third empirical paper will use an experience sampling methodology to examine significant other behavioural responses in association with patient outcomes during momentary assessments, conducted within the course of everyday life. Both patients and their significant others will report on the occurrence of solicitous and negative behaviours; analyses will examine momentary associations between significant other responses and patient outcomes, in addition to potential changes in patient outcomes following significant other responses.

Chapter 2: Methods

After providing an overview to the empirical papers, the following sections will first discuss general methodological considerations common across each of the studies, followed by detailed discussion of specific aspects of the methodologies employed in each of the empirical papers. A brief description of each methodology is outlined within each of the empirical papers presented subsequently within the thesis, however, due to journal word limit constraints additional relevant information will be considered here, such as CFI adaption and coding (paper 1), dyadic belief incongruence calculation (paper 2), and experience sampling methodology (paper 3).

2.1 Overview of the empirical papers

The first chapter presented within this thesis has provided a review of the literature, including a systematic review of the literature examining significant other responses to CFS/ME, and the association between these responses and patient outcomes. The following chapters will present the empirical studies included within the current thesis; these will be presented in the format appropriate for submission in peer-reviewed journals.

The data presented within the current thesis was collected as part of two studies. The data collected from the first study contributed to the first and second empirical papers presented within this thesis. Where aspects of the methodology are relevant for both empirical papers 1 and 2; study 1 will be referred to. The data collected as a part of the second study contributed to the third empirical paper presented within this thesis. Therefore, for clarity, each of the empirical studies presented within this thesis will be numbered as outlined below. The title and a brief description of each paper are presented here:

Paper 1: The impact of significant other Expressed Emotion (EE) on patient outcomes in chronic fatigue syndrome. This paper reports on the association between significant other EE and patient outcomes measured cross-sectionally, and longitudinally at six-month follow-up.

Paper 2: Understanding Expressed Emotion in CFS/ME: an investigation into significant other illness beliefs and dyadic belief incongruence. This paper examines factors that may contribute to EE, namely significant other illness beliefs. In addition, the association between dyadic belief incongruence and EE is explored.

Paper 3: Significant other behavioural responses and patient CFS/ME symptom fluctuations in the context of daily life: An experience sampling (ESM) study. This paper examines the temporal associations between significant other responses and patient outcomes in using an experience sampling methodology (ESM) paradigm.

2.2 General methodological issues

2.2.1 Sample size calculations

A priori power calculations were calculated for each of the studies, and are outlined below.

Although testing hypotheses in study 1 involves comparing variables of interest based upon the EE rating of the significant other, it was not possible to estimate the likely proportion of significant others in high- and low-EE categories within a CFS/ME sample due to the lack of previous data within this patient group. As correlational analyses were planned for paper 1 in addition to the group comparisons, the sample size calculation for study 1 was based upon previous research in to interpersonal processes in CFS/ME (Romano, et al., 2009; Schmaling, et al., 2000). These studies primarily employ correlational analyses; the significant effect sizes reported within previous

studies ranged from 0.25-0.3 (Pearson r values). Therefore, the estimated sample size was therefore calculated using the critical values reported for Pearson's coefficient and a significance value of 0.05; an r of 0.304 would require 40 participants to demonstrate statistical significance at $p < .05$, whereas an r of 0.25 would require a sample of 60 participants. The target sample size was set at 60 participant dyads to ensure sufficient participants were recruited to provide adequate statistical power, particularly considering the longitudinal design, and potential participant attrition.

The sample size for the second (ESM) study was also calculated based on conventions within previous studies of this kind. Traditional methods for power calculation are not appropriate, as they do not account for the multi-level structure of ESM data; the combined random effects associated with the fixed effects of X must also be taken into account, in addition to traditional assumptions (Bolger & Laurenceau, 2013). Each participant could potentially contribute a total of 60 momentary assessments to the dataset, however, as these assessments are nested within individual days and participants, statistical techniques are required that account for the lack of independence between observations. In addition, there is currently no guidance in relation to minimum sample sizes necessary when recruiting participants as dyads for ESM studies. Therefore, the convention of 30 participants was followed (Oorschot, Kwapil, Delespaul, & Myin-Germeys, 2009), and the target sample size was set at 30 participant (patient-significant other) dyads.

2.2.2 Recruitment

Recruitment for both studies was conducted through UK North-West NHS services or self-referral arising as a result of study advertisements distributed to local and national CFS/ME support groups and organisations. The author collected all of the data for both Study 1 and Study 2.

The general procedure for recruitment was the same for both Study 1 and Study 2; the primary source of participants was through liaising with North West Specialist CFS/ME services and clinicians. Initially, prior to study commencement, presentations were made to clinicians working within regional CFS/ME services, outlining the study details and eligibility criteria. Routes to recruitment were flexible so that potential participants could have included those patients currently on treatment waiting lists, those newly inducted in to the service and those currently on clinician case-loads. R&D approvals were granted from all respective NHS trusts.

Those potential participants who expressed an interest in the study were given a Participant Information Sheet (PIS; Appendix 2, Study 1; Appendix 4, Study 2); they then either took these away and contacted the author directly, or alternatively provided their contact details, or expressed verbal consent for the clinician to do so. Potential participants who provided their contact details were then contacted by telephone after a period of 3-5 days; during this initial telephone correspondence a study screen was completed. This screening ensured that the patients met study inclusion criteria using a checklist according to the Oxford criteria for CFS/ME (Sharpe, et al., 1991). In addition, significant other inclusion criteria were fully explained to ensure that the patient had an appropriate significant other who would also be willing to take part in the study; the procedure for significant other opt-in to the study was also explained. Any questions arising about the research or the procedure were also addressed during this initial telephone contact.

Subsequently, for those patients and significant others who were willing to participate, an arrangement was made for a research meeting with the author. These were organised at a time and place most convenient to the participant, and were flexible so that interviews could have been conducted at their own or a relative's home, within the CFS/ME clinic, or at the University. Patient and significant other interviews could be

conducted during the same research visit or individually, depending upon the preferences of the participant. All participants were posted questionnaire measures to complete at home prior to the research meeting.

For any individuals who self-referred to the study, leaflets and advertisements about the study were distributed with local CFS/ME support groups (such as Bolton/Bury ME/CFS support group) and national CFS/ME organisations (such as AYME). A PIS was sent to the patient in the first instance if they had not already received a copy of this information, and subsequently the procedure followed was that outlined above.

The procedure for recruitment for Study 2 varied from that outlined above in one respect only; those participants who had completed Study 1 and had consented to be contacted about future, linked studies were also approached with information about Study 2. Therefore, this was an additional route to recruitment for Study 2. Furthermore, Study 2 was adopted on to the CLRN Portfolio (UKCRN ID 12696) and therefore received Clinical Research Network support.

2.2.2.1 Inclusion and exclusion criteria

Inclusion and exclusion criteria were imposed on both studies to optimise the possibility of valid and generalisable conclusions arising from the data; therefore ensuring that all research questions posed within these studies could be addressed. Participants were recruited as dyads, and therefore the study criteria outlined for both studies included both general and specific criteria.

All patients were required to have received a diagnosis of CFS/ME, made by a specialist clinician, and confirmed by administration of a checklist according to the Oxford Criteria (Sharpe et al, 1991) for CFS/ME (see Appendix 5) to be eligible for inclusion within the current studies. The Oxford Criteria for CFS/ME were selected as

they require that fatigue must affect both physical and mental functioning (Sharpe, et al., 1991), and are easier to operate than the CDC criteria for CFS/ME (K Fukuda et al., 1994); the Oxford Criteria have also been previously used to determine eligibility for CFS/ME treatment trials conducted within the UK (Wearden et al., 2010; P. White, et al., 2011). In addition, patients were required to have an appropriate significant other who was willing to participate in the study. It was explained to patients that significant others should be the individual with the most day-to-day involvement with the patients' life. Inclusion restrictions were therefore set so that significant others must live with, or have over ten hours of face-to-face contact with the patient per week.

Further general inclusion criteria were set for all participants, and included:

- Sufficient levels of English comprehension and production to complete all study measures
- Aged 18 years or above
- Able to provide fully informed consent
- Significant others had to provide consent to record the Camberwell Family Interview

A general exclusion criterion was outlined for significant others, so that any participant experiencing an on-going physical or mental health condition which impacted on their ability to participate in study procedures were not eligible for inclusion in the study. The significant other inclusion and exclusion criteria were explained to patients within the initial study brief to ensure there was a suitable significant other who was eligible for participation. This exclusion criterion was set to avoid recruiting dyads where the significant other may also have been experiencing a chronic disorder; it was expected that the role of significant other factors would be qualitatively different within these

dyads. No specific exclusion criteria were outlined on the basis of patient co-morbid disorders, although they were recorded, where applicable.

Following the inadvertent recruitment of two participants aged 17 years old into Study 1, substantial amendments were submitted to each of the NHS research ethics committees (for studies 1 and 2) in order to reduce the minimum age for inclusion to 16 years of age or above, in line with the regional adult CFS/ME services. This request received approval for Study 2, and therefore the study inclusion criteria were modified to include all participants over the age of 16. For Study 1, the ethics committee deemed that the original inclusion criteria should be maintained. The data from these two participants was retained within the study on the provision that participant and parental consent to do so was obtained.

2.2.3 Ethical considerations

2.2.3.1 Approval

Prior to commencement, the author compiled each study protocol and documentation in preparation for review by an NHS Research Ethics Committee; specific details for each study are outlined below.

Study 1: The study was granted approval from the North West 3 Research Ethics Committee, Liverpool East on 31st May 2011 (reference 11/NW/0198; Appendix 1) following attendance at the research ethics committee meeting. The study protocol outlined that a series of studies would be nestled within this study; for the current thesis this included an examination of significant other Expressed Emotion in association with patient outcomes (cross-sectionally and longitudinally); and an examination of dyadic illness perceptions. In addition, 4 NHS Research and Development departments granted approval for the study, however, recruitment primarily took place in 2 of these:

Lancashire Care and The Liverpool Royal and Broadgreen University Hospitals NHS Trusts.

Study 2: This study was granted approval from the North West 9 Research Ethics committee, Greater Manchester West on 11th August 2011 (reference 11/NW/0495; Appendix 3) following attendance at the research ethics committee meeting. In total, 3 NHS Research and Development departments granted approval for the study, but similarly to Study 1, participants were recruited primarily from Lancashire Care and The Liverpool Royal and Broadgreen University Hospitals NHS Trusts.

2.2.3.2 Participant burden

Participant burden was identified as an ethical consideration that was relevant for both Study 1 and Study 2, particularly given the nature of the principle symptoms, such as severe fatigue, associated with the experience of CFS/ME. Therefore, the procedure for each study was designed recognising potential participant burden, and minimising this where possible to avoid risk to potential participants. In Study 1, self-report questionnaires were posted to participants ahead of the research visit to allow participants sufficient time to complete these at a pace that was convenient to them (see Appendix 6). In addition, patients could post these back to the researcher at a later date if they had not managed to complete them by the research meeting. Interview schedules were limited so that patient interviews lasted approximately 30-45 minutes, and significant other interviews approximately 1 hour. Patients were also offered the opportunity to complete the interview in a second research meeting should they experience high levels of fatigue during the interview.

In preparing Study 2, it was recognised that ESM protocols can be time consuming and burdensome for participants. In an attempt to keep this to a minimum, each momentary sampling assessment was restricted, and items included within the protocol were

research hypothesis driven. Each assessment took approximately 2-3 minutes to complete. A thorough individual briefing session was provided to each participant ahead of the ESM phase of the study. In addition, all newly developed items were piloted to identify potential issues in clarity; these steps were taken to ensure that participants fully understood the items and procedure, therefore reducing effort and potential attrition from the study. Furthermore, to avoid unnecessary duplication and burden to those participants recruited from Study 1, baseline measures completed in Study 1 were used as the non-ESM measures in Study 2.

2.2.3.3 Participant distress

As the studies outlined in this thesis involved the discussion and disclosure of personal and potentially sensitive information it was possible that participants may have experienced distress as a result of participation. Firstly, all participants were made aware of the procedure, so that they were informed about the nature of the questions, particularly during interview. A number of safeguards were put in place, should participants become distressed during their involvement within the study. These included an offer for the participant to pass over any questions that may have been uncomfortable, or to interrupt or terminate the interview. It was decided that if any worrying levels of distress were uncovered during the interview (such as suicidal ideation), discussion would first take place with the supervisory team, or if deemed necessary, with the participant's GP. The author was to ask the patients' permission to disclose such information, with the exception that in the extremely unlikely event of severe and imminent risk to self or other, such disclosure would be made without the patients' permission.

2.2.3.4 Participant confidentiality

All participant interviews were conducted individually, and privately. However, it was necessary to audiotape all interviews, to allow for later EE codings to be made. All audio-recordings were numbered to ensure that participants could not be identified, and in accordance with the University of Manchester policy all audio recordings, transcripts derived from them, and all paper questionnaires were stored in secure locked filing cabinets, or password protected files on encrypted password protected hard-drives. All individuals involved in data transcription, or any other aspect of access to the data were asked to sign a confidentiality agreement beforehand.

In study 2, participant confidentiality was a key consideration to overcome; the study protocol was designed so that both patient and significant others would complete momentary assessments at the same time for the duration of the study. As the primary hypotheses were concerned with assessing the impact of significant other responses, it was identified that partners viewing the other participants' responses may result in difficulties for participants, and may impact upon the truthfulness of data reporting. To address this issue, it was stressed to both participants during the study briefing that it was highly important to answer all assessments confidentially and as independently from the other participant, as was reasonably practicable. Additionally, to minimise the risk of any participant breach of confidentiality, electronic data collection was used, so that all assessments, including data on significant other responses were unable to be viewed again by the participant (or any other individual) once entered. Data was uploaded from the individual Smartphone using a specialised set of platform tools only accessible to the authors, once the study was completed.

2.2.3.5 Safe Lone working

To ensure that the author was safe whilst out in the community particularly during home visits, University lone working policies were followed. All details of home visits

were provided to a nominated individual whilst out of the office on research visits. In addition, clinicians within the specialist services agreed to identify any individual cases where they felt a home visit may pose a particular risk to the author.

2.3 Specific methodological considerations

2.3.1 Paper 1: The impact of significant other Expressed Emotion on patient outcomes in chronic fatigue syndrome.

Paper 1 involved the cross-sectional and longitudinal investigation of the association between significant other Expressed Emotion (EE) and patient outcomes; the role of high levels of significant other critical comments and emotional over-involvement (EOI) were examined separately. The aim of the study therefore was to identify if patient outcomes such as fatigue, disability and depression are linked with these EE subscales in meaningful ways. These relationships were investigated cross-sectionally, and the predictive power of EE on over time was also investigated in a longitudinal design. The methodological considerations of these designs are addressed below.

2.3.1.1 Cross-sectional

Cross-sectional designs involve the assessment of relationships between two constructs or variables, occurring at the same time point. Cross-sectional designs may assess statistical associations between variables within an individual, or within pairs of individuals; differences between groups based upon a variable of interest can also be explored. In study 1, group comparisons were conducted examining potential differences in patient CFS/ME outcomes according to the EE-status (that is, high- or low-EE) on the relevant EE subscales (critical comments and EOI). Correlational analyses were also planned in addition to the group comparisons; however, these are not reported within the empirical paper. There are a number of limitations associated with cross-sectional research, namely that the direction of associations cannot be

ascertained due to both measurements occurring at the same point. In addition, correlation analyses may also be limited by the effect of unmeasured or unaccounted for confounding variables. Therefore, a longitudinal design element was also incorporated in to study 1; the advantages will be discussed below.

2.3.1.2 Longitudinal

A longitudinal design assesses the relationship between variables of interest at two separate time points; typically a ‘baseline’ assessment is completed, and subsequent follow-up assessments are made at a later time point, such as several months later. In study 1, a six-month patient follow-up assessment was included within the protocol; at this follow-up, all patient outcomes assessed at baseline were repeated. The methodological advantage of such a design is that it allows the predictive validity of variables, in this case, significant other EE, to be assessed in association with outcomes over time. Furthermore, assessment of patient outcomes at baseline allowed previous level of functioning to be controlled for in multivariate analyses conducted on the follow-up data. This enables the effect of predictor variables to be determined. However, a potential issue with longitudinal designs is retention of participants within the sample at follow-up; initial power calculations identified that a sample size of between 40 and 60 participants should be recruited in order to enable planned analyses to be conducted. The target baseline sample size was therefore set at 60 participant dyads to protect against longitudinal participant attrition, and ensure sufficient power was retained (that is >40 participant dyads) at follow-up.

A further consideration with respect to the longitudinal design employed in study 1 is the extent to which change was anticipated to be observed in outcomes over time within the patient sample. In order to meet the target sample sizes required, the principle route for recruitment within the current study was through contact with

regional specialist CFS/ME services; often a long duration of time elapsed between patient diagnosis and induction to these services. Consequently, the majority of the patients included within the sample had established CFS/ME. In spite of this, many of these participants were beginning treatment programs for the first time; both of these factors may be important to consider when examining change in patient outcomes at the follow-up assessment. An additional section addressing the change in patient outcomes within the current sample has been presented in Chapter 3 (see section 3.6); it is presented separately as, due to the journal word count, these data were not included within the empirical paper submitted for publication. The data are presented after Paper 1 (page 125).

2.3.1.3 CFI adaption for CFS/ME

The Camberwell Family Interview Schedule (Vaughn & Leff, 1976) was used within the current study to determine significant other EE ratings. The CFI was developed originally for use with relatives of people with a schizophrenia diagnosis (Brown & Rutter, 1966; Leff & Vaughn, 1985) but can be adapted for use within other patient populations (Wearden, Tarrier, Barrowclough, et al., 2000). Therefore, several modifications were necessary in order to make the conventional interview schedule applicable to CFS/ME. In its original format, section A of the CFI first enquires about the onset of the patients' troubles, and then focuses on the current episode; this is less appropriate for the illness course typically associated with CFS/ME, and as such, this section was modified. In the current version, the period between the initial onset and the current functioning was explored, focusing upon difficulties associated with diagnosis, and fluctuations in symptom experience across this period. Section B of the interview focuses upon symptoms; this section was also modified within the current study. Sections that focused upon symptoms such as overactivity or hallucinations and delusions were removed, as were sections referring to destructive or bizarre behaviours,

violence, and those focusing on gambling, drinking and street-drug use. More relevant sections focusing on aspects of fatigue and bodily complaints typical of CFS/ME (such as pain, nausea, headaches) were included instead. Further topics focusing on illness management (such as types of treatments explored, and the involvement and impact on the family), and the impact of CFS/ME on day-to-day life were also included. An example of the modified CFI schedule can be found in the appendices (Appendix 7).

2.3.1.4 CFI coding and reliability estimates

The CFI interviews were coded by the author, in line with the EE training manual (Leff & Vaughn, 1985), with a selection of interviews independently rated by a second trained rater. After a small selection of the first interviews had been coded it was clear that the interviews contained very little material relevant for critical comments. As a result, a manual outlining further guidance for determining borderline and dissatisfied comments was created (Appendix 8), and all borderline and dissatisfied statements were subsequently extracted and coded from all CFI interviews. In line with the EE training manual, borderline statements were identified as those which ‘felt’ critical, but did not meet the standard criteria on the basis of sufficient content or tone. Dissatisfaction was coded when the significant other expressed some dissatisfaction or regret concerning the behaviour, or a desire for thing to be different, without explicitly blaming the patient. After discussion with Dr Christine Vaughn, the reliability estimates for the current study were calculated in line with conventional methods. Complete agreement was established for overall EE status ratings and significant other EOI. Reliability estimates for the other EE subscales of critical comments ($r = 0.89$), positive comments ($r = 0.78$), warmth ($r_s = 0.95$) and hostility ($k = 0.5$) were also found to be acceptable.

2.3.2 Paper 2: Understanding Expressed Emotion in CFS/ME: an investigation into significant other illness beliefs and dyadic belief incongruence.

The aim of the second paper presented within this thesis was to investigate significant other illness beliefs about CFS/ME in order to develop an understanding of the development of significant other EE. As previous research has also identified that relationship quality may be associated with dyadic belief incongruence, this was also investigated with respect to significant other EE status. A discussion about the calculation of dyadic incongruence will be presented in a subsequent section.

Level of significant other EE was derived from the CFI ratings as outlined above for Paper 1. The overall EE status (that is, high- or low-EE) was operationalised as the measure of EE; a cross-sectional design was also employed, with all participant measures of illness perceptions collected at the same time point as the CFI was conducted. Patients completed a standard version of the revised Illness Perception Questionnaire (IPQ-R; Moss-Morris, et al., 2002) for CFS/ME. Significant others completed an adapted version of this; the modifications will be discussed in the following section. However, perceptions of illness identity were derived from the Cognitive Behavioural Response Questionnaire (CBRQ; Skerrett & Moss-Morris, 2006) rather than the IPQ-R. The rationale for including this version was due partly to the increased number of symptom items included in the CBRQ (27 vs. 13). In addition, the CBRQ asks participants to make judgements about the cause of the symptom. Those items which are endorsed can be attributed to various causes; symptoms attributed to the condition, stress and reduced activity are discriminated (see Appendix 9).

2.3.2.1 Significant other IPQ-R adaption

The IPQ-R was adapted so that significant others were asked to respond in line with their own personal beliefs about the patients' CFS/ME. Consequently, the instructions

and items were modified to reflect this; therefore an item such as ‘I have the power to influence my CFS/ME’ taken from the patient version was presented as ‘They have the power to influence their CFS/ME’ in the significant other version. These changes were applied to each of the 38 items in the standard version of the IPQ-R. In addition, a further 16 items were included in the significant other version; these were modified from the IPQ for Schizophrenia: Relatives’ version (IPQS-Relative; Lobban, Barrowclough, & Jones, 2005). This measure was developed to assess relatives’ beliefs about Schizophrenia, and includes four additional subscales not included in the IPQ-R version. Two of these subscales reflect significant other versions of those subscales included in the patient version of the IPQ-R; one assesses beliefs about significant other personal control, whilst the other explores beliefs about the negative consequences experienced by the significant other. Two further subscales reflect beliefs about self-blame, either with respect to the patient or the significant other (Lobban, et al., 2005). The subscales assessing significant other consequences (9 items), significant other perceived control (4 items) and significant other self-blame (3 items) were also included with the current study. The significant other personal negative consequences subscale was previously shown to correlate with a number of other factors, including significant other negative emotional responses, objective burden and a trend towards associating with higher critical comments (Lobban, et al., 2005). In addition, controlling behaviours are thought to be important for the development of EE (Hooley & Campbell, 2002); therefore these additional subscales were included to assess additional information that may be potentially relevant in understanding of the expression of EE within this population. The wording of these 16 items was also modified for relevance to CFS/ME rather than Schizophrenia; references to ‘mental health problems’ were adapted to ‘CFS/ME’ where applicable, for example, ‘To some extent, what I do can determine whether their mental health problems get better or

worse’ was modified to ‘To some extent, what I do can determine whether their CFS/ME gets better or worse’. Significant other versions of the IPQ-R are provided in Appendix 10. The internal consistencies calculated for each subscale are provided within the tabular information for the empirical paper (see Table 10).

2.3.2.2 Calculating dyadic belief incongruence

Across the wider literature, illness representation “congruence” has been measured primarily in two ways. Patient illness representation ratings are subtracted from those made by the significant other (or the other way around) to create a mean difference score (Heijmans, et al., 1999). Alternatively, a median split is conducted for each illness representation dimension, therefore categorising patients and their significant other as high or low scorers for that dimension, grouping dyads according to similarity or dissimilarity (Karademas, Zarogiannos, & Karamvakalis, 2010). Similar and dissimilar (or congruent and incongruent) beliefs can be further categorised to take into account the direction of the beliefs, accounting for positive and negative beliefs. Therefore, patients and significant others may share positive or negative representations (although congruent) or two different types of incongruent beliefs (Figueiras & Weinman, 2003). However, there are potential issues with interpretation of this method. For example, if the majority of patients reported holding strong negative beliefs on a subscale, such as personal control, the median point may therefore discriminate those who ‘strongly disagree’ from all others including those that may ‘disagree’ up to those who ‘strongly agree’ with the statements. This may result in participants with largely negative beliefs being classified as those in the ‘positive’ domain, and raises questions about the validity of such methods for categorisation of dyadic belief congruence. Given that IPQ responses are rated on a likert scale, with two points either side of a neutral point, there may be difficulties with interpretation of incongruence no matter

which way it is calculated, which may account for the generally inconsistent relationship to illness outcomes and psychological adjustment throughout the literature.

There has been limited examination of significant other illness perceptions or indeed, dyadic belief incongruence, in relation to Expressed Emotion. However, of those studies identified, dyadic belief incongruence was calculated by subtracting patient scores from significant other scores (Kuipers et al., 2007; Lobban, et al., 2006); a similar procedure was reported in the only paper examining dyadic belief incongruence in CFS/ME (Heijmans, et al., 1999), whereby significant other scores were subtracted from those reported by the patient. Therefore, in line with the relevant literature it was decided that dyadic belief incongruence would also be calculated by subtraction on the individual IPQ subscales for which data was available for both patients and significant others, and that this would follow the methodology outlined within the previous EE research within this area (Kuipers, et al., 2007; Lobban, et al., 2006). The rationale for subtracting patient scores from significant others' scores was to aid interpretation of the direction of results; a positive score would therefore represent a higher significant other score on the dimension (i.e. significant other maximisation), whilst a negative score would indicate a stronger belief held by patients (i.e. significant other minimisation).

2.3.3 Paper 3: Significant other behavioural responses and patient CFS/ME symptom fluctuations in the context of daily life: An experience sampling (ESM) study.

The aim of paper 3 was to investigate whether significant other negative and solicitous responses were associated with changes in patient symptom severity and reported disability on a moment-to-moment basis. Specifically, the relationship between negative significant other responses and symptom severity was investigated; the meditational role of patient distress was also examined. In addition, the relationship

between solicited significant other responses and patient disability was investigated; activity limitation as a mediating factor was examined. An experience sampling methodology was therefore employed as it offers several advantages; namely that temporal associations between variables, such as significant other responses, and fluctuations in experiences, such as symptom severity can be explored. Previous cross-sectional research has examined significant other responses reported by the significant other, in addition to those perceived by the patient; it is unclear whether there are any systematic differences in the relationships identified with outcomes according to the respondent. Therefore, both patients and their significant others were recruited and reported on significant other responses at those time points where dyadic contact occurred. The following sections will provide an in depth discussion of experience sampling methodology, and the key methodological considerations in designing study 2 will be outlined.

2.3.3.1 Experience Sampling Methodology

Experience Sampling Methodology (ESM) (Csikszentmihalyi & Larson, 1987) also known as ecological momentary assessment (EMA) (Stone & Shiffman, 1994) utilises repeated participant assessments over a specific period of time. ESM was developed from daily diary methods, whereby repeated daily assessments are made within the flow of daily life (Myin-Germeys, Delespaul, & van Os, 2003). Participants may be asked to report on a number of variables such as their affects, beliefs, behaviours, the social context and appraisal of the social context; this can refer to the very moment when the prompt arrives, or alternatively, participants can be asked to report on the above variables in reference to the time elapsed between the most recent and preceding beep (Myin-Germeys & van Os, 2007; Palmier-Claus, et al., 2011). Typically, ESM protocols require participants to respond immediately after a signal, such as a beep, on ten occasions throughout waking hours on each day, for a period of consecutive days

(Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001; Palmier-Claus, et al., 2011). It is suggested that ESM has high levels of ecological validity, as a result of the often naturalistic setting (Stadler, Snyder, Horn, Shrout, & Bolger, 2012).

2.3.3.1.1 The emergence of computerised ESM (ESMc) formats

ESM assessments can be carried out in different formats, broadly grouped into paper (ESMp) or computerised (ESMc) formats (Kimhy et al., 2006). Paper formats typically include a daily diary, whilst computerised ESM techniques include the use of watches, personal digital assistants (PDAs) and Smartphones (Palmier-Claus, et al., 2011). With the advancing technological developments over recent years, an increasing number of investigations have utilised computerised forms of ESM data collection. Recently, the feasibility of electronic ESM data collection, particularly using mobile phone technology has been explored; these methods have been shown to be valid and acceptable for participants (Ainsworth et al., 2013; Kimhy, Myin-Germeys, Palmier-Claus, & Swendsen, 2012; Palmier-Claus et al., 2013), including patients where pain and other physical symptoms are the primary outcomes of interest (Burton, Weller, & Sharpe, 2007).

A central problem associated with ESM research is the extent to which researchers can be confident that participants complete diary entries in response to the signal, known as participant compliance, (Kimhy, et al., 2006). This is a particular problem for ESMp, with the estimates of compliance of paper-and-pen methods having varied considerably (Stone, Shiffman, Schwartz, Broderick, & Hufford, 2002). Computerised methods of ESM assessment offer the advantage of enabling ‘time-stamping’ of data entries, and so can avoid back or forward-filling of entries by locking momentary assessments after a certain period (Palmier-Claus, et al., 2011; Sorbi et al., 2006a). This ensures that any assessments that are gathered truly reflect the time course being sampled (Trull &

Ebner-Priemer, 2009), which allows for greater confidence in the reliability of data gained. ESMc techniques also readily offer the possibility of branching of items (Le, Hat, & Beal, 2006), whereby the items presented within the momentary assessment can vary dependent upon participant responses to earlier items. A further advantage of ESMc is the ability to ensure confidentiality with respect to participant responses (Kimhy, et al., 2012).

2.3.3.1.2 The utility of ESM in chronic health conditions

A large number of studies have usefully employed ESM to examine various aspects of mental health difficulties, particularly psychosis (Myin-Germeys, et al., 2003; Myin-Germeys et al., 2009; Oorschot, et al., 2009; Palmier-Claus et al., 2010). However, there are a number of methodological advantages that have been identified with respect to employing ESM protocols in the assessment of physical health outcomes; namely that these methodologies overcome some of the difficulties associated with symptom reporting in traditional cross-sectional research (Stone & Broderick, 2007).

Consequently, several studies have examined the potential utility of momentary assessment techniques in the experience of chronic pain (Broderick, Schwartz, Schneider, & Stone, 2009; Litcher-Kelly, Stone, Broderick, & Schwartz, 2004; Schneider et al., 2012; Stone, Schwartz, Broderick, & Shiffman, 2005). ESM techniques offer the advantage of attempting to assess temporal relationships between variables (Stadler, et al., 2012), and therefore, for research examining changes in patient outcomes linked to a particular event, ESM techniques appear to be highly appropriate (Kim, Kikuchi, & Yamamoto, 2013). Empirical comparisons of momentary, daily and recalled reports of symptoms over equivalent time periods have been explored within patients experiencing chronic pain, and large differences between these measurements have often been noted. Level of pain reported at a momentary level has

been shown to be significantly lower than that recalled and reported retrospectively for the same week (Stone, Broderick, Shiffman, & Schwartz, 2004; Stone, et al., 2005). ‘Peak’ and ‘end’ effects are phenomena thought to bias traditional symptom recall, whereby extreme or recent symptom experience may influence judgments of pain or fatigue (Redelmeier & Kahneman, 1996). Indeed, research into chronic pain has suggested that patients do not systematically aggregate or average reports of experienced pain when asked to recall over a given period, such as the previous week (Broderick, Stone, Calvanese, Schwartz, & Turk, 2006). Furthermore, estimates are likely to be biased by a number of factors; concurrent experience of symptoms at the time of reporting, and salient events that occurred in conjunction with the symptom experience increase the likelihood of symptom recall, whilst periods of non-symptom experience are likely to be omitted from memory when making these judgements (Broderick, et al., 2006; Stone & Broderick, 2007; Stone et al., 2003). A further consideration that has been explored within the chronic pain literature is the extent to which ESM paradigms are able to capture the within-person variability; this has been shown to be an important factor predictive of increased symptom recall over the same period (Stone, et al., 2005). In addition, within-person variance has been shown to be almost as great as the variability between participants (Sorbi, et al., 2006a; Stone & Broderick, 2007), and associated with a number of indicators of adjustment, such as depression and interference in social relationships (Schneider, et al., 2012). It has been suggested that it is necessary to understand the within-person variance as a meaningful way of measuring change in symptom severity over time (Litcher-Kelly, et al., 2004).

However, these methodological issues appear to be less clear-cut when examining reports of fatigue within this patient population (Broderick, et al., 2009; Schneider, Stone, Schwartz, & Broderick, 2011). It is possible therefore that the challenges associated with examining momentary assessments of chronic fatigue may differ when

recruiting a CFS/ME sample. The small body of literature using momentary paradigms with patients experiencing chronic fatigue syndrome will be outlined below.

2.3.3.1.3 Momentary assessments in chronic fatigue syndrome

In comparison to chronic pain, relatively few published articles have utilised experience sampling (or similar momentary) paradigms to examine patient outcomes in CFS/ME. Interestingly, the associations between weekly reports of fatigue were identified to be inflated in comparison to momentary reports of fatigue, although these were highly associated (Friedberg & Sohl, 2008), in line with the chronic pain literature (Stone, et al., 2005). Reports of momentary fatigue were also found to significantly associate with momentary negative affect and cross-sectional reports of anxiety, depression and catastrophising (Sohl & Friedberg, 2008). However, the majority of studies have focused upon aspects of patient activity. Patients experiencing CFS/ME have shown significantly reduced activity levels relative to controls especially during afternoon and evening periods of the day (Evering, Tonis, & Vollenbroek-Hutten, 2011); greater physical and psychological symptoms have also been found to be reported during these later parts of the day (Yoshiuchi et al., 2007). In addition, patients' activity was more likely to be classified at 'low' levels for longer periods throughout the day and less likely to be classified as 'high activity' (Evering, et al., 2011). Elsewhere it has been noted that patient reports of fatigue were predicted by engaging in activities that patients found to be fatiguing, and not engaging in activities which patients identified as meaningful (Jason et al., 2009). The conclusions drawn by these authors are, however, limited by the analyses conducted; correlational analysis of the repeated assessments do not take in to account the multi-level structure of the data, which is necessary if these types of investigations are to develop understanding of these complex processes (Stadler, et al., 2012). Further studies have identified that worsening patient physical symptoms occurred five days subsequent to participating in laboratory-

based exercise. Physical symptoms progressively worsened over the remaining period; these effects were not observed in association with cognitive functioning or sleep, and were independent of changes in patient affect (Yoshiuchi, et al., 2007). However, there are a number of methodological issues within this small body of research; patient CFS/ME symptom severity seems to be very seldom measured using these ESM paradigms, instead often measured by traditional cross-sectional methods (Evering, et al., 2011; Jason, et al., 2009; Sohl & Friedberg, 2008). Whilst this may be useful in examining fluctuations in variables of interest, such as activity, with well validated patient outcome measures, the temporal associations between these variables are ignored. This limitation also applies to averaged momentary assessments (Jason, et al., 2009; Sohl & Friedberg, 2008). Yet, these studies identify that electronic data collection methods appear to be acceptable within this population; reported patient compliance within these studies is high. It is clear that there is currently great potential to utilise ESM paradigms further, particularly with respect to understanding the relationship between psychological variables and physical outcomes in CFS/ME (Yoshiuchi, et al., 2007).

2.3.3.1.4 Investigating dyads using ESM

A recent review of the evidence examining social interactions measured using daily experience sampling paradigms identified that patient reports of somatic symptoms, such as levels of pain, in addition to observed changes in physiological functioning, such as blood pressure, are associated with the quality and quantity social support (Stadler, et al., 2012). It has been suggested that examining dyadic interactions within ESM paradigms may be advantageous for a number of reasons. Firstly, it is impossible to tease apart associations in cross-sectional reports, to determine if significant other responses are an antecedent or consequence of patient symptom experience (Itkowitz, et al., 2003); ESM paradigms offer the possibility of investigating the temporal order of

relationships between variables (Stadler, et al., 2012). Furthermore, significant other responses are likely to vary across time and context (Newton-John & Williams, 2006). Indeed, it has been highlighted that the association of responses to patient factors such as catastrophising, may vary over the course of chronic illnesses (Boothby, et al., 2004), and that significant other coping and acceptance of CFS/ME may vary across time (Ax, et al., 2002). Finally, ESM offers the possibility of capturing dyadic interactions as they happen within the natural environment (Janicki, Kamarck, Shiffman, & Gwaltney, 2006). Previously, ESM has been used to examine the role of significant other responses to chronic pain in association with patient pain intensity (Sorbi, et al., 2006a), and disability (Sorbi et al., 2006b). Pain intensity was significantly associated with perceived significant other responses that included reinforcement of pain behaviour and punishment of well behaviours (Sorbi, et al., 2006a). Patient immobility was associated with significant other punishment of well behaviours and patient avoidance behaviours (Sorbi, et al., 2006b). There has been increasing interest the in the use of intensive longitudinal designs for examining dyadic interactions in association with psychological and health outcomes (Bolger & Laurenceau, 2013; Stadler, et al., 2012).

The cross-sectional CFS/ME literature outlined within the systematic review presented in Chapter 1 identified that solicitous responses have been previously associated with greater levels of fatigue and disability, whilst negative responses have shown preliminary relationships with illness behaviours and patient distress (Romano, et al., 2009; Schmalting, et al., 2000). Therefore, the current study was included to extend our understanding of the role of significant other responses by exploring the temporal relationships between responses and fluctuations in patient outcomes.

2.3.3.2 Key methodological considerations for the present study

2.3.3.2.1 Sampling schedule

The current study employed a typical sampling schedule protocol; assessments were made using a stratified sampling strategy, so that one assessment would occur within each 90-minute period throughout the day. No two consecutive beeps would occur later than three hours apart, nor sooner than 15 minutes following the preceding beep. In addition, the sampling schedule employed was synchronised for both participants so that each individual within the dyad was signalled to respond at the same momentary time point. In line with previous research, assessments were sampled between 7.30am and 10.30pm for a period of six days.

2.3.3.2.2 ESM format

The current study followed an ESMc format for signalling participants to complete momentary assessments and for data entry completion. It was decided that this was essential, given that the aim of the study was to assess, primarily, contact with the significant other, and the interactions associated with dyadic contact. It was thought that these questions might potentially be viewed as sensitive, or be uncomfortable for patients to answer, especially if they felt that their significant other may view their responses. Therefore, to ensure that patient confidentiality was maintained, Android (San Francisco) Smartphones were used in the current study, and items presented through the ClinTouch app software (Ainsworth, et al., 2013; Palmier-Claus, Rogers, et al., 2013). At any given momentary assessment participants were signalled by a beep, and presented with a screen alerting them that it was time to complete the questionnaire. Participants had three potential options; they could press the 'ok' button, therefore beginning the momentary assessment; press 'snooze', whereby they would be prompted by a second beep 2 minutes later; or do nothing, in which case, after 15 minutes they would receive a second message informing them that they had run out of time to complete the questions. When participants responded to a momentary assessment they were presented with items individually, and asked to indicate the extent to which they

endorsed the item on the touch screen of the phone (on a scale anchored with ‘not at all’ to a lot2’; see Appendix 12 for screen shots). The screen could be rotated so that items were presented in portrait or landscape orientation, dependent upon participant preference at the time of completion. Patient familiarity with the technology has been previously highlighted as a potentially important factor affecting user acceptability (Burton, et al., 2007; Kimhy, et al., 2012), therefore a full briefing was undertaken with each participant. Participant briefing and debriefing will be addressed in the following section, and the items sampled are discussed subsequently.

2.3.3.2.3 Participant briefing and debriefing

It was important to ensure that participants were comfortable with the equipment and procedure for the current study therefore a detailed briefing procedure was developed. Given the high levels of burden associated with the ESM procedure, thorough briefing was also conducted to help reduce participant attrition as a result of potential lack of adherence to the protocol. The briefing session was usually completed at the participants’ home, and was either conducted separately (for patients and their significant others) or together, depending upon the preferences of the dyad. A briefing procedure was developed (see Appendix 13) which first described the purpose of the study and then addressed the functional aspects of the Smartphone. ESM item-specific information was provided, such as explaining rating scales and ensuring participants understood the meaning of items. This helped increase confidence that participants would complete the assessments in a valid way. In addition, a number of key principles underlying the ESM paradigm were stressed to participants during the briefing session. These included the importance of answering questions as soon as possible after the beep; it was also explained to participants that their responses should be spontaneous, reflecting their feelings in that given moment, and not how they felt in general. The rationale for this was to acquire momentary snapshots throughout the ESM period, in

an attempt to capture potential fluctuations in these variables. Furthermore, participants were reminded that the study was attempting to assess the associations of variables within the flow of daily life, and therefore it was important to fill out as many assessments as possible without changing their typical routine to fit in with the study. Finally, participant confidentiality was addressed; it was explained to participants that once they had completed an assessment none of their answers could be accessed by themselves or another individual other than the researchers, to reassure participants that their responses would remain confidential. It was also stressed that although the schedules were synchronised for both participants, it was important that participants should answer questions as independently as practicably possible.

Contact with participants was maintained throughout the ESM phase of the study and a full debrief was completed at the end of the study. During this debriefing session participants were asked to discuss their experiences of the study; any verbal feedback given with respect to the items, protocol or software was noted. Participants were also provided with a quantitative feedback form (see Appendix 14) to complete and return to the author, either during the debrief session or later by post.

2.3.3.2.4 ESM item inclusion and development

The ESM items included within the current study were based predominantly on the standard diary items (Myin-Germeys, et al., 2001). However, as the research for which the items were developed has largely focused upon psychosis, these diary items were modified in several ways; new items that were more relevant to patient experiences of CSF/ME, and to the testing of the study research questions were developed. Care was taken not to include too many items within each assessment to avoid participant overburden. Furthermore, development of items took in to account current recommendations; the use of extreme items was avoided and both positively and

negatively phrased items were included, particularly with reference to symptom experience (Kimhy, et al., 2012; Palmier-Claus, et al., 2011). The rationale for this was to include items which are likely to vary over the sampling period; increased variability in patient reports result in greater statistical power (Bolger & Laurenceau, 2013). In addition, it was important that the language used for the items was clear and familiar to patients (Kimhy, et al., 2012); this was addressed in a number of ways. Firstly, items from well validated measures, such as the Chalder fatigue questionnaire (Chalder, et al., 1993) and the Work and Social adjustment scale (Marks, 1986) were examined, to develop appropriately worded items, in addition to utilising the expertise within the supervisory team. Finally, items were piloted with a student volunteer, diagnosed with CFS/ME and his partner. Further extensive piloting was conducted with healthy controls in order to establish that the procedural aspects of the methodology (such as beep synchronisation, appropriate item branching and the sampling schedule) were as intended.

All items were rated on a 7-point likert scale and were anchored with ‘not at all’ to ‘a lot’; the only exception being the appraisal of significant other contact items, rated on a 7-point bipolar scale where -3 = very unpleasant, 0 = neutral, 3 = very positive. No numbers were provided on the scales that participants were presented with on the phones. The following momentary items (i.e. referring to the moment immediately preceding the signal to complete the questionnaires) presented below were included in both patient and significant other versions: all momentary items began with the phrase “Before the beep went off I was...” or “Right now I am...”. All ESM items are presented in Appendix 11.

2.3.3.2.4.1 Affect

12 items were included to assess participant affect; 9 of these items were based up previously developed positive (happy, cheerful, relaxed, and satisfied) and negative (guilty, lonely, anxious, irritated and sad) affect subscales (Myin-Germeys, et al., 2001). Two further items (excited and annoyed) were included (Vasconcelos e Sa, Wearden, Hartley, Emsley, & Barrowclough, in preparation), and the item ‘distressed’ was included as a measure of momentary distress.

2.3.3.2.4.2 Activity

Four activity appraisal items were also included, based upon previous ESM items (Myin-Germeys, et al., 2001).

2.3.3.2.4.3 Dyadic contact and Significant other responses

All participants were asked to identify if they were with their significant other at the time of the assessment alert. For those momentary assessments where participants reported contact, four subsequent items were presented relating to the contact (such as, ‘I feel comfortable with this person’ or ‘I would rather be alone’). Additionally, participants were presented with eight significant other response items, thought to reflect the two response styles of interest, in line with the research questions presented throughout this thesis. The wording of these significant other response items were developed based upon the critical and EOI EE subscales (Leff & Vaughn, 1985), solicitous and negative significant other behavioural responses (Kerns & Rosenberg, 1995), and previously developed ESM items examining behavioural control (Vasconcelos e Sa, et al., in preparation). The items were thought to reflect two types of responses, labelled as negative (‘nagging me’, ‘leaving me alone’, ‘irritated with me’ and ‘pushing me to do things’) and solicitous responses (‘checking up on me’, ‘doing things for me’, ‘looking after me’ and ‘helping me’). The order of presentation of these items was randomised. At the end of this section participants were also asked to

appraise the contact with the significant other on a 7-point bipolar scale (as outlined above). Dyadic contact and significant other responses were also assessed at a between beep level (that is, for the time elapsed between the preceding and current momentary assessment) to maximise available sampling opportunities.

2.3.3.2.4.4 Patient only items

2.3.3.2.4.4.1 CFS/ME symptom severity

These items were designed to capture the principal characteristics of CFS/ME, including fatigue, pain and concentration problems, and developed from widely used CFS/ME outcome measures (Chalder, et al., 1993). In total, seven ESM items were developed and included feeling weak, tired, active, well, sleepy, and experiencing pain and ‘mental fog’.

2.3.3.2.4.4.2 Activity management strategies

Four items were designed to assess patient illness management techniques. These items were based upon two subscales included in the CBRQ (Skerrett & Moss-Morris, 2006); activity limiting (‘resting to control my symptoms’ and ‘avoiding activities that might make my symptoms worse’), and all-or-nothing behaviours (‘rushing to get things done whilst I feel able’ and ‘doing things whilst I can’).

2.3.3.2.4.4.3 Patient disability

Six items were included to assess commonly reported aspects of disability, based upon widely used self-report measures of functional disability (Marks, 1986); these referred to work, socialising, leisure activities, household tasks, leaving the house and general activity. A higher score indicated greater patient activity levels in the period elapsed between the previous and current beep.

Each of the newly developed subscales was assessed using a standard factor analysis in STATA, and Cronbach alpha's calculated; these values are reported in paper 3. Although the limitations associated with such an approach for validating ESM subscales were recognised, that is, that these analyses do not account for the multi-level structure of the data, no better alternative was available at present.

2.4 Summary

The information outlined within this chapter highlights the common and novel methodological approaches that have been employed between the empirical papers presented within the current body of work. Each of these empirical papers has been written in the format suitable for publication in peer-reviewed journals; information regarding the context and dissemination of the paper will be provided under the chapter headings, and the empirical paper presented subsequently.

Chapter 3: Paper 1 - The impact of significant other Expressed Emotion on patient outcomes in chronic fatigue syndrome

The following paper reports on significant other EE in association with patient outcomes in cross-sectional and longitudinal analyses. In order to examine the proposed mechanisms identified within the review, patient outcomes were examined in association with the two principal, but contrasting, EE constructs of critical comments and EOI.

This paper is currently under review for publication in *Health Psychology*. The findings arising from this study have also been disseminated as oral presentations at the 2012 UKSBM conference (Manchester), the 2013 EHPS conference (Bordeaux) and the 2013 DHP conference (Brighton). Poster presentations have also been given at the 2013 Postgraduate DHP conference (Northampton) and the 2013 University of Manchester Faculty Graduate Society Showcase.

The impact of significant other Expressed Emotion on patient outcomes in chronic fatigue syndrome

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Running head: *Expressed emotion and patient outcomes in chronic fatigue syndrome*

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3.1 Abstract

Objective: Previous literature has identified the importance of interpersonal processes for patient outcomes in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), particularly in the context of significant other relationships. The current study investigated Expressed Emotion (EE), examining the independent effects of critical comments and emotional over-involvement (EOI) in association with patient outcomes.

Methods: Fifty-five patients with CFS/ME and their significant others were recruited from specialist CFS/ME services. Significant other EE status was coded from a modified Camberwell Family Interview. Patient outcomes (fatigue severity, disability, and depression) were derived from questionnaire measures. Forty-four patients (80%) completed follow-up questionnaires six-months after recruitment.

Results: Compared with low-EE, high-EE categorized by both high levels of critical comments and high EOI was predictive of worse fatigue severity at follow-up. High-EE as a result of critical comments was also associated with increased patient depression longitudinally; this was observed to mediate the relationship between high critical comments and fatigue severity reported at follow-up. Significant differences were identified within the prevalence of high-EE observed between the parent and partner significant other subgroups, particularly for the EOI subscale.

Conclusions: Patients with high-EE significant others demonstrated poorer outcomes at follow-up compared to patients in low-EE dyads. One mechanism for this appears to be as a result of increased patient depression. Future research should seek to further clarify the role of interpersonal processes, particularly within different significant other relationships in CFS/ME. The development of significant other-focused treatment interventions may be particularly beneficial for both patients and significant others.

Keywords: Chronic Fatigue Syndrome; Significant others; Expressed Emotion; Critical comments; Emotional over-involvement.

3.2 Background

Chronic fatigue syndrome (or myalgic encephalomyelitis; CFS/ME) is a complex condition characterized by severe, persistent fatigue, together with other symptoms including headaches, sleep disturbances, cognitive complaints and muscular and joint pain (K. Fukuda, et al., 1994). The estimated prevalence of the condition has varied widely; ranging from approximately 0.2-2.6% within adult populations (Prins, et al., 2006). The occurrence of fatigue in CFS/ME is unexplained by the presence of other medical conditions, and diagnoses are made by exclusion (K. Fukuda, et al., 1994). However, explanatory models propose that the maintenance of established symptoms may be influenced by a number of factors, such as patient symptom preoccupation, beliefs and behaviours in response to the condition (Deary, et al., 2007; Surawy, et al., 1995).

Social factors, such as medical uncertainty and illness legitimacy are also identified as potential perpetuating factors (Deary, et al., 2007); previous literature has demonstrated that these factors may shape patient experience of the condition, and consequently, the role of significant others. The challenges associated with negotiating a diagnosis (Dickson, et al., 2007; Larun & Malterud, 2007) have been proposed to increase the importance of significant others' views in informing patient understanding of their condition (Cordingley, et al., 2001); both patients and significant others report explanation seeking with respect to the condition as a collaborative process (Brooks, et al., 2013). Furthermore, the functional role of significant others may become more important over time (Melamed, 2003), in association with high levels of patient disability, reduced social contact and shifting roles within the family (Ax, et al., 2002; McCrone, et al., 2003). In contrast, the lack of established biomedical markers for the condition often results in delegitimizing experiences for patients from both healthcare professionals and significant others (Dickson, et al., 2007). Patients report these

interactions with significant others as the most difficult to deal with and they are associated with patient accounts of poor coping and feeling unsupported (Dickson, et al., 2007). There is accumulating evidence to suggest that an integrated investigation of interpersonal factors in the perpetuation of CFS/ME would be beneficial (Blazquez & Alegre, 2012).

Empirical studies examining significant other behaviours in response to patient symptom experiences, such as fatigue or pain, have noted associations with patient illness outcomes, including symptom severity and psychological wellbeing. In particular, solicitous responses, for example comforting the patient or helping with practical tasks (Kerns & Rosenberg, 1995), have been associated with increased fatigue severity and disability (Romano, et al., 2009; Schmalting, et al., 2000). In comparison, negative responses, for example expressing anger or frustration at the patient (Kerns & Rosenberg, 1995) have been associated with poorer psychological outcomes and increased depression (Romano, et al., 2009). These findings suggest there are two potential interpersonal mechanisms that may be important in symptom perpetuation, and provide the rationale for further exploration of significant other responses in CFS/ME.

A well-established framework for empirically examining significant other factors in association with patient outcomes is the multi-component Expressed Emotion (EE) construct (Vaughn & Leff, 1976). EE provides a measure of several aspects of the patient-significant other relationship; it is thought to represent the affective quality of the relationship, related to significant other distress and burden (Barrowclough & Parle, 1997; Tarrier et al., 2002), and has been shown to reflect typical patterns of reciprocal interaction within the dyad (Hooley, 1986, 2007; Miklowitz, Goldstein, & Nuechterlein, 1995). Significant others are conventionally conceptualized as high- or low-EE on the basis of ratings of three key components of the construct, critical comments, hostility

and emotional over-involvement (EOI). Hostility is rarely observed in the absence of highly critical attitudes (Leff & Vaughn, 1985) and therefore is often considered as an extreme form of criticism (Wearden, Tarrier, Barrowclough, et al., 2000). Ratings are made on the basis of evidence for these constructs during the semi-structured Camberwell Family Interview (CFI; Vaughn & Leff, 1976); the CFI is considered to be the ‘gold standard’ for determining EE (Hooley & Parker, 2006). Alongside consideration of the content of speech, which may include evidence of significant other beliefs, attitudes and responses towards the patient, ratings are made on the basis of the tone of speech and significant other behaviours at interview, such as dramatization or emotional display. A robust association has been documented between the presence of a high-EE relative and poorer patient illness and treatment outcomes, particularly across psychiatric conditions, but also among patients who are experiencing physical health problems (Bebbington & Kuipers, 1994; Butzlaff & Hooley, 1998; Hooley, 2007; Tarrier, Sommerfield, & Pilgrim, 1999; Wearden, Tarrier, Barrowclough, et al., 2000; Wearden, Tarrier, & Davies, 2000).

The assumption that significant other EE may drive significant other behavioural responses towards the patient has received some support in the form of observational data (Hooley, 1986; Miklowitz, et al., 1995). Much of the previous EE research has focused upon criticism, although it has been noted that significant other emotional and behavioural responses are likely to be different when arising as a result of high EOI (Vasconcelos e Sa, Wearden, & Barrowclough, 2013; Wearden, Tarrier, Barrowclough, et al., 2000). The previous literature examining significant other behavioural responses in CFS/ME suggests that there are two distinct response styles (that is, solicitous and negative) that are important for patient outcomes (Romano, et al., 2009; Schmalin, et al., 2000); the constituent behaviours for these response styles (Kerns & Rosenberg, 1995), appear to overlap with the responses that would be relevant for the EOI and

critical comments EE subscales. For example, solicitous behaviours such as showing high levels of concern for the patient or engaging in tasks on the patients' behalf would count towards the rating of EOI. Additionally, behaviours that are reportedly associated with negative responses, such as expressing frustration, overlap with the EE construct of criticism. It was therefore hypothesized that solicitous responses may reflect behaviours driven by high levels of EOI, whilst negative responses may be associated with high levels of critical comments. No previous study has considered the role of significant other EE as a framework for examining interpersonal processes in CFS/ME. Therefore, the aim of the current study was to extend the previous literature by being the first to examine how significant other EE is associated with patient outcomes in a CFS/ME population. The proposed relationships between the behavioural responses previously associated with CFS/ME outcomes and the principle EE subscales were utilized to guide study hypotheses.

Within the wider CFS/ME literature, research examining significant other factors have tended to focus exclusively upon romantic partners or spouses. However, within EE research, significant others have typically been defined as the person with the most daily involvement in the patients' illness management (MacCarthy, Hemsley, Shrank-Fernandez, Kuipers, & Katz, 1986), often with a minimum limit of weekly contact specified (Onwumere et al., 2008); consequently, a variety of significant other relationship types have been examined, often reflecting the characteristics of the disorder under examination. These relationship types are seldom distinguished between when examining the predictive validity of EE, although there are some findings of note in the literature. Investigations of the role of EE in depression, have tended to study spouses (Hooley, 1986; Hooley & Teasdale, 1989; Meuwly, Bodenmann, & Coyne, 2012) and have identified the role of criticism as particularly important within these relationships (Butzlaff & Hooley, 1998; Hooley, 2007). In studies of patients with

dementia where the significant other may include the offspring of the patient, EOI in appears to be very low indeed (Bledin, MacCarthy, Kuipers, & Woods, 1990; Orford, O'Reilly, & Goonatilleke, 1987; Tarrier, et al., 2002). Thus there may potentially be differences in the mechanisms of EE on patient outcomes, according to the nature of the relationship between the patient and the significant other. With respect to CFS/ME, it is likely that significant others' experience of the condition may differ dependent on factors such as patient age and the nature of the relationship. Given the novel nature of the present study, and in line with the wider EE literature, significant others were identified by patients and not restricted to partner relationships only.

3.2.1 Hypotheses

It was hypothesized that significant other high-EE (as defined by conventional criterion levels) would be associated with poorer patient outcomes, in comparison to significant other low-EE. Specifically, in line with the literature, it was predicted that high levels of significant other critical comments during the CFI would be associated with higher levels of patient depression and fatigue severity. It was also hypothesized that patient depression would mediate the association between critical comments and increased fatigue severity. Furthermore, it was predicted that high levels of significant other EOI during the CFI would be associated with increased disability and fatigue severity. All patient outcomes were examined both cross-sectionally and longitudinally, at six-month follow-up. No specific a priori hypotheses were formulated with regards to the distribution of high-EE according to the nature of the significant other relationship type; however, it was expected that there would be differences in the prevalence of EE observed within different patient-significant relationships.

3.3 Method

3.3.1 Participants

To be eligible for participation patients had to have received a specialist diagnosis of CFS/ME, which was confirmed by a clinical study checklist based on the Oxford criteria for CFS/ME (Sharpe et al, 1991). In addition, patients had to have a willing significant other who had the most day-to-day involvement in the patients' activities, and had a minimum of ten hours face-to-face contact per week. Both participants were required to have sufficient fluency in English to complete the assessments. Any ongoing condition that may have impacted upon the significant others' ability to complete the procedure was set as an exclusion criterion; however, no participants were excluded during recruitment. Ethical approval was granted from a UK National Health Service (NHS) research ethics committee (11/NW/0198). Participants were recruited primarily from specialist NHS CFS/ME services. These included patients who were newly inducted in to the specialist services, currently receiving treatment or individuals on clinician case-loads. 38% of patients approached within these services consented to being contacted by the researcher ($n = 89$), and of these, 52 consented to participating within the study (22% of those approached). Participants were also able to enter the study through self-referral as a result of advertisements with CFS/ME support organizations ($n = 3$). No incentives were offered in return for participation, and written informed consent was obtained from all participants. Participants aged 17 and over were recruited for the study as dyads; the final sample included 55 patients and their significant others. The patient sample ranged from 17 to 58 years old, with a mean age of 38 (12.25), and 91% of the sample were female ($n = 50$). The mean illness duration of the sample was 6.8 years upon entry into the study (range: 8 months -25 years). 93% ($n = 51$) of the patient sample were White British. Mean (*SD*) scores on patient outcome measures at baseline and follow up are shown in Table 3. The age of significant others ranged from 19-72, with a mean age of 48 (12.87) years old, and 51%

were female (n= 28). The majority of significant others were partners (n= 30, 55%), or parents (n= 20, 36%), whilst the remaining significant others included daughters (n= 3, 5%), sisters (n= 1, 2%) and close friends (n= 1, 2%). Ten patients (18%) did not live with their significant others, but in each case the significant other was the individual with the most daily contact with the patient.

3.3.2 Measures

3.3.2.1 Measures completed by the patient.

Patient measures assessing CFS/ME outcomes were those widely reported within the literature (Dittner, Wessely, & Brown, 2004), and where possible, were those included in the UK CFS/ME national outcomes database (Collin, et al., 2011). Reliability estimates for the current dataset are provided in Table 3.

3.3.2.1.1 *Fatigue.*

Chalder Fatigue Questionnaire (Chalder, et al., 1993). Patient fatigue severity within the last month was assessed using the Chalder fatigue scale. Eleven items assess both mental and physical fatigue severity; each item is rated on a 4-point scale from 0-3 (ranging from better than usual – much worse than usual). Individual scores are then summed to give a total fatigue score (0-33). The scale has been widely used (Cella & Chalder, 2010) and had excellent internal consistency at baseline and follow-up in the current sample (Table 3).

Visual analogue scales of fatigue (VAS-F; Lee, Hicks, & Nino-Murcia, 1991). A visual analogue scale was also used to assess fatigue severity and energy levels experienced at the time of completion. The scale consists of 18 items (13 measuring fatigue and 5 energy) each anchored with ‘not at all – extremely’ and rated from 0-100; mean scores are calculated for each subscale. One item on the fatigue subscale was removed after

piloting due to difficulties in comprehension in UK English (not at all bushed – totally bushed), resulting in a final 17-item scale. The measure has previously demonstrated good psychometric properties (Dittner, et al., 2004).

3.3.2.1.2 Disability.

The Short Form (36) Health Survey (SF-36; Ware & Sherbourne, 1992). Two subscales widely used in CFS/ME research were included as measures of patient disability; these were physical functioning and bodily pain experienced within the last month. Ten items assessed physical functioning; participants were asked to indicate the extent to which they were able to perform typical daily activities (three possible response items: limited a lot; limited a little; not limited at all). Bodily pain was measured using two items assessing level of pain (rated on a 6-point scale from ‘none’ to ‘very severe’) and pain interference (rated on a 5-point scale from ‘not at all’ to ‘extremely’). Each scale is converted in to a score ranging from 0-100, with a higher score indicating better patient functioning. The psychometric properties of the SF-36 have been extensively tested across countries (Gandek & Ware, 1998); the current data demonstrated reliability estimates in line with this (Table 3).

3.3.2.1.3 Anxiety and depression.

Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). All patients completed this scale designed to assess anxiety and depression during the previous week in patient populations. It consists of 14 items which are rated on a 4-point scale from 0-3 (not present – substantial). Each subscale consists of 7 items which are summed to calculate a total score (ranging from 0-21), with higher scores indicating higher anxiety and depression. These subscales showed acceptable internal consistencies at baseline and follow-up within the current study (Table 3).

Table 3: Mean (*SD*) scores for patient outcome measures at baseline and six-month follow-up

Outcome measure		Baseline		α	Follow-up		α
		Mean	<i>SD</i>		Mean	<i>SD</i>	
Fatigue							
Total fatigue (CF)		26.75	6.53	.938	19.73	9.65	.970
Fatigue (VAS)		60.59	17.75	.927	56.80	21.38	.947
Energy (VAS)		24.96	17.54	.909	31.55	22.77	.930
Disability							
Physical functioning (SF36)		34.73	24.73	.992	44.66	30.30	.949
Bodily pain (SF36)		40.13	26.90	.798	43.35	29.10	.928
Anxiety and Depression							
Anxiety (HADS)		9.19	4.60	.820	9.30	5.19	.889
Depression (HADS)		9.46	3.99	.774	9.11	5.19	.884

Note. CF = Chalder fatigue Scale; VAS = Visual Analogue Scale; SF36 = Short Form (36) Health Survey; HADS = Hospital Anxiety and Depression Scale.

3.3.2.2 Measures completed by significant others.

3.3.2.2.1 Expressed Emotion (EE).

Camberwell Family Interview (CFI; Vaughn & Leff, 1976). All significant others took part in a semi-structured interview used to assess levels of Expressed Emotion in patient populations. The standard interview schedule was modified for relevance to CFS/ME; the symptom section was adapted by removing symptoms specific to psychosis, and symptoms typical of CFS/ME were added. Additionally, the period following the initial illness onset and preceding the current time was explored in greater depth, and sections addressing illness management strategies and the impact of the condition on daily life were expanded. The interviews lasted approximately 1 hour. The full interview may be obtained from the first author.

Table 4: Examples of statements similar to those extracted from the CFI interview: rated critical comments and evidence for EOI.

Examples of significant other critical comments:
<ul style="list-style-type: none"> • “I get frustrated with the fact that you know, sometimes we can’t go into town because it takes her a long time to get, you know, I’m ready to go with my coat on for 40 minutes like a kid who’s waiting to go to the sweet shop, and its taking her all this time just to get dressed or just to do her hair or, it takes its toll actually...” • “Usually after tea she’s just laying on that couch, which annoys me because it’s not to be laid on” • “It can be 8 o’clock when I come home and then sometimes as soon as I walk through the door I start, I’ll kick off because I’m thinking ‘I’ve just done a 12 hour day and you’ve just got out of bed and you can’t even tidy up a bit. I’m sure you’ve got the energy to do that!’ and then it just kicks off because I can’t hold it anymore you know what I mean? At first it used to be like, ‘come on love’, I used to be so much more patient but I’m not anymore, I’m really not” • “I get very frustrated when she doesn’t remember things, ‘cos I’ve got quite a good memory I think, and so there’s a lot of writing things down but even then she doesn’t look at it, so I get frustrated by that”
Examples of significant other statements relevant for EOI:
<ul style="list-style-type: none"> • “I’ll come over and make her bed and make her a bit of breakfast and she usually just sits on the sofa until she’s strong enough to have a shower or a bath. I’ll pop to the shop and get her shopping, milk and fresh things that you know she needs. If it’s a good time, like at the moment, she gets up about lunchtime, you know about 12, and I’ll come and help her get ready and then she’ll go to work and immediately she comes home from work at about 5 or 6, I’ll come again just to help her in the evening, having made her tea and bring it round, and again usually she’s taken herself off to bed by 8o’clock” • “I worry constantly about how she’s feeling” • “What I would say is that his decision-making isn’t as good and what I would say is that he is forgetful and he gets things confused and I do put safeguards in place. I sound like a control-freak now but if you’re making important decisions, they have to be the right decisions so if it’s going to be an important decision which I can control I’ll ask him to check that out with me to make sure that’s okay.” • “The only time I really go out is to go down check on her mother, make sure she’s okay, you know what I mean, make sure she’s alright. I’ll go to my friend’s house for about an hour about twice a week, that’s it. I just don’t like leaving her in the house by herself, in case she feels worse and needs me to do something” • “In the end it was towards the end of last year I thought I can’t cope with this anymore it’s driving me insane you know, and I feel sorry for [patient], so sorry for him because he’s the one got it, but it really affects everybody and this is why I’ve been upset, [patient]’s been upset, I’m gonna get upset again, because it just takes over”

3.3.3 Procedure

Questionnaire measures were posted to each of the patients to complete prior to significant other interviews. All significant others were interviewed individually in their own or patients' homes. All interviews were conducted confidentially, and audio-recorded. At six months following the baseline assessments, patients were sent a second copy of the fatigue, disability, anxiety and depression measures, to complete and return by post.

3.3.4 Statistical Analysis

3.3.4.1 EE coding.

All CFI interviews were conducted by the first author and rated using the conventional criteria; the rating for each EE subscale was recorded. Critical comments are extracted when significant other utterances display strong tonal criticism or provide unambiguous evidence for disapproval of patient behaviours or characteristics. EOI is characterized by over-identification with the patient, or self-sacrificing, overprotective or emotionally exaggerated behaviours (Leff & Vaughn, 1985). Examples of statements similar to those extracted and coded are provided in Table 4. Conventionally, global high-EE status is assigned to significant others who make six or more critical comments, and/or display evidence of hostile attitudes, and/or those who demonstrate evidence for at least moderately high levels of EOI (equivalent to a score of 3 or above on the 0-5 scale) (Leff & Vaughn, 1985). To enable assessment of study hypotheses, significant others were first classified as high- or low-EE as above (henceforth designated HEE and LEE). Second, significant others were reclassified on the basis of critical comments subscale only (designated HEE-C and LEE-C), with a HEE-C rating assigned to those who made 6 or more critical comments. Third, significant others were reclassified according to their EOI status only (HEE-EOI and LEE-EOI); HEE-EOI was determined by a score

of 3 or greater, in line with the conventional criterion levels. An independent, EE-trained psychology doctoral student blind to the study hypotheses also second coded a selection of the interviews, and where there was disagreement on any rating, a third opinion was sought ($n = 1$). A random sample of these second rated interviews were selected to establish rating reliability ($n = 9$). Complete agreement was established for global EE status and significant other EOI ratings, in addition to acceptable agreement on the critical comments subscale ($r = 0.89$).

3.3.4.2 Data analysis strategy.

SPSS version 20 was used to conduct all statistical analyses. Initial Kolmogorov-Smirnov tests were conducted to examine the distribution of the data; only VAS-fatigue and HADS subscales were normally distributed. Comparisons of patients who completed follow-up and those who did not were conducted for demographic variables, illness related variables and EE measures using χ^2 (or Fishers exact test where appropriate) for categorical variables, and Mann-Whitney U tests for continuous variables. Demographic variables (age, gender); illness related variables (illness duration, length of treatment) and level of patient depression were correlated with both patient outcome variables (fatigue and disability) and predictor variables (EE) to identify any significant associations that may potentially inflate the relationship between predictor and outcome variables. These variables are henceforth referred to as confounding variables.

Comparisons of patient outcomes in HEE-C vs. LEE-C, and HEE-EOI vs. LEE-EOI dyads were performed using Mann-Whitney U tests. These comparisons were conducted at baseline and repeated at follow-up. Where a significant difference in outcome had been identified on Mann-Whitney U tests for both HEE-C vs. LEE-C and HEE-EOI vs. LEE-EOI, multivariate analyses were first conducted including overall

EE status (HEE vs. LEE) in order to include all significant others who received a high-EE rating. Baseline outcomes were included within the models to control for previous level of functioning; further non-EE variables that were associated with outcomes at follow-up were identified as additional potential predictor variables. Subsequently, regression analyses were conducted to assess EE-C and EE-EOI in combination with additional predictor variables in predicting patient outcomes at six-month follow-up. Mediation analyses were conducted using bootstrapping procedures to assess the mediational role of depression between HEE-C and fatigue severity. Finally, due to the heterogeneous nature of the significant other sample, exploratory analyses were conducted on the partner and parent subgroups. Comparisons between these groups were conducted using X^2 (or Fishers exact test) for categorical variables, and Mann-Whitney U tests for continuous variables (Table 5).

3.4 Results

3.4.1 CFI rated EE.

Twenty significant others (36%) received a rating of overall high-EE (HEE). Very few critical comments were made overall within the sample; twenty-six significant others made no critical comments (47%). The mean number of critical comments was 1.91 (2.62); the median was 1 critical comment. Only 8 (15%) significant others made six or more critical comments, meeting the conventional threshold for a HEE-C rating. On the EOI scale, 14 (25%) significant others demonstrated no EOI (that is, a rating of zero), and the median level was rated as ‘some EOI’ within the sample. Using the conventional criterion level of 3 or above, 16 significant others (29%) were classified as HEE-EOI, with 12 significant others (22%) achieving HEE status based on evidence for HEE-EOI only.

3.4.2 Preliminary Analyses

At baseline, patient levels of fatigue (VAS) were correlated with longer illness duration ($r_s = .277$, $p = .045$). Older patient age was significantly correlated with poorer physical functioning ($r_s = -.448$, $p = .001$). Longer treatment length was correlated with reduced patient anxiety ($r_s = -.291$, $p = .040$) and depression ($r_s = -.352$, $p = .012$). Additionally, patient level of depression (HADS) was significantly correlated with all patient fatigue outcomes (Chalder total fatigue; VAS fatigue and energy) and disability outcomes (SF36 physical functioning and bodily pain) (ranging from $r_s = .189$ to $.473$). Gender was not found to significantly relate to any of the outcome variables. All other correlations between potential confounding variables and patient outcome measures were non-significant. There were no significant associations between any of the potential confounding variables and the EE variables (critical comments and EOI). At follow up, patient depression (HADS) was significantly associated with all patient outcomes, and therefore baseline depression was included as a potential predictor variable in regression analyses, as were the baseline scores for the respective outcome measures to control for previous level of functioning.

3.4.3 Expressed Emotion and Cross-sectional Patient Outcomes

Contrary to predictions, there were no significant cross-sectional associations between significant other EE and patient outcomes (see Table 5).

3.4.4 Expressed Emotion and Longitudinal Patient Outcomes

3.4.4.1 Six-month follow-up.

Forty-four participants returned completed follow-up questionnaires (80% of baseline sample); of these, 41 were female participants (93%). Comparison analyses identified that there were no significant differences on demographic or illness related variables at

baseline for those participants who completed follow-up compared to those who did not. Additionally, no significant differences were identified in significant other EE variables (overall EE, critical comments or EOI).

Comparisons of high- and low- EE groups (HEE-C vs. LEE-C and HEE-EOI vs. LEE-EOI) were conducted for patient outcomes at follow-up using Mann-Whitney U tests. In line with study predictions, patients whose significant other was rated as HEE-C at baseline had significantly higher levels of depression and fatigue at follow-up (Table 5). As hypothesized, HEE-EOI at baseline was also associated with worse fatigue severity, but, contrary to predictions, not disability reported at follow-up (Table 5).

Table 5: Patient Mean outcome measures at baseline and six-month follow-up by low- and high-EE subscales, and significant Mann-Whitney U tests

	Patient mean at baseline				Patient mean at follow-up			
	Low-EE	High-EE	U	p	Low-EE	High-EE	U	p
Critical comments								
CF Total	26.5	29.38	235	.223	18.67	27.29	194.5	.022
VAS fatigue	61.04	63.35	188.5	.914	54.03	73.03	187	.045
VAS energy	26.03	17.85	126.5	.164	31.65	23.46	89.5	.236
HADS depression	9.5	10.13	194.5	.802	8.36	13.43	201	.012
EOI								
CF Total	26.84	21.29	272	.690	18.03	26.80	254	.009
VAS fatigue	62.37	60.60	259.5	.524	51.86	74.51	264	.003
VAS energy	24.77	24.39	296.5	.524	32.51	23.18	104.5	.082
SF36 Physical functioning	35.77	31.43	274.5	.606	46.36	39.50	135	.402
SF36 Bodily Pain	40	40	273.5	.697	42.58	35	139.5	.786

Note. p<.05 is in boldface.

3.4.4.2 Regression analyses.

A series of regression analyses were conducted to examine if significant other EE independently predicted patient scores on outcome measures at follow-up. Predictor variables were selected as outlined in preliminary analyses.

As significant differences in fatigue severity were observed between groups for both HEE-C vs. LEE-C and HEE-EOI vs. LEE-EOI comparisons, multivariate analyses were first conducted examining overall EE status (HEE vs. LEE). This enabled the predictive validity of an overall high-EE rating to be explored before investigating the individual impact of critical comments and EOI. Significant other overall high-EE significantly predicted increased fatigue severity on the Chalder Fatigue scale (that is, fatigue experienced within the last month) reported at follow-up (see Table 6). Once the other potential predictor variables were added to the model, overall EE and depression remained significant predictors. These results were replicated when HEE-C was included as the predictor variable within the model. When examining EOI only, HEE-EOI was the only significant predictor of fatigue severity at follow-up (see Table 6).

The above analyses were repeated for VAS fatigue scores (that is, fatigue severity experienced at the point of follow-up); when entered alone, significant other overall high-EE status predicted greater fatigue at follow-up. However, overall EE became non-significant following the addition of patient depression (Table 6). These findings were replicated for HEE-EOI. However, when examining the predictive validity of HEE-C only, both high critical comments and depression were predictive of greater fatigue severity in the final model.

Table 6: Summary of Hierarchical Regression analysis for variables predicting patient scores on outcome measures at six-month follow-up (*N* = 44)

Variable	R ²	ΔR ²	B	SE B	β	P
Outcome: Chalder fatigue scale scores at six-month follow-up						
Step 1	.164	.164				
High/low EE			8.46	2.99	.41	.007
Step 2	.308	.145				
High/low EE			7.24	2.87	.35	.016
Baseline fatigue			.24	.26	.13	.379
Baseline depression			.80	.37	.32	.036
Outcome: VAS fatigue scale scores at six-month follow-up						
Step 1	.161	.161				
High/low EE			18.99	6.78	.40	.008
Step 2	.385	.225				
High/low EE			12.69	6.27	.27	.05
Baseline fatigue			-.23	.185	-.18	.227
Baseline depression			3.07	.82	.54	.001
Outcome: Chalder fatigue scale scores at six-month follow-up						
Step 1	.115	.115				
High/low critical comments			8.62	3.73	.34	.026
Step 2	.292	.177				
High/low critical comments			7.92	3.44	.31	.027
Baseline fatigue			.04	.27	.05	.724
Baseline depression			1.90	.36	.40	.009
Outcome: VAS fatigue scale scores at six-month follow-up						
Step 1	.109	.109				
High/low critical comments			19.04	8.49	.33	.030
Step 2	.398	.289				
High/low critical comments			16.16	7.21	.28	.031
Baseline fatigue			-.27	.18	-.21	.134
Baseline depression			3.37	.78	.60	<.001
Outcome: HADS depression scale scores at six-month follow-up						
Step 1	.131	.131				

	High/low critical comments			5.07	2.04	.36	.017
Step 2		.581	.450				
	High/low critical comments			4.53	1.44	.323	.003
	Baseline depression			.924	.141	.672	<.001
Outcome: Chalder fatigue scale scores at six-month follow-up							
Step 1		.156	.156				
	High/low EOI			8.77	3.18	.40	.009
Step 2		.277	.121				
	High/low EOI			6.78	3.23	.31	.043
	Baseline fatigue			.24	.27	.13	.391
	Baseline depression			.74	.39	.29	.069
Outcome: VAS fatigue scale scores at six-month follow-up							
Step 1		.202	.202				
	High/low EOI			22.65	7.02	.45	.002
Step 2		.383	.181				
	High/low EOI			13.75	6.92	.27	.054
	Baseline fatigue			-.22	.19	-.17	.240
	Baseline depression			2.87	.86	.51	.002

Finally, HADS depression scale scores were examined (Table 6). Having a significant other who was categorized as HEE-C, that is who made six or more critical comments during the CFI, was predictive of increased depression at follow-up. Baseline level of depression also significantly predicted depression reported at follow-up.

3.4.4.3 Relationships among patient fatigue severity, depression and significant other critical comments.

Having established that high levels of significant other criticism were predictive of increased levels of patient fatigue severity and depression, mediation was formally tested using the bootstrapping procedures outlined in Preacher and Hayes (2008) The basis for these analyses is that the indirect effect of HEE-C on the dependent variable

(i.e., fatigue severity) is the product of the paths between HEE-C and mediator (i.e., depression), and between mediators and dependent variable. However, such indirect effects are not normally distributed, meaning that bootstrapping is necessary (Preacher & Hayes, 2008). Bootstrapping involves resampling random subsets of data in order to gain a nonparametric approximation of the sampling distribution of the product of the implementation intention-mediator and mediator-dependent variable paths. The analyses presented here are based on 1,000 resamples. The confidence intervals associated with the indirect effect of depression did not contain zero (95% CI = 2.01, 11.71). Thus, the effect of HEE-C on fatigue severity was significantly ($p < .05$) mediated by level of patient depression.

Table 7: Exploratory analysis of significant other subgroups

	Partners (n = 30)		Parents (n = 20)		p
	Mean	SD	Mean	SD	
Patient demographics					
Patient age (years)	42.59	9.39	28.85	10.50	<.001
Patient illness duration (years)	6.44	5.51	6.24	5.65	.719
	n	%	n	%	p
Female	27	90	19	95	.641
Living with the significant other	28	93	14	70	.096
Significant other variables					
Female	4	13	19	95	<.001
HEE-C	3	10	5	25	.240
HEE-EOI	5	17	10	50	.025
HEE- C and EOI	0	0	4	20	.019

Note. HEE-C denotes high-EE as a result of critical comments. HEE-EOI denotes high-EE as a result of EOI. HEE-C and EOI refers to those significant others who received a high-EE rating on the basis of evidence for both critical comments and EOI.

$p < .05$ is in boldface.

3.4.5 Exploratory Analysis of Significant Other Subgroups

Patients who nominated their parent as their significant other were significantly younger than those with a partner; significant others within this group were also significantly more likely to be female (that is, mothers compared to male partners). Significant differences were observed between partners and parents with respect to EE status; parents were significantly more likely to receive a high-EOI rating in comparison to partners. Furthermore, parents were the only group of significant others to receive a high-EE rating on the basis of evidence for both critical comments and EOI (Table 7). No significant differences in significant other criticism were observed between these groups. Lack of statistical power prohibited any further exploration of potential differences between relationship subgroups.

3.5 Discussion

This study examined the impact of significant other Expressed Emotion in a CFS/ME sample. The main findings demonstrate that significant other high-EE is associated with poorer longitudinal patient outcomes, particularly with respect to fatigue severity and depression. The predictive validity of overall high-EE is in line with the wider EE literature, which has demonstrated poorer illness and treatment outcomes for patients in high-EE dyads (Butzlaff & Hooley, 1998; Tarrier, et al., 1999; Wearden, Tarrier, Barrowclough, et al., 2000).

In line with study hypotheses the role of the critical comments and EOI subscales were investigated separately. It was identified that high levels of critical comments were predictive of greater fatigue severity at follow-up compared to patients within low-EE dyads; these findings were evident irrespective of the way in which fatigue was measured. Furthermore, on each outcome measure, both high critical comments and high levels of patient depression predicted greater fatigue at follow-up. Further

analyses revealed that HEE-C was associated with, and predictive of, higher levels of patient depression at follow-up. It was hypothesized that the relationship between significant other HEE-C and poorer patient outcomes would be, at least, partially accounted for by increased levels of patient depression; the findings reported within this paper demonstrated that depression did significantly mediate the relationship between HEE-C and fatigue severity. These findings appear to support the contention that significant other critical comments as measured by the CFI are theoretically linked with negative response styles; the associations reported here between HEE-C and patient outcomes are in line with the previous literature documenting an association between negative significant other responses and increased patient depression in CFS/ME (Romano, et al., 2009; Schmaling, et al., 2000). In addition, this evidence implies that these interpersonal processes may be more enduring than cross-sectional associations would suggest, or indeed that the effect of criticism is only observable when examining longitudinal associations within subjects. The association between HEE-C and depression may be particularly important clinically, since patient level of depressive symptoms have been previously found to be associated with poorer long-term outcomes following treatment in CFS/ME (Bentall, Powell, Nye, & Edwards, 2002), and recently was found to moderate the efficacy of pragmatic rehabilitation treatment in reducing patient fatigue severity (Wearden, Dunn, Dowrick, & Morriss, 2012). Furthermore, the findings provide further evidence for a potential underlying interpersonal mechanism; we speculate that highly critical EE may drive negative significant other responses.

In contrast to high levels of critical comments, HEE-EOI was only observed to predict fatigue severity experienced across the last month. In this model, significant other EOI was found to be the only significant predictor of fatigue severity (whilst baseline fatigue and depression were non-significant). The results of this analysis suggest that

EOI is potentially impacting upon fatigue severity through a separate mechanism other than increased depression, supporting the differentiation of these EE subscales acknowledged within the literature (Vasconcelos e Sa, et al., 2013; Wearden, Tarrier, Barrowclough, et al., 2000). The finding that parents of patients were significantly more likely to be rated as HEE-EOI than partner significant others has been observed within other patient groups (Goldstein, Miklowitz, & Richards, 2002). Increased stress has often been cited as a potential mechanism through which EE may impact upon patient functional outcomes (Hooley, 2007), as previous evidence has suggested that interactions with high-EE significant others are experienced as more stressful by patients compared to interactions with low-EE significant others (Cutting, Aakre, & Docherty, 2006). It is possible that the beliefs and responses associated with EOI, such as over-protective and self-sacrificing behaviours, may be more or less acceptable and appropriate when considered within the context of these different groups (that is, parents and partners). Lack of statistical power prevented further exploratory analyses of these processes within significant other subgroups within the current study; however, these outstanding questions surrounding the importance of the principle significant other relationship for patient outcomes in CFS/ME provide a clear direction for future research within this area. Additionally, it was proposed that high levels of EOI would be associated with increased patient disability, based upon the cross-sectional associations with solicitous responses reported in the literature (Romano, et al., 2009; Schmaling, et al., 2000). It is possible that this association was not observed within the current study due to the predominance of EOI in the parent significant other subgroup; previous research examining significant other responses within CFS/ME has focused solely on significant others involved in a romantic relationship with the patient.

Although we have noted potential variations within the distribution of EE within significant other subgroups, as this is the first study to examine significant other EE in

a CFS/ME sample, it is instructive to compare the distribution of high-EE across the subscales of interest in comparison to those reported with other patient populations. The number of critical comments made within the overall sample was very low, although the distribution was comparable to other samples where patients were experiencing a physical health problem (Wearden, Tarrier, & Davies, 2000). Patients within the sample had been ill for a long duration before entering the study; many reported waiting a long time to engage with specialist services. It is possible that this may reflect the experiences and difficulties commonly reported by patients when interacting with healthcare providers (Larun & Malterud, 2007). Furthermore, it is possible that this long process of obtaining medical recognition and support in CFS/ME resulted in reduced criticism within these close relationships (Blazquez & Alegre, 2012), out of increased pressure to formulate joint explanatory narratives of the condition (Brooks, et al., 2013). However, despite the generally low levels of criticism within the sample, it is worth noting that when high levels of critical comments were present, patient outcomes at follow-up were poorer.

In comparison, a high proportion of significant others demonstrated high EOI; many of these receiving a high-EE rating on the basis of evidence for EOI only. Almost one quarter of significant others received a HEE-EOI only rating within the current study; other samples have identified much lower proportions of this classification across a range of conditions, (Barrowclough, Johnston, & Tarrier, 1994; Tarrier, et al., 2002; Wearden, Tarrier, & Davies, 2000). Evidence for self-sacrificing behaviours, intrusive over-protection and emotional display at interview were most commonly observed. The prevalence of HEE-EOI ratings may reflect the high number of parents involved as significant others within the study, but may also be due, in part, to the characteristics of the condition. High symptom severity and beliefs reflecting the potential beneficial effects of resting upon symptoms (Moss-Morris, 2005) may engender higher levels of

self-sacrificing or overprotective behaviours from significant others. These significant other response styles may be in contrast to the general strategies recommended by the current UK management guidelines (NICE, 2007), therefore, inclusion of significant others in treatment programs may alleviate some of the impact of EE on patient outcomes (Brooks, et al., 2013). Additionally, the high levels of emotional display reflect the difficulties experienced by this significant other group, and indicate that relatives of patients may also benefit from individual support or psycho-education in relation to the condition.

3.5.1 Study Limitations

Although the majority of patients were newly inducted in to specialist treatment programs at the time of recruitment, there was variation in the level of service engagement within the sample. Additionally, no information was available at follow-up with regards to the precise treatment that patients had received in the intervening period. Therefore, the data has been analyzed acknowledging the place of recruitment where possible, using the available data. The low rates of EE, particularly critical comments, may lead to reduced power in detecting significant associations. Evidence of high-EE observed within the sample was due predominantly to EOI, and consequently, those few significant others rated as high-EE on the basis of critical comments only may have introduced additional noise in to the analysis. The low prevalence of critical comments may be representative of the population of significant others of patients with CFS/ME but it may also reflect a self-selection bias; it is possible that highly critical significant others may have been less likely to participate, possibly because of beliefs about illness legitimacy. Future research should attempt to examine beliefs about the condition in association with significant other EE. As previously acknowledged, the heterogeneous nature of the current sample further limited statistical power and analyses examining the impact of EE within specific patient-significant other relationship types. The

possibility of Type 1 errors arising as a result of conducting multiple statistical tests must also be acknowledged. A final additional limitation is the lack of independent measures of patient functioning; all patient outcome measures were assessed by patient self-report.

3.5.2 Conclusions

The current study is the first to document the prevalence of significant other EE within a CFS/ME sample. The findings suggest that significant other high-EE is associated with poorer longitudinal patient fatigue outcomes, which may be partially accounted for by increased levels of patient depression, particularly where there are high levels of significant other criticism. The results therefore provide the rationale for the integration of significant other psycho-education into current clinical interventions, to address significant other responses that may inadvertently contribute to symptom maintenance within this condition. To achieve this, future research should further clarify these interpersonal processes in CFS/ME by examining the associations between significant other relationship type and the development of EE. Research examining the associations between significant other beliefs and their emotional and behavioural responses in CFS/ME would also be beneficial. Finally, a reduction of significant other distress may also be a target for family-oriented interventions.

3.6 Change in patient outcomes over time

The following section was not included within the empirical paper that is currently under review, however, in order to assist the reader additional data will be presented here on the change in primary outcome variables over time within the current sample. After discussing change in outcome scores, the change data for the whole sample will be presented (means and standard deviations). Subsequently, the data will be presented for high- and low-EE subgroups (LEE vs. HEE, LEE-C vs. HEE-C, and LEE-EOI vs. HEE-EOI); significant differences observed between these subgroups will also be reported.

3.6.1 Calculating change in outcomes

There has been debate within the literature surrounding the psychometric and statistical properties of change scores (Edwards, 1994). However, change in patient outcomes over time is of interest to clinicians and researchers, and in particular, with reference to change arising following patient involvement in therapeutic interventions. The extent to which change may be anticipated within the current sample has been previously addressed within the thesis (chapter 2, point 3.1.2); the mean and standard deviation change scores for those patients who completed the follow-up assessment are displayed in Table 8. A recent randomised trial comparing various interventions for CFS/ME defined a clinically interesting change in primary outcome variables (total fatigue and physical functioning) as an improvement approximate to half of the baseline standard deviation (P. White, et al., 2011). Within the current sample this was equivalent to a 3-point change on the Chalder fatigue questionnaire and a 12-point change in SF-36 physical functioning subscale. The data presented in Table 8 suggests that patients reported change (improvements) over the follow-up period across the sample as a whole. Furthermore, standard deviations are high; therefore identifying that patient

change in outcomes was also highly variable within the sample. These findings are in line with changes in patient outcomes reported over a 12-month follow-up period and collected across several specialist NHS services within England (Crawley, et al., 2013), suggesting that the amount of change observed within the current sample was at an expected level for patients engaged with specialist NHS services.

Table 8: Patient mean (SD) change scores on outcome measures at six-month follow-up

	Patient mean (SD) change at follow-up	
	Mean	SD
CF Total	-8.17	10.07
VAS fatigue	-3.34	27.85
VAS energy	8.85	23.99
SF36 Physical functioning	9.25	16.85
SF36 Bodily Pain	-3.00	24.00
HADS depression	-.55	3.84

Note. A higher score on the fatigue, pain and depression subscales represent poorer outcomes. A higher score on the energy and physical functioning subscales represent better outcomes. Therefore, all change scores shown here represent improvements over the follow-up period (i.e. a negative value on the fatigue, pain and depression subscales indicates a reduction calculated at follow-up; a positive value on the energy and physical functioning subscales indicate an increase in functioning).

3.6.2 Change in outcomes according to significant other EE status

As the primary aim of this thesis was to examine patient outcomes in association with significant other factors, patient change in outcomes was also examined comparing those patients within high- and low-EE dyads; these analyses were conducted separately for overall EE status, EE-C and EE-EOI. Furthermore, Mann-Whitney U tests were conducted to identify significant differences in change scores between these subgroups (Table 9). These findings suggest that patients within low-EE dyads on average, reported improvements in outcomes at follow-up, whilst patients within high-EE dyads reported little improvement, or in some cases, poorer outcomes than observed at baseline. In line with study hypotheses reported in Paper 1, critical comments were

associated with significant differences in change in patient fatigue severity and depression reported at follow-up; increased depression and poorer fatigue outcomes were observed in high-EE dyads (>6 critical comments) in comparison to low-EE dyads. Similarly, dichotomous EOI ratings were associated with significant differences in change in patient fatigue severity and physical functioning; these subscales improved to a significantly greater degree in low-EOI dyads in comparison with high-EOI.

Table 9: Patient mean change scores on outcome measures at six-month follow-up by low- and high-EE subscales, and Mann-Whitney U tests

Patient mean change at follow-up					
Overall EE	Low-EE	<i>SD</i>	High-EE	<i>SD</i>	p
CF Total	-10.26	10.01	-1.27	5.08	.002
VAS fatigue	-10.38	25.27	14.84	24.70	.003
VAS energy	11.62	21.82	-1.65	26.15	.032
SF36 Physical functioning	12.26	16.32	-.045	12.54	.019
SF36 Bodily Pain	-6.45	22.14	11.36	18.99	.089
HADS depression	-1.06	3.52	1.82	4.05	.049
Critical comments	Low-EE	<i>SD</i>	High-EE	<i>SD</i>	p
CF Total	-8.92	10.15	-1.83	3.43	.016
VAS fatigue	-7.44	25.39	18.25	29.91	.038
VAS energy	8.71	22.06	4.72	33.0	.339
HADS depression	-1.06	3.41	4.17	3.37	.007
EOI	Low-EE	<i>SD</i>	High-EE	<i>SD</i>	p
CF Total	-9.84	9.90	-0.78	5.07	.002
VAS fatigue	-9.79	24.65	18.32	25.95	.002
VAS energy	10.81	21.37	-1.62	29.24	.044
SF36 Physical functioning	12.12	15.96	-2.78	12.02	.019
SF36 Bodily Pain	-4.85	22.38	9.44	20.68	.321

**Chapter 4: Paper 2 - Understanding Expressed Emotion in CFS/ME:
an investigation into significant other illness beliefs and dyadic belief
incongruence**

The following paper reports on significant other beliefs about CFS/ME in association with significant other EE, to investigate those beliefs that may contribute to high- and low-EE status. In addition, previous research has identified that incongruence of beliefs within the patient-significant other dyad is associated with poorer relationship satisfaction; dyadic belief incongruence was also therefore examined in association with EE.

This paper is currently under review at *British Journal of Health Psychology*.

Running head: *Expressed Emotion and illness beliefs about chronic fatigue syndrome*

**Understanding Expressed Emotion in chronic fatigue syndrome: an investigation
into significant other illness beliefs and dyadic belief incongruence**

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4.1 Abstract

Objectives: A number of factors are thought to be important in the perpetuation of chronic fatigue syndrome (CFS/ME), including patient beliefs about the condition and social factors, such as close interpersonal relationships. The current study aimed to examine the relationship between the presence of significant other Expressed Emotion (EE) and illness perceptions about CFS/ME. Dyadic belief incongruence was also explored in association with EE status.

Design: Cross-sectional interview and questionnaire survey.

Methods: Fifty-five patient-significant other dyads were recruited from specialist CFS/ME services. Significant other EE status was derived from a modified version of the Camberwell Family Interview. Illness perceptions were measured using the IPQ-R (CFS version) and CBRQ.

Results: In comparison to low-EE significant others, high-EE significant others held more negative illness models, attributing significantly more physical symptoms to CFS/ME. More negative beliefs about the consequences of the CFS/ME for themselves and the patient were reported, in addition to more negative emotional representations. Dyadic belief incongruence differed between high- and low-EE dyads; high-EE significant others reported more negative emotional representations and beliefs about patient consequences, whilst low-EE significant others reported more positive beliefs on these dimensions, relative to the patient. However, significant other EE was not associated with overall belief dissimilarity within dyads.

Conclusions: Significant other beliefs about the negative consequences and emotional impact of CFS/ME appear to be important correlates of significant other high-EE. The development of significant other-focused interventions addressing these negative

beliefs about the condition may be beneficial in potentially reducing significant other high-EE.

4.2 Background

Chronic fatigue syndrome, also known as myalgic encephalomyelitis (CFS/ME) is characterized by the experience of persistent and severe fatigue, in addition to other symptoms such as pain, sleep disturbance and reported cognitive deficits (K. Fukuda, et al., 1994). Symptoms may develop after an infection or other trigger, or may develop gradually, and result in high levels of functional impairment (Afari & Buchwald, 2003; Collin, et al., 2011; McCrone, et al., 2003). Cognitive-behavioural models outline factors such as fear-driven avoidance of activity thought to be important in the maintenance of symptoms of CFS/ME; these in turn may be influenced by social factors (Deary, et al., 2007). Close interpersonal relationships with significant others have been identified as particularly important in guiding patient understanding of CFS/ME (Brooks, et al., 2013; Cordingley, et al., 2001), and an association between significant other responses and patient outcomes has previously been documented (Romano, et al., 2009; Schmaling, et al., 2000; K. White, et al., 2006).

One well-established methodology for conceptualising the patient-significant other relationship with respect to patient outcomes has been the Expressed Emotion (EE) framework (Leff & Vaughn, 1985). EE examines aspects of the relationship across a number of core constructs, and is typically derived from significant other utterances and behaviours during the semi-structured Camberwell Family Interview (CFI) (Vaughn & Leff, 1976). Conventionally, significant others are conceptualised as high- or low-EE. High-EE ratings are ascribed to significant others who display high levels of criticism, hostility, or emotional over-involvement (EOI) - a composite measure including over-protective, self-sacrificing and emotionally exaggerated attitudes or behaviours (Leff & Vaughn, 1985). The link between poorer patient illness outcomes and the presence of significant other high-EE across a range of psychiatric and physical health conditions is well established (Butzlaff & Hooley, 1998; Wearden, Tarrier,

Barrowclough, et al., 2000). Despite this, the role of EE has not been explored in association with patient outcomes in CFS/ME until recently (Band, Barrowclough, & Wearden, in submission). In this study, the presence of significant other high-EE was associated with poorer patient outcomes longitudinally, with higher levels of fatigue severity and depressive symptoms reported, in comparison to patients within low-EE dyads. Furthermore, high-EE was predictive of unimproved patient fatigue severity over time (Band, et al., in submission).

Attempts to examine the development and maintenance of high-EE within the wider literature have focused predominantly upon significant others' underlying explanations for the illness and related symptoms and behaviours (Lobban, Barrowclough, & Jones, 2003; Wearden, Tarrier, Barrowclough, et al., 2000), commonly exploring significant other attributional beliefs for patient problems (Berry, Barrowclough, & Haddock, 2011). A comprehensive review of the EE literature identified that significant other criticism and hostility are consistently associated with patient responsibility attributions, that is, making more attributions about problems to factors personal, internal and controllable by the patient (Barrowclough & Hooley, 2003). In comparison, individuals rated as high-EOI tend to attribute symptoms to factors related to the illness rather than the individual (Barrowclough & Hooley, 2003). Barrowclough and colleagues (Barrowclough, Lobban, Hatton, & Quinn, 2001) suggested that significant other responses to illness, such as EE, may also be understood by examining illness beliefs in general, guided by Leventhal's self-regulation model (SRM) (Leventhal, Nerenz, & Steele, 1984). This paper focuses on such an approach in relation to CFS/ME; the illness models that significant others hold about the condition in general will be examined in order to develop understanding of significant other responses to CFS/ME.

Within the SRM, a number of dimensions are defined, along which cognitive representations of illness are thought to be organised (Leventhal, et al., 1984). These

dimensions include the *identity* (that is, the label attributed to the condition, and the symptoms that appear to be associated with the condition), the perceived *cause*, *consequences*, *controllability* (that is, the extent to which the condition may be cured or kept under control), and the expected duration (or *time-line*) of the condition (Leventhal, Benyamini, Brownlee, & al, 1997). It is proposed that in parallel to these cognitive representations, emotional representations are also generated in response to the health threat; these are interdependent processes, both of which are thought to guide different patient coping strategies. Individual illness models are proposed to be dynamic, and may be modified over time as outcomes and coping strategies are appraised against earlier representations (Leventhal, et al., 1984).

Typically, the Illness Perception Questionnaire (IPQ) (Weinman, et al., 1996) has been used to quantify patient illness representations. Patients are asked to report their beliefs about the illness along those dimensions outlined above; a higher score reflects a more strongly held belief on that dimension. A revised version of the questionnaire (IPQ-R) (Moss-Morris, et al., 2002) added subscales assessing *illness coherence* (that is, the extent to which patients have a clear sense of their illness) and included a measure of *emotional representations*. In addition, individual beliefs about *personal control* over the illness, and beliefs about *treatment control* were differentiated, and a scale measuring beliefs about the extent to which the symptoms fluctuate (*timeline-cyclical* dimension) was added. Significant other versions of the IPQ have been developed, including one for dyads where the patient was experiencing schizophrenia (IPQS-Relative) (Lobban, et al., 2005), which has additional subscales assessing significant others' perception of the consequences, control and blame in relation to themselves and the patient.

Using the IPQ, a consistent pattern of patient illness beliefs about CFS/ME has been identified within the literature. Typically, patients strongly endorse beliefs related to

illness identity, timeline and consequences; that is, patients attribute a high number of physical symptoms to CFS/ME, report a high number of serious consequences, and believe that the condition will last for a long time (Moss-Morris & Petrie, 2001; Moss-Morris, Petrie, & Weinman, 1996; Weinman, et al., 1996). Only one paper has previously examined significant other illness beliefs in relation to patient illness beliefs and CFS/ME outcomes (Heijmans, et al., 1999). Dissimilarity of beliefs was found to be associated with decreased relationship satisfaction within the dyad. In addition, poorer patient outcomes and psychological adjustment were associated with significant other minimization, that is, believing that the illness has fewer symptoms, less serious consequences and is more treatable, relative to the patient (Heijmans, et al., 1999).

To date, the relationship between significant other EE status and illness beliefs has only been studied in the context of psychosis, where high-EE significant others were found to hold more negative general illness models than those rated as low-EE (Lobban, et al., 2006). In addition, dissimilarity of beliefs within the dyad was greater when the significant other was rated as high-EE; these significant others demonstrated more negative beliefs about the illness relative to the patient, particularly in relation to illness identity and consequences (Lobban, et al., 2006).

The aim of the current study was to examine significant other illness perceptions in association with significant other EE status within a CFS/ME sample. On the basis of previous literature, it was hypothesized that significant other beliefs about the condition would differ according to their EE status; in particular, that significant others rated as high-EE would report more negative illness models in comparison to low-EE significant others. Furthermore, previous literature has identified that dissimilarity of beliefs about the illness within the dyad may impact upon the quality of the relationship (Heijmans, et al., 1999), which would be expected to impact upon the EE rating of the significant other (Lobban, et al., 2006). The current study therefore aimed to explore

dissimilarity in beliefs between patients and significant others in association with the EE status of the significant other. It was predicted that higher levels of dissimilarity in patient and significant other illness beliefs would be observed in dyads where the significant other had received a high-EE rating and that in comparison to low-EE dyads, high-EE significant others would report more symptoms associated to the illness (that is, a stronger illness identity), and more negative consequences as a result of the CFS/ME relative to the patient.

4.3 Method

4.3.1 Participants

55 patients and their significant others were recruited to the study as dyads, from specialist North-West CFS/ME services or through self-referral. All participants were aged 17 or above. To be eligible for inclusion, patients were required to have received a specialist diagnosis for CFS/ME, confirmed by a study checklist according to the Oxford criteria (Sharpe, et al., 1991). Significant others were required to live with patients or have a minimum of 10 hours face-to-face contact per week. All participants were required to have sufficient English fluency to complete all study assessments. Any ongoing medical condition which would potentially impact upon the participants' ability to complete the procedure was defined as a general exclusion criterion. Ethical approval was granted from the North West 3 NHS research ethics committee, and written informed consent was obtained from all participants.

4.3.2 Illness belief measures

Illness belief measures were completed by both the patient and the significant other.

4.3.2.1 Illness Perception Questionnaire (IPQ-R) (Moss-Morris, et al., 2002). The 38-item IPQ-R for CFS/ME was used to assess patient illnesses perceptions along the

dimensions of consequences; personal control; treatment control; timeline (acute/chronic) and timeline cyclical; illness coherence; and emotional representations of CFS/ME. Individual items are scored on a 5-point likert scale (ranging from *strongly disagree* – *strongly agree*), responses to which are combined to form dimension subscale scores. The significant other version was adapted from the patient IPQ-R version for CFS/ME to reflect significant other beliefs about the patients' illness. For example, 'My CFS/ME will last for a long time' was adapted to 'Their CFS/ME will last for a long time'. In addition, 16-items from the IPQS-Relatives version (Lobban, et al., 2005) were included in the significant other version. These items assessed three additional illness perception subscales, referring to consequences of the illness for the significant other (9 items), significant others' perceptions of control (4 items), and significant other self-blame (3 items). These items were modified so that 'mental health problems' were replaced with 'CFS/ME' where applicable, for example, 'Their mental health problems make it more difficult for me to do day to day things' was modified to 'Their CFS/ME makes it more difficult for me to do day to day things'. In total, 54 items were included in the significant other version; items and subscale scores were calculated in the same way as the patient version.

4.3.2.2 Cognitive Behavioural Responses Questionnaire (CBRQ) (Skerrett & Moss-Morris, 2006). The 27-item CBRQ symptom list was used to assess beliefs about CFS/ME illness identity. For each item, participants were asked to identify if the patient had experienced the symptom since the onset of the condition. In addition, for all endorsed symptom items, participants were also asked to identify whether they believed the symptom to be a result of the illness, stress, or activity limitation. A measure of the total number of symptom items endorsed, and those attributed to illness only, were calculated for both patients and significant others.

4.3.3 Patient fatigue severity

4.3.3.1 Chalder Fatigue Questionnaire (Chalder, et al., 1993). The 11-item Chalder Fatigue scale was used to assess total patient fatigue severity within the previous four weeks. The scale assesses both mental and physical fatigue; each item is rated on a 4-point scale, (ranging from *better than usual* – *much worse than usual*). Responses are then summed to give a total fatigue score (0-33).

4.3.4 Significant other Expressed Emotion

4.3.4.1 Camberwell Family Interview (CFI) (Vaughn & Leff, 1976). Significant other Expressed Emotion ratings were derived from a modified version of the CFI. The symptom section was adapted to be relevant to the core symptoms associated with CFS/ME. In addition, further sections were included to explore the period between the initial onset and the current period, illness management strategies, and the impact of the condition on daily life. The interviews lasted approximately 1 hour. Global EE ratings were made according to conventional criterion levels (≥ 6 critical comments, hostility and ≥ 3 EOI rating) by the first author; complete agreement on global EE ratings was observed on a selection of interviews (n=9) with a second trained rater.

4.3.5 Procedure

Questionnaire measures were posted to all participants and collected by the first author prior to the participant interviews. All significant others interviews were conducted individually in their own or patients' homes, and audio recorded for later transcription and coding.

4.3.6 Statistical analysis

Internal consistencies for each IPQ-R dimension were determined by calculating the alpha coefficient. Independent t-tests were conducted to compare dyads with low- and high-EE rated significant others for all analyses involving normally distributed

variables. Where a significant ($<.05$) result was obtained on Kolmogorov-Smirnov tests, Mann-Whitney U tests were performed. Comparisons between high- and low-EE dyads were initially conducted to examine significant other CFS/ME beliefs reported on individual subscales, and overall negative illness models. Significant other illness models were calculated by summing scores reported for the CFS/ME specific symptoms (CBRQ), patient consequences, significant other consequences, timeline, timeline cyclical and emotional representations subscales, minus their belief in treatment control. Subsequently, univariate ANOVAs were conducted to examine these associations controlling for patient fatigue severity. These analyses were then repeated to examine differences in patient reported CFS/ME beliefs, and patient overall negative illness models (calculated by summing scores on the CFS/ME specific symptoms (CBRQ), consequences, timeline, timeline cyclical and emotional representations subscales, minus their belief in personal control and treatment control). Dissimilarity scores within the dyad were calculated by subtracting the patient score on each dimension from that reported by the significant other; a positive dissimilarity score indicated a higher significant other score on the dimension and a negative score indicated a higher patient score on the dimension. Total dissimilarity was calculated by summing dissimilarity scores within the dyad for each of the IPQ subscales and the CBRQ identity subscale. Comparison analyses were then conducted examining dissimilarity scores for high- and low-EE dyads. Finally, the proportion of dyads where the significant other reported a more negative belief compared to the patient was calculated for high- and low-EE dyads, and compared using Fishers exact test statistic.

4.4 Results

4.4.1 Participants

The mean age of patients within the sample was 38 years old ($SD = 12.25$ years, range = 17-58 years). Fifty patients recruited were female (91%) and 5 were male (4%), and

the majority of patients were White British ($n = 51$; 93%). At the time of recruitment, the median patient illness duration was 4.75 years ($IQR = 10$) and 52 (95%) participants were undergoing specialist CFS/ME treatment programs. Ten patients (18%) did not live with their significant others. The mean score for patient fatigue severity on the Chalder fatigue scale was 26.68 ($SD = 6.51$).

The mean age of significant others was 48 years old ($SD = 12.87$ years, range = 19-72 years). Twenty-eight of significant others were female (51%), and 27 were male (49%). All significant others were the individual with the most daily face-to-face contact with the patient and included partners ($n = 30$, 55%), parents ($n = 20$, 36%), daughters ($n = 3$, 5%), sisters ($n = 1$, 2%) and close friends ($n = 1$, 2%).

4.4.2 Significant other expressed emotion

In total, 20 of the 55 significant others (36%) were rated as high-EE. Of these, 4 (7%) were rated on the basis of critical comments only, 12 (22%) were rated on evidence for EOI only and 4 (7%) were rated on the basis of both critical comments and EOI.

4.4.3 Comparison of significant other beliefs between low- and high-EE dyads

Significant others who were rated as high-EE attributed a significantly higher number of patient symptoms to the illness compared to low-EE significant others (Table 10). In addition, high-EE significant others reported significantly more negative beliefs about patient and significant other consequences as a result of CFS/ME, relative to those rated as low-EE. High-EE significant others also reported significantly more negative emotional representations. These effects remained significant when controlling for patient level of fatigue severity. High-EE significant others were observed to have more negative overall illness models than low-EE significant others (Table 10). This remained significant when controlling for fatigue severity.

Table 10: Comparison of mean significant other CBRQ/ IPQ subscale scores and the modified IPQS between high- and low-EE dyads

CBRQ/ IPQ subscale	Mean (SD) subscale score		T-test/ Mann Whitney U (p value)	Dimension α
	Low EE	High EE		
Total illness Identity	16.59 (4.94)	18.72 (6.29)	375 (.162)	-
Symptoms attributed to illness	12.75 (6.09)	16.56 (6.52)	393 (.003)*	-
Timeline	20.76 (3.53)	20.26 (4.16)	309 (.794)	.764
Timeline cyclical	14.79 (2.28)	13.95 (3.78)	284.5 (.467)	.768
Patient consequences	23.44 (2.88)	26.37 (2.89)	495 (.001)*	.694
Patient control	22.09 (2.69)	20.63 (3.99)	264.5 (.274)	.674
Treatment control	17.09 (2.38)	16.16 (2.41)	238 (.111)	.657
SO illness coherence	12.91 (3.57)	13.74 (3.96)	360.5 (.482)	.877
SO emotional representations	19.18 (3.55)	23.53 (3.86)	-4.14 (<.001)*	.776
SO consequences	23.38 (4.03)	27.37 (5.71)	458.5 (.012)*	.694
SO control	14.41 (2.80)	13.00 (3.79)	258.5 (.226)	.818
SO blame	7.5 (1.56)	6.95 (2.07)	275 (.363)	.269
Overall negative illness model	97.26 (11.81)	111 (16.29)	-3.54 (.001)*	-

^a SO denotes significant other

*p<.05.

4.4.4 Comparison of patient beliefs between low- and high-EE dyads

Patients who had a low-EE significant other had significantly stronger beliefs about the cyclical nature of CFS/ME in comparison to patients with a high-EE significant other (Table 11). This remained significant when controlling for patient fatigue severity. No further significant differences in patient beliefs were observed on the remaining IPQ or CBRQ subscales according to the EE status of the significant other, nor for overall patient illness models.

Table 11: Comparison of mean patient CBRQ/ IPQ subscale scores between high- and low-EE dyads

CBRQ/ IPQ subscale	Mean (SD) subscale score		T-test/ Mann Whitney U (p value)	Dimension α
	Low EE	High EE		
Total illness Identity	21.16 (4.28)	21.44 (5.12)	382 (.574)	-
Symptoms attributed to illness	15.97 (5.87)	18.67 (5.98)	465.5 (.062)	-
Timeline	21.17 (4.54)	22.0 (3.82)	374 (.451)	.832
Timeline cyclical	14.80 (3.06)	12.76 (2.63)	225.5 (.028)*	.727
Patient consequences	24.74 (2.83)	25.53 (2.94)	421.5 (.207)	.508
Patient control	22.86 (3.71)	21.06 (3.05)	241 (.055)	.696
Treatment control	17.16 (3.38)	16.47 (2.74)	303.5 (.597)	.785
SO illness coherence	16.26 (3.98)	15.41 (3.41)	281.5 (.352)	.784
SO emotional representations	20.22 (5.00)	20.35 (4.00)	-.609 (.545)	.854
Overall negative illness model	57.48 (16.44)	62.53 (17.77)	-9.71 (.336)	-

*p<.05.

4.4.5 Comparison of dissimilarity of patient and significant other beliefs between low- and high-EE dyads

Significant differences in patient-significant other dissimilarity scores were observed on the patient consequences and emotional representations subscales between high- and low-EE dyads. Significant others rated as high-EE reported more severe patient consequences and more negative emotional representations in comparison to patients, whilst low-EE significant others rated less severe patient consequences and less negative emotional representations than patients (Table 12).

The total dissimilarity scores between patients and significant others across all IPQ and CBRQ (illness specific symptoms) subscales did not reach significance. Although there was considerable variability within these subgroups, there was a trend for low-EE

significant others to report more positive beliefs about the illness, relative to the patient, whilst high-EE significant other beliefs were overall very similar to patient beliefs (Table 12).

Table 12: Comparison of patient and significant other dissimilarity scores on the CBRQ/ IPQ and modified IPQS between high- and low-EE dyads

CBRQ/ IPQ subscale	Mean (SD) dissimilarity score		T-test/ Mann Whitney U (p value)
	Low EE	High EE	
Total illness Identity	-4.56 (4.48)	-2.72 (5.52)	360.5 (.141)
Symptoms attributed to illness	-3.22 (7.01)	-2.11 (5.22)	318 (.543)
Timeline	-.56 (4.54)	-2.18 (4.76)	.98 (.331)
Timeline cyclical	.029 (3.12)	1.00 (3.32)	-1.25 (.217)
Patient consequences	-1.35 (3.17)	.88 (4.01)	-2.08 (.043)*
Patient control	-.74 (4.03)	.41 (4.10)	347 (.655)
Treatment control	-.19 (3.72)	-.29 (3.14)	307 (.985)
Illness coherence	-3.38 (5.19)	-1.35 (5.45)	-1.32 (.193)
Emotional representations	-1.17 (6.62)	3.41 (6.49)	413.5 (.038)*
Total dissimilarity	-9.30 (16.16)	-.89 (16.01)	-1.82 (.075)

^aA positive dissimilarity score indicates that the significant other reported higher scores than the patient (i.e. SO maximisation), and negative dissimilarity scores indicate that the patient reported higher scores than the significant other (i.e. SO minimisation).

*p<.05.

4.4.5.1 Comparison of negative significant other beliefs (relative to the patient) between low- and high-EE dyads.

The number of dyads in which the significant other had more negative illness beliefs relative to the patient was compared for high- and low-EE dyads (Table 13). A significant difference was identified for the emotional representations subscale; 70% of significant others rated as high-EE reported more negative emotional representations

relative to the patient, in comparison to 46% of significant others rated as low-EE ($F = .026$).

Table 13: Comparison of the number of dyads in which the significant other had a more negative illness model than the patient between high- and low-EE dyads

CBRQ/ IPQ subscale	No (%) of dyads where the SO scored higher than the patient		
	Low EE	High EE	Fishers exact statistic (1-sided)
Total illness Identity	5 (14%)	3 (15%)	.482
Symptoms attributed to illness	10 (29%)	6 (30%)	.508
Timeline	15 (43%)	6 (30%)	.295
Timeline cyclical	13 (37%)	10 (50%)	.353
Patient consequences	9 (26%)	9 (45%)	.107
Patient control	15 (43%)	9 (45%)	.532
Treatment control	16 (46%)	8 (40%)	.581
Illness coherence	17 (49%)	9 (45%)	.443
Emotional representations	16 (46%)	14 (70%)	.026*

* $p < .05$.

4.5 Discussion

The main findings were in line with hypotheses, namely that significant others rated as high-EE reported significantly more negative illness models than those rated as low-EE. Specifically, high-EE significant others attributed more symptoms to the condition, perceived more negative patient and significant other consequences, and had more negative emotional representations arising from the condition. Contrary to hypotheses, total concordance across all illness belief dimensions did not significantly differ between high- and low-EE dyads. However, significant differences were evident for some dimensions of illness beliefs: high-EE significant others reported more severe consequences of the illness and more negative emotional representations than patients,

whilst low-EE significant others reported more positive beliefs on both dimensions. However, patient-significant other dissimilarity scores did not significantly differ for illness identity beliefs.

The current results concur with previous findings examining significant other illness representations in association with EE (Lobban, et al., 2006); demonstrating that high-EE was associated with negative overall illness models for CSF/ME in comparison to low-EE. High-EE significant others attributed more symptoms experienced by the patient to CFS/ME, although the total number of symptoms reported between significant other groups did not differ. In addition, more negative beliefs about the consequences of CFS/ME for themselves and the patient, and more negative emotional representations associated with the condition were reported; these differences remained significant even when controlling for level of patient fatigue severity. The results therefore indicate that these significant others perceive a greater number of negative consequences arising from the condition, which are not merely a result of the symptom severity experienced by patients within these dyads. Furthermore, within high-EE dyads, significant others reported more negative beliefs relative to the patient with reference to consequences and emotional representations, whilst low-EE significant others reported more positive beliefs than patients. Considering the predominantly high-EOI status of significant others (80% of those rated as high-EE) within the current sample, these observations are in line with the wider attributional research, which has identified that high-EOI is typically associated with stronger attributions to illness than other EE groups (such as highly critical, or low-EE subgroups) (Barrowclough & Hooley, 2003). Although patient outcomes were not directly reported within the current paper, high-EE within this sample was found to be associated with poorer patient outcomes longitudinally (Band, et al., in submission), in line with the wider EE literature (Butzlaff & Hooley, 1998; Wearden, Tarrier, Barrowclough, et al., 2000).

It has been documented that patients with CFS/ME often hold strong, negative beliefs about various aspects of the condition (Moss-Morris & Petrie, 2001; Moss-Morris, et al., 1996; Weinman, et al., 1996). Heijmans et al., (1999) suggested that significant other minimisation may have been associated with poorer outcomes within their sample as a result of patients feeling delegitimized by significant other beliefs. However, the current findings identified that significant other low-EE was associated with belief minimisation relative to the patient, therefore questioning the extent to which it is acceptable to equate significant other minimising beliefs with delegitimizing responses. Previously, within the wider literature, it has been noted that significant others rated as low-EE tend to report overly optimistic views when appraising patients' symptoms or the condition, even relative to the patient (Barrowclough & Parle, 1997; MacCarthy, et al., 1986). Since low-EE is generally associated with better patient outcomes across conditions (Wearden, Tarrier, Barrowclough, et al., 2000), and was found to be predictive of longitudinal patient improvement within CFS/ME (Band, et al., in submission), the current study suggests that significant other minimisation when associated with optimism about the condition is beneficial for patient outcomes. As delegitimizing experiences with significant others have been highlighted as important factors associated with patient well-being (Dickson, et al., 2007), future research should seek to specifically identify the beliefs associated with delegitimizing (as contrasted with optimistic) responses.

Moreover, dissimilarity in patient-significant other CFS/ME illness beliefs was previously found to impact upon the relationship satisfaction within the dyad (Heijmans, et al., 1999). However, the current results revealed that low-EE significant others reported discordant, but overall positive beliefs across belief dimensions, whilst high-EE significant others tended to hold similar beliefs to patients; possibly reflecting the high rates of EOI and lower rates of critical and hostile attitudes presented in

comparison other samples (Lobban, et al., 2006). The dimensions that significantly differentiated dissimilarity in high- and low-EE dyads were beliefs about consequences and emotional representations, therefore suggesting that strong negative beliefs with respect to these aspects of the condition may result in difficulties within the relationship, as observed by a high-EE rating (Lobban, et al., 2006), rather than dissimilarity in general.

There are several key differences that may account for inconsistencies between Heijmans and colleagues' study (Heijmans, et al., 1999) and that reported here. In Heijmans' study all the significant others were spouses, whereas in the current study, significant others were the individuals with the most involvement in patients' daily life. Illness perceptions were measured in Heijmans' study using the original IPQ questionnaire (Weinman, et al., 1996), and therefore did not take into account the additional dimensions or differentiation of beliefs on dimension such as controllability and timeline, which were reported on here, using the revised version (Moss-Morris, et al., 2002). In addition, in Heijmans' study, patient illness perceptions were derived from an interview measure whilst significant other beliefs were self-reported, therefore, the beliefs elicited may not be directly comparable in this case (Heijmans, et al., 1999).

4.5.1 Strengths and Limitations

There are a number of strengths associated with the current study. As significant other illness beliefs were not derived from the CFI interviews used to determine EE ratings, the associations between significant other beliefs and EE are methodologically less likely to be confounded by common method bias (Lobban, et al., 2006). In addition, the significant differences in beliefs identified between high- and low-EE significant others, particularly with respect to emotional representations, concur with observations made during the CFI; exaggerated emotional responses, and emotional display at interview,

are relevant for high-EOI ratings (Leff & Vaughn, 1985), and were common within the current sample (Band, et al., in submission). The current findings emphasize the negative consequences experienced by some significant others, and highlight the impact that significant other distress may have on the relationship quality.

However, the limitations associated with statistical power limit further analyses such as the consideration of important covariates such as the relationship status of the significant other, and in addition, comparison of individual EE subscales being conducted. Interpretation of dissimilarity scores can be challenging, yet these are important methodological and theoretical questions which future research should attempt to address. Furthermore, the possibility of Type I errors must be acknowledged due to the number of ANOVAs conducted with the current sample size. Finally, the cross-sectional nature of the current analysis limits strong conclusions regarding the direction of effects, and consequently for potential significant other interventions.

4.5.2 Conclusions

The current study is the first to examine the associations between significant other EE and illness beliefs in relation to CFS/ME. The results suggest that stronger illness models, particularly with reference to the symptoms, consequences and emotional representations attributed to the condition by significant others are associated with high-EE in a CFS/ME sample. Low-EE however, appears to be characterized by positive, optimistic beliefs about the condition. Dissimilarity of beliefs in general does not appear to be a significant factor in determining significant other EE; although dissimilarity on emotional representations and beliefs about the consequences associated with CFS/ME between significant others and patients may also distinguish between low- and high-EE dyads. The development of significant other interventions

specifically addressing these negative beliefs about the may be beneficial in potentially reducing significant other high-EE within CFS/ME populations.

Chapter 5: Paper 3 - Significant other behavioural responses and patient CFS/ME symptom fluctuations in the context of daily life: An experience sampling (ESM) study.

This paper utilised an experience sampling methodology (ESM) to examine the impact of those significant other behavioural responses outlined within the cross-sectional literature (that is, solicitous and negative responses) on a momentary basis. This enabled changes in patient outcomes following significant other responses to be explored. Using the novel ESM design allowed several of the methodological issues outlined within the systematic review of the literature to be addressed.

The following paper is currently under review for publication at *Psychological Medicine*.

Significant other behavioural responses and patient CFS/ME symptom fluctuations in the context of daily life: An experience sampling (ESM) study.

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Running head:

Daily interactions and symptom fluctuations in CFS/ME

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5.1 Abstract

Background: Significant other responses to patients' symptoms are important for patient illness outcomes in CFS/ME; negative responses have been associated with increased patient depression, whilst increased disability and fatigue have been associated with solicitous significant other responses. The current study aimed to examine the relationship between significant other responses and patient outcomes within the context of daily life using Experience Sampling Methodology (ESM).

Methods: Twenty-three patients with CFS/ME and their significant others were recruited from specialist CFS/ME services. Sixty momentary assessments, delivered using individual San Francisco Android Smartphones, were conducted over a period of six days. All participants reported on affect, contact with each other and significant other responses to the patient. Patients reported on symptom severity, disability and activity management strategies.

Results: Negative significant other responses were associated with increased patient symptom severity and distress reported at the same momentary assessment; there was evidence of a mediating role of concurrent distress on symptom severity. Patient-perceived solicitous responses were associated with reduced patient activity and disability reported at the same momentary assessment. Lagged analyses indicate that momentary associations between significant other responses and patient outcomes are largely transitory; only significant other-reported negative responses were associated with symptom severity at the subsequent assessment.

Conclusions: The results indicate that significant other responses are important influences on the day-to-day experience of CFS/ME. Further research examining patient outcomes in association with specific significant other behavioural responses is

warranted and future interventions that target such significant other behaviours may be beneficial.

5.2 Background

Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a symptomatically defined condition, characterised by severe fatigue and pain (K. Fukuda, et al., 1994). Current explanatory models suggest that patients' cognitive, behavioural and affective responses to symptoms are important for symptom perpetuation (Deary, et al., 2007; Surawy, et al., 1995). Interpersonal relationships are also considered as further potential maintaining factors (Deary, et al., 2007), and interactions with significant others have been highlighted as important in the patient illness experience (Dickson, et al., 2007).

Significant other behavioural responses to the patient have been examined cross-sectionally in association with patient-reported CFS/ME outcomes. Significant other negative responses, such as ignoring, or expressing frustration at the patient (Kerns & Rosenberg, 1995) have been found to be associated with increased patient depression (Romano, et al., 2009). Patient depression has been shown to be important for long-term patient illness outcomes and responses to treatment (Bentall, et al., 2002; Wearden, et al., 2012). In addition, solicitous significant other responses, such as encouraging patients to rest or doing tasks on their behalf (Cordingley, et al., 2001; Kerns & Rosenberg, 1995), have been associated with increased levels of fatigue severity and disability (Brooks, et al., 2012; Romano, et al., 2009; Schmalings, et al., 2000). It is proposed that these solicitous responses may promote decreased patient activity levels (Itkowitz, et al., 2003). Activity limitation has been observed to mediate treatment efficacy on fatigue severity (Wearden & Emsley, in press), and furthermore, current UK CFS/ME management guidelines recommend graded increases in patient activity levels (NICE, 2007). However, significant other responses observed during dyadic interaction tasks did not replicate the associations identified for self-reported responses; negative responses were associated with less patient illness behaviour and better

physical functioning (Romano, et al., 2009). Given these inconsistencies, and the possibility that responses elicited in experimentally induced situations may not accurately reflect typical interactions within the dyad, alternative methodological techniques are required to assess interpersonal processes.

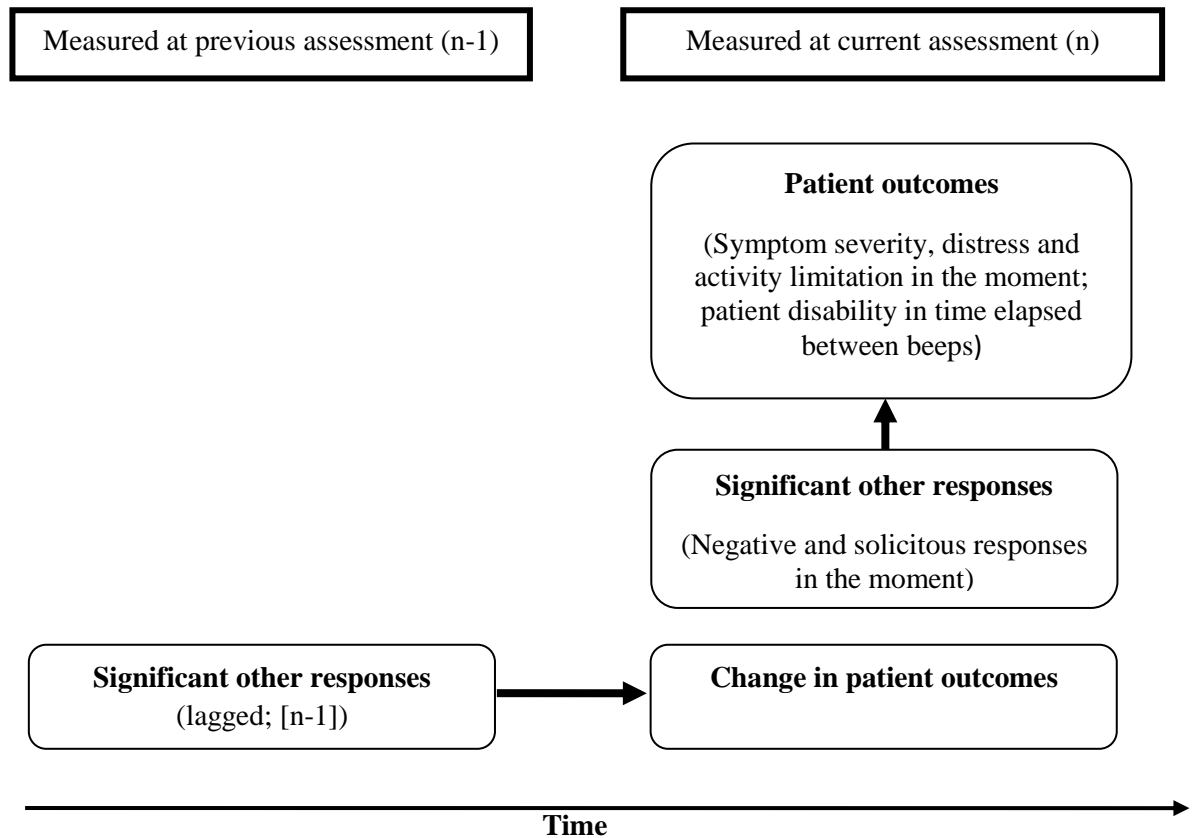
Experience Sampling Methodology (ESM; Csikszentmihalyi & Larson, 1987) utilises repeated participant assessments made within the flow of daily life to assess temporal associations between variables (Myin-Germeys, et al., 2003). Typically, participants are prompted several times during the day to record what they are feeling or doing at that particular moment. This may include current mood, actions, situational factors, and appraisal of the situation within that given moment (Myin-Germeys & van Os, 2007). ESM techniques have predominantly been employed to assess factors associated with mental health difficulties, within various populations (Myin-Germeys & van Os, 2007; Myin-Germeys, et al., 2001; Palmier-Claus, Shryane, Taylor, Lewis, & Drake, 2013; Thewissen, Bentall, Lecomte, van Os, & Myin-Germeys, 2008; Udachina et al., 2009). However, symptoms of chronic conditions often fluctuate considerably over short periods of time, and therefore ESM techniques seem particularly appropriate to capture this. ESM also offers the advantage of potentially addressing some of the methodological issues associated with symptom reporting in cross-sectional research (Redelmeier & Kahneman, 1996; Stone & Broderick, 2007; Stone, et al., 2003).

Furthermore, it has been suggested that ESM is a suitable methodology for examining dyadic interactions, as significant other responses are likely to vary across context (Newton-John & Williams, 2006). Additionally, ESM offers the possibility of capturing dyadic interactions as they happen within the natural environment (Janicki, et al., 2006). Comparisons of ESM and day reconstruction methods (DRM) for assessing fluctuations in mood and fatigue in healthy controls suggested that ESM is the most appropriate methodology for examining specific changes in outcomes occurring as a

result of particular events, such as dyadic interactions (Kim, et al., 2013). Previous ESM investigations have examined patient-perceived significant other responses to chronic pain in association with patient pain intensity (Sorbi, et al., 2006a), and disability (Sorbi, et al., 2006b). Pain intensity was significantly associated with perceived significant other responses that included reinforcement of pain behaviour and punishment of well behaviours (Sorbi, et al., 2006a). Patient immobility was associated with significant other punishment of well behaviours and patient avoidance behaviours (Sorbi, et al., 2006b). This suggests that ESM is a feasible methodology for examining dyadic interactions within chronic conditions such as CFS/ME.

The current study aimed to utilise ESM to investigate the role of significant other responses in association with patient reported outcomes within the course of daily functioning. In line with the literature, it was hypothesised that negative responses would be associated with increased patient distress and symptom severity. In addition, it was predicted that significant other solicitous responses would be associated with increased patient activity limitation and disability. Patient-perceived and significant other-reported responses were investigated separately. In addition to momentary analyses (that is, exploring associations between responses and patient outcomes at the same momentary assessment) lagged analyses were also conducted, to assess the significant other response reported at the previous momentary assessment in association with change in outcome at the current assessment (see Figure 2). Finally, it was predicted that the relationship between patient-perceived negative significant other responses and symptom severity would be mediated by level of patient distress, whilst the relationship between patient-perceived solicitous significant other responses and levels of disability would be mediated by patient activity limitation.

Figure 2: Depiction of the main effects analyses



5.3 Method

5.3.1 Design

The ESM protocol was completed by patients and significant others. In addition, patients completed standardised self-report outcome measures at a non-momentary level.

5.3.1.1 ESM sampling schedule, hardware, and software.

A typical ESM protocol was followed (Myin-Germeys, et al., 2001); participants were alerted to complete assessments at ten time points, occurring between typical waking hours of 7.30am and 10.30pm, for a period of six days. A semi-random sampling schedule was used to ensure a representative sample of time points was collected; one assessment was made within each 90 minute period throughout the day. Consecutive

beeps occurred after a minimum of 15 minutes and a maximum of three hours. Following the alert to signal an assessment, participants had 15 minutes to access the questions, after which time the assessment became unavailable. All alerts and ESM data collection was completed on San-Francisco Android Smartphones using specialist ClinTouch software (Ainsworth, et al., 2013). Data entry was completed using a sliding scale on the touch-sensitive screen (see Ainsworth et al, 2013).

5.3.2 Participants

Participants were recruited from regional North-West CFS/ME services. All patients had received a specialist clinical diagnosis of CFS/ME, confirmed by administration of a checklist according to the Oxford Criteria for CFS/ME (Sharpe, et al., 1991). To be eligible for inclusion, all patients were required to have a willing significant other with whom they lived or had at least ten hours face-to-face contact per week. All participants had to be aged 16 or above, able to provide fully informed consent, and have sufficient English comprehension to complete all study measures. Ethical approval was granted from the North West 9 NHS research ethics committee.

5.3.3 Measures

5.3.3.1 Non-ESM Measures.

Patients provided demographic information on illness duration, time of diagnosis and current CFS/ME treatment. In addition, validated and frequently used outcome measures assessing patient fatigue severity and disability were completed prior to the ESM phase of the study.

5.3.3.1.1 Patient fatigue and disability.

Fatigue was measured using the *Chalder Fatigue Questionnaire* (Chalder, et al., 1993). It consists of 11 items rated on a 4-point scale (*better than usual – much worse than usual*; total score range 0-33); higher scores indicate greater fatigue severity.

The *Work and social adjustment scale* (WSAS; Marks, 1986) measures functioning across 5 areas: work, home management, social and private leisure activities, and family relationships. Overall scores are summed from each item (total score range 0-40); higher scores indicate greater disability.

5.3.3.2 ESM measures.

As the current study examined patient outcomes associated with CFS/ME, several modifications to standard ESM diaries (Myin-Germeys, et al., 2003; Myin-Germeys, et al., 2001) were necessary in order to be relevant to symptom experience within this patient group.

5.3.3.2.1 Item development.

In line with current recommendations, validated non-ESM measures (Chalder, et al., 1993; Marks, 1986; Spence, et al., 2005) were utilised for item development (Palmier-Claus, et al., 2011). The items were phrased in language that was familiar to patients; positively and negatively worded items were developed to avoid extreme response bias (Kimhy, et al., 2012). All items were rated on a 7-point likert scale anchored with *Not at all* to *A lot* (scored from 1-7), and were piloted with patients and healthy controls prior to the study commencement in order to ensure comprehensibility and acceptability. Momentary items began with the phrase “Before the beep went off I was...” or “Right now I am...”.

STATA (version 11) was used to conduct preliminary analyses assessing the factor structure of the ESM items for individual subscales (Myin-Germeys, et al., 2001), using the FACTOR command. The factor solution was determined by identifying the number of factors with an Eigenvalue of greater than one, and individual items with a loading of >0.4 were included within the subscale. Subsequently, internal consistencies of subscales were assessed using the ALPHA command.

5.3.3.2.1.1 Symptom severity.

Seven items were developed to assess symptom severity, reported ‘in the moment’, that is, at the time immediately preceding the alert, and were completed by patients only. These items reflected core CFS/ME symptoms, including concentration difficulties, termed “mental fog” by UK sufferers. Items were feeling weak, active, tired, well, experiencing pain, experiencing mental fog, and being sleepy. Preliminary principal components analyses indicated that all items loaded on to a one factor solution ($\alpha = .79$).

5.3.3.2.1.2 Distress.

Distress was assessed using a single item (‘feeling distressed’), which was included with standard items examining participants’ affect at a momentary level.

5.3.3.2.1.3 Activity limitation.

Two items were included at the momentary level to assess patient activity limitation. These items were ‘resting to control my symptoms’ and ‘avoiding activities that might make my symptoms worse’, completed by patients only. The alpha coefficient for these items was calculated at $\alpha = .80$.

5.3.3.2.1.4 Disability.

Six items were developed to assess patient disability during the time elapsed since the previous momentary assessment. The phrase “Since the last beep I was able to” preceded items examining household tasks, socialising, leisure activities, leaving the house, work and general activity; a higher score indicated less disability. All items loaded on to one factor solution ($\alpha = .82$). These items were completed by patients only.

5.3.3.2.1.5 Significant other contact and responses.

Significant other responses were reported on following participant endorsement of dyadic contact at the momentary level. These items were developed to reflect negative and solicitous responses as defined within the wider literature (Kerns, et al., 1985; Vaughn & Leff, 1976). Analyses revealed that significant other responses loaded on to a two factor structure; the first factor was labelled as negative responses and included nagging me, irritated with me, and pushing me to do things ($\alpha = .92$). The second factor was labelled as solicitous responses and included the following behaviours: doing things for me, looking after me, helping me, and checking up on me ($\alpha = .95$).

5.3.3.2.2 Associations with Non-ESM measures.

Correlations were conducted between mean levels of ESM reported outcomes (across all valid beeps) with validated non-ESM outcome measures (Palmier-Claus, et al., 2011). Symptom severity reported during the ESM phase was found to be significantly correlated with patient reported fatigue severity (Chalder Fatigue scale; $r_s = .567$, $p = .005$). High levels of ESM reported disability were found to be correlated with total levels of WSAS disability ($r_s = -.538$, $p = .010$).

5.3.4 Procedure

5.3.4.1 ESM briefing.

All participants were given a thorough briefing about the study, which included an ESM practice session to ensure that participants understood the meaning of ESM items and ESM rating scales. This allowed the researcher to ensure that participants were comfortable with the procedure during the briefing session. Researcher and participant contact details were confirmed to maintain contact during the ESM period. Written informed consent was obtained from all participants. Patient non-ESM measures were completed prior to the ESM phase of the study.

5.3.4.2 Six-day ESM phase.

The ESM phase began on the day following the briefing session and the sampling schedule was synchronised for both patients and significant others. Patients were contacted on Day 2 of the ESM phase to discuss any potential problems and to ensure that participants were happy to continue with the study. Participants were contacted again two days later if requested. The ESM phase ended after a period of six days.

5.3.4.3 ESM debriefing.

After the completion of the ESM phase, all participants were debriefed. All participants were asked to provide evaluative feedback about their experiences of the study.

5.3.5 Statistical Analysis strategy

5.3.5.1 Hypothesis testing.

ESM has a hierarchal structure, whereby measures are clustered in three levels: beeps are nested in days which are nested within participants; therefore multilevel models were used to assess all main study effects. The XT MIXED command was used for all continuous outcome variables with a random intercept for each participant and for each

day within participant; betas, 95% CI and p-values are reported for all associations between independent and dependent variables. To test the first set of hypotheses, significant other responses were entered as predictor variables into the models with patient outcome variables as the dependent variable for the same momentary assessment (see Figure 2). The main effects were calculated separately for significant other-reported responses and then repeated for patient-perceived responses.

Subsequently, to test hypotheses relating to associations between the previous and current assessment, lagged significant other responses were included as predictors with change in patient outcomes as the dependent variable. Lagged significant other responses were those reported at the preceding assessment (n-1), and changes in outcome variables were calculated as the difference between the current (n) and previous (n-1) assessment. Analyses were conducted for both significant other-reported and patient-perceived responses.

Mediation hypotheses were assessed using a procedure similar to that outlined by Baron and Kenny (1986). Using the XTMIXED command, we fitted a model without the putative mediator and subsequently including the mediator as a predictor. A change in the coefficient of the main predictor between these two models can be interpreted as evidence of mediation and the size of the indirect effect can be calculated by taking the difference of these coefficients.

5.4 Results

5.4.1 Description of sample

The patient sample (n = 23) ranged in age from 17 to 58, with a mean age of 35.5 (*SD* = 13.96) years. Twenty (87%) of the sample were female and 21 (91%) were White British. At the time of recruitment, the median patient illness duration was 5 years (IQR

= 10) and 22 (96%) participants were undergoing specialist CFS/ME treatment programmes. Three patients (13%) did not live with their significant others. Significant others' ($n = 23$) ages ranged from 19-72, with a mean age of 45 ($SD = 13.35$) years old. Thirteen (57%) significant others were female; 11 (48%) were partners, 9 (39%) were parents, and 3 (13%) were daughters of the patient.

5.4.1.1 Patient adherence.

None of the 46 participants dropped out before the completion of the study. Three patients (7%) and 2 significant others (4%) did not complete the level of valid assessments ($n = 20$) traditionally recommended to be retained for analyses (Palmier-Claus, et al., 2011). Analyses were conducted including all participants, and then repeated excluding these participants. No differences were observed in the findings in subsequent analyses; therefore the analyses including all participants are presented here to exploit all available data. Patients completed a mean of 38.74 beeps ($SD = 14.88$), whilst significant others completed a mean of 34.52 beeps ($SD = 14.93$). Patients reported a mean of 18.97 momentary significant other contacts ($SD = 11.42$), and significant others reported a mean of 13.26 ($SD = 10.90$) momentary patient contacts.

5.4.2 The effects of significant other responses upon patient outcomes

5.4.2.1 Significant other-reported negative responses.

To investigate the effect of significant other-reported negative responses on patient symptom severity and distress, four regression analyses were conducted. In the first two analyses, significant other-reported negative responses were entered as the independent variable. In separate analyses, patient symptom severity and distress at the same momentary assessment were entered as dependent variables. The results indicated that significant other negative responses were associated with increased symptom

severity and with increased distress at the concurrent momentary assessment (see Table 12).

Secondly, the negative response variable was lagged to create a measure of significant other-reported negative responses at the previous (n-1) assessment. In addition, change in levels of patient symptom severity and distress, from the previous (n-1) to the current (n) assessment, were calculated. Analyses one and two were then repeated with the lagged significant other response entered as the independent variable, and the change in patient symptom severity and distress variables entered as the dependent variables in separate analyses. The results indicated that lagged significant other negative responses were significantly associated with a reduction in patient symptom severity over the period elapsed between the previous and current assessment. No significant relationship was identified between lagged negative responses and change in patient distress (Table 12).

5.4.2.2 Significant other-reported solicitous responses.

Four further regression analyses were conducted to assess the effect of significant other-reported solicitous responses on patient disability and activity limitation. In the first two analyses, significant other-reported solicitous responses were entered as the independent variable, and patient disability and activity limitation at the same beep assessment were entered as dependent variables. The results indicated that significant other solicitous responses were not significantly associated with patient disability or activity limitation at the concurrent momentary assessment (Table 14).

Secondly, the solicitous response variable was lagged, and change in levels of patient disability and activity limitation were calculated. The previous analyses were then repeated with the lagged solicitous response entered as the independent variable, and the change in patient disability and activity limitation variables entered as the

dependent variables. No significant relationship was identified between lagged solicitous responses and change in patient disability or activity limitation between the previous and current assessment (Table 14).

Table 14: The association between significant other-reported responses and patient outcomes in momentary and lagged analyses

Momentary association between significant other responses and patient reported outcomes

Negative responses and symptom severity	$\beta = 2.295$, 95% CI: 1.458 - 3.131, $p < 0.001$
Negative responses and patient distress	$\beta = .173$, 95% CI: .0572 - .289, $p = .003$
Solicitous responses and disability	$\beta = .034$, 95% CI: -.026 - .093, $p = .272$
Solicitous responses and activity limitation	$\beta = .046$, 95% CI: -.057 - .148, $p = .384$

Lagged association between significant other responses and change in patient outcomes

Negative responses and symptom severity	$\beta = -1.543$, 95% CI: -2.572 - -.514, $p = .003$
Negative responses and patient distress	$\beta = -.045$, 95% CI: -.285 - .195, $p = .712$
Solicitous responses and disability	$\beta = -.039$, 95% CI: -.109 - .032, $p = .285$
Solicitous responses and activity limitation	$\beta = .084$, 95% CI: -.043 - .211, $p = .193$

5.4.2.3 Patient-perceived negative responses.

The analyses outlined for significant other-reported negative responses were repeated, with patient-perceived negative responses included in the model as the independent variable. The results revealed that patient-perceived negative responses were associated with increased symptom severity and distress at the concurrent momentary assessment (Table 15). As before, lagged patient-perceived negative responses were then calculated and subsequently included in the model, with patient change in symptom severity and distress. These analyses indicated that there was no significant association between patient-perceived negative responses at the previous assessment and change in

symptom severity or distress reported between the previous (n-1) and current (n) assessment (Table 15).

Table 15: The association between patient-perceived responses and patient outcomes in momentary and lagged analyses

Momentary association between patient-perceived responses and patient reported outcomes

Negative responses and symptom severity	$\beta = .505$, 95% CI: .214 - .797, $p = .001$
Negative responses and patient distress	$\beta = .188$, 95% CI: .107 - .269, $p < 0.001$
Solicitous responses and disability	$\beta = .080$, 95% CI: .035 - .124, $p < 0.001$
Solicitous responses and activity limitation	$\beta = .094$, 95% CI: .020 - .169, $p = .013$

Lagged association between patient-perceived responses and change in patient outcomes

Negative responses and symptom severity	$\beta = -.048$, 95% CI: -.767 - .671, $p = .896$
Negative responses and patient distress	$\beta = -.027$, 95% CI: -.193 - .140, $p = .755$
Solicitous responses and disability	$\beta = -.039$, 95% CI: -.093 - .016, $p = .164$
Solicitous responses and activity limitation	$\beta = -.029$, 95% CI: -.123 - .064, $p = .541$

5.4.2.4 Patient-perceived solicitous responses.

The analyses outlined for significant other-reported solicitous responses were repeated, with patient-perceived solicitous responses entered as the independent variable. The results revealed that patient-perceived solicitous responses were associated with decreased levels of patient reported disability at the concurrent momentary assessment (Table 15). Additionally, patient-perceived solicitous responses were associated with an increase in patient activity limitation at the same momentary assessment. As before, lagged patient-perceived solicitous responses were then calculated and included in the model, with change in patient disability and activity limitation as dependent variables.

These analyses indicated that there was no significant association between patient-perceived solicitous responses at the previous assessment and change in patient disability or activity limitation reported between the previous and current assessment (Table 15).

Table 16: The mediating effect of patient distress and activity limitation on the relationship between patient-perceived responses and patient outcomes in momentary analyses

The mediating effect of distress on the relationship between patient-perceived negative responses and symptom severity

Model 1: Negative responses and symptom severity	$\beta = .505$, 95% CI: .214 - .797, $p = .001$
Model 1 including patient distress (mediator)	$\beta = .384$, 95% CI: .093 - .674, $p = .01$
Indirect effect of distress	0.122

The mediating effect of activity limitation on the relationship between patient-perceived solicitous responses and disability

Model 2: Solicitous responses and disability	$\beta = .080$, 95% CI: .035 - .124, $p < 0.001$
Model 2 including activity limitation	$\beta = .099$, 95% CI: .056 - .141, $p < 0.001$
Indirect effect of activity limitation	-0.019

Note. Patient-perceived responses are included as the IV and patient reported outcomes (symptom severity and disability) as the DV within these models. Indirect effects are estimated by subtracting the β coefficient of the effect of the IV in the model including the mediating variable from the original model (without the mediating variable).

5.4.3 Testing the meditational role of patient distress and activity limitation

To assess the potential mediating effect of distress, the multi-level model for patient-perceived negative responses and patient symptom severity was recalculated including the potential mediating variable, distress, in the model. The results of these analyses revealed that the coefficient for the effect of negative responses was reduced in the

subsequent model, and there were small indirect effects (Table 16). Similar results were observed when examining the potential mediating effect of activity limitation between patient-perceived solicitous responses and patient disability (see Table 16). However, there were significant direct effects in both models, therefore only providing evidence for partial mediation in each case.

5.5 Discussion

The current study aimed to examine two types of significant other responses in association with patient reported CFS/ME outcomes within the context of daily life. As hypothesised, patient-perceived significant other negative responses were associated with increases in reported symptom severity and distress at the same momentary assessment. These associations were also observed for significant other-reported momentary responses. These results extend the existing literature, which demonstrates an association between negative significant other responses, as reported by both the patient and significant other, and increased patient depression (Romano, et al., 2009; K. White, et al., 2006). Within the literature, patient depression has been associated with poorer patient illness outcomes (Bentall, et al., 2002; Wearden, et al., 2012), and the results of the current study indicated that patient distress partially mediated the relationship between perceived negative responses and increased symptom experience at a momentary level. Overall, the results indicate that on a momentary basis, negative responses are associated with increased patient distress, and that this may also partially account for the relationship with increased symptom severity.

However, since it is not possible to infer causal relationships from ESM data, alternative explanations for these observations must be explored. It is possible that increased patient symptom severity at the momentary level elicited negative significant other responses. Additionally, patient perception, and therefore reporting, of negative

significant other responses may be elevated whilst experiencing increased symptom severity; it may be important to also consider variables unaccounted for in the current analysis, such as patient negative affect.

In contrast to momentary associations, lagged significant other-reported negative responses were associated with a reduction in symptom severity at the subsequent momentary assessment. There are a number of possible explanations for this unexpected finding; symptom severity reported at the following assessment may have simply returned to the level reported prior to the dyadic contact and negative significant other response (that is, the symptom severity reported at the [n-2] assessment). This would suggest that the impact of significant other responses on symptom fluctuations is, at a momentary level at least, fairly transitory. These results may also be consistent with previous observational data, whereby fewer patient illness behaviours and better patient physical functioning were associated with observed negative significant other responses (Romano, et al., 2009).

It was also hypothesised that significant other solicitous responses would be associated with increased patient disability and activity limitation. Patient-perceived solicitous responses were observed to be associated with increased activity limitation at the same momentary assessment, in line with study hypotheses. Cross-sectionally, increased patient disability and fatigue have been associated with increased significant other solicitous responses (Brooks, et al., 2012; Romano, et al., 2009; Schmaling, et al., 2000). The current results do not however, concur with the cross-sectional associations with significant other behaviours and disability observed within the wider literature. The association with patient disability was in the opposite direction to that predicted, with increased solicitousness associated with reduced patient reported disability at the same momentary assessment. The interpretation of the direction of these results is limited by the correlational associations of these variables; however, the results may

indicate that when patients perceive themselves as more able to engage in activities such as work, leisure and social activities, they also report their significant other as engaging in more solicitous behaviours (for example, helping or looking after them). The items developed to assess patient disability showed a significant, moderate correlation with the WSAS measure of disability, suggesting that patients reporting greater levels of disability in the ESM measures also reported higher levels of ongoing disability. However, the inconsistency between our findings with respect to solicitous significant other responding and patient disability, and those previously reported may reflect the methodological differences between measuring patient disability within an ESM paradigm and using traditional cross-sectional questionnaire reports; the ESM data may potentially reflect more state-like reports of disability, whereas cross-sectional reports may reflect more stable, global perceptions of disability.

ESM data offers the potential to examine temporal relationships between variables as they occur, or between current events (for example, significant other responses) and subsequent changes in patient outcomes. However, the current study did not assess the impact of repeated interactions or cumulative significant other responses in association with patient outcomes. On a momentary level, patient-perceived solicitous responses may be experienced as helpful and facilitative by patients, but repeated solicitous exchanges with significant others may impact upon patient outcomes differently over time, as the wider cross-sectional literature would suggest. The current analyses suggest that increased activity limitation may be a potential mediating factor between solicitous responses and disability. These results are in line with previous research indicating that the efficacy of treatment programmes on reducing fatigue severity is mediated by activity limitation (Wearden & Emsley, in press). Future research examining the impact of significant other behaviour might usefully examine those dyads where the significant

other has a persistent and frequent response style (i.e. negative or solicitous) compared with dyads where behavioural interactions with the patient are more variable.

However, significant other-reported solicitous responses were not found to be significantly associated with patient disability or activity limitation, nor were there any significant associations between solicitous responses and change in patient outcomes at the subsequent momentary assessment. It is possible that the items included within the study to assess solicitous responses do not accurately reflect the extremely solicitous behaviours typically found to associate with poorer patient outcomes.

Although ESM offers the potential advantage to overcome some of the difficulties associated with cross-sectional symptom reporting (Redelmeier & Kahneman, 1996; Stone & Broderick, 2007; Stone, et al., 2003), there are also a number of limitations that need to be acknowledged. As noted above, the temporal associations identified between variables of interest are limited by their correlational nature. Further statistical limitations have been outlined in relation to the mediation analyses; such as the possibility of unmeasured confounders accounting for relationships between predictors, mediators and outcomes; hence only tentative conclusions have been drawn. Additionally, a further limitation is the reliance upon participant self-report in generating momentary data, particularly in relation to potentially sensitive questions such as significant other responses. However, confidential electronic data collection ensured that all participants' data entry remained private from the other participant and was inaccessible to either participant following assessment completion. In addition, the inclusion of significant other-reported responses was beneficial for examining these processes from both a patient and significant other viewpoint. Inherently subjective sensations such as fatigue or pain cannot be objectively measured, however, where possible, the development and inclusion of objective measures into ESM paradigms, such as measures of activity, would help overcome some of these difficulties.

The novel findings from this study demonstrate that significant other responses are important for patients' day-to-day experience of CFS/ME. In particular, the results indicate that targeting significant other negative responses may be beneficial for reducing fluctuations in patient experience of symptom severity and distress. The association between solicitous responses and patient activity limitation is important, given the impact of activity limitation on fatigue severity during patient treatment programmes. The results also indicate that perceived helpful responses may be important in facilitating patient perception of increased ability to participate in daily activities. Future research should seek to examine which specific significant other responses elicit increased levels of patient activity, and which associate most strongly with unfavourable activity management strategies, such as activity limitation. This may inform potentially helpful significant other focused interventions.

Chapter 6: General discussion

The following chapter will provide a summary of the key findings presented within the previous thesis chapters; these findings will then be discussed in the context of the previous literature. In addition, the strengths and limitations of the body of work within this thesis will be addressed. Finally, the implications of the findings and key questions for future research will be discussed.

6.1 Key findings

6.1.1 Systematic review

The systematic review identified a small quantity of literature closely related to the research questions explored within this thesis; a total of 13 published articles were uncovered examining significant other experiences of CFS/ME, and the impact of significant other responses upon patient illness outcomes. A key number of findings were identified with respect to significant others' experiences of the condition. Specifically, a number of negative consequences for significant others were noted in the literature, such as relationship difficulties, as well as more practical problems including changes to family roles and financial difficulties. Significant others reported increasing acceptance and adjustment to the condition over the illness course, however, significant other coping strategies varied depending on the nature of the relationship with the patient and significant other gender; male partners reported utilising the fewest coping strategies.

Significant other beliefs, behavioural responses, and dyadic relationship quality had received the most attention in the previous literature. The review identified that significant others tend to hold beliefs that are highly congruent with the patient, in relation to beliefs about the illness onset and ongoing symptom factors; incongruent dyadic beliefs were found to be associated with poorer patient outcomes.

The remaining evidence pointed to two potentially contrasting interpersonal mechanisms; each associated with different beliefs, behavioural responses and relationship quality. The first mechanism appeared to be characterised by beliefs attributing responsibility for the condition to the patient, significant other negative responses (including those described as unhelpful) and low levels of relationship quality, including high conflict, low support and low empathy. These factors appear to be associated with increased patient depression and higher symptom severity. The second potential interpersonal mechanism appeared to be associated with those significant other responses which may reinforce patient illness beliefs or behaviours, such as helping the patient, discussing the illness or encouraging the patient to rest; these have been referred to as solicitous responses throughout the thesis. The evidence suggests that these are associated with significant other beliefs suggesting that patients may control their symptoms by engaging in activity limitation. These significant other responses appear to be associated with patient higher levels of fatigue severity, disability, and expressions of pain and fatigue, but also higher levels of relationship satisfaction.

A number of methodological limitations were identified with the current evidence base, namely that the majority of those studies reviewed (particularly with respect to patient outcomes) relied heavily on cross-sectional associations, whereby reports of significant other factors and patient outcomes arose from self-reported patient accounts. Furthermore, inconsistencies between studies were evident particularly in the measurement of constructs (such as beliefs or responses); other issues included the use of non-specific measures and the lack of theoretical underpinning guiding the previous research. These methodological limitations identified within the primary literature were also important in determining the format of the review. It has been suggested that meta-analyses are inappropriate when the quality of the literature is variable and the

relationships of interest are poorly understood; in circumstances where hypothesis generation is required, narrative reviews can be more informative (Bailar, 1995).

With these key findings and methodological limitations in mind, the rationale for Study 1 was formed; a well-validated, theoretically driven methodological framework was required, not only to examine the proposition of two contrasting interpersonal mechanisms, but to also integrate those factors that had been identified as important (such as significant other beliefs, responses, relationship quality). The Expressed Emotion (EE) construct seemed to fulfil these requirements, particularly given the overlap with the principle EE subscales and significant other behavioural responses previously examined. This also offered the advantage of including a longitudinal design in Paper 1, and integrating the examination of significant other beliefs, dyadic belief incongruence and significant other EE in Paper 2. The design of 3 was also in line with the review conclusions that alternative methodological techniques such as experience sampling (ESM) may overcome some of the limitations of the current evidence base; the momentary assessment of variables within the natural environment offered the potential to address some of the biases inherent in traditional cross-sectional self-reporting particularly with reference to symptom experience. Furthermore, temporal associations between significant other responses and change in outcomes were addressed.

6.1.2 Paper 1: The impact of significant other Expressed Emotion on patient outcomes in chronic fatigue syndrome.

The aim of Paper 1 was to assess the impact of significant other high-EE upon patient outcomes in comparison to low-EE. Specifically, in line with the previous literature, the associations between patient outcomes and high-critical comments were investigated separately from the outcomes associated with high-EOI. In addition, the predictive

validity of EE was assessed by the inclusion of a longitudinal patient follow-up. The sample recruited consisted of patients with a specialist diagnosis of CFS/ME who had selected the individual with the most daily involvement in their life as their significant other.

As this was the first study to explore EE within a CFS/ME sample, the prevalence and distribution of significant other EE was considered; the findings revealed that significant other EE was generally low within the sample. However, the prevalence of high-EE based upon evidence for EOI-only was higher than previously observed in a range of other patient samples, including those consisting of patients experiencing schizophrenia (Barrowclough, et al., 1994), depression (Hooley & Licht, 1997), Alzheimer's disease (Tarrier, et al., 2002) and diabetes (Wearden, Tarrier, & Davies, 2000). This high-EOI classification was significantly more likely to be assigned to parent-significant others than to partners; previous research has also identified that high-EOI is more likely to be observed in parents than spouses (Goldstein, et al., 2002). With respect to patient outcomes, no cross-sectional associations were identified in association with significant other EE. However, as predicted, high-critical comment ratings on the CFI at baseline (≥ 6 critical comments) were predictive of higher fatigue severity and patient depression longitudinally. Further analyses revealed that depression mediated the relationship between critical comments and fatigue severity. High-EOI was also predictive of higher fatigue severity at follow-up, but not level of disability, as predicted.

The results of Paper 1 extend the previous literature, particularly with reference to the association between negative significant other responses and poorer patient outcomes. Furthermore, the findings suggest that the impact of EOI on fatigue severity is not occurring as a result of increased depression, therefore indicating that the mechanism is

different to that of high-critical comments. The longitudinal impact of high-EE upon patient outcomes suggests that this may be an important future target for therapeutic interventions, although further clarification of these interpersonal processes would be important.

6.1.3 Paper 2: Understanding Expressed Emotion in CFS/ME: an investigation into significant other illness beliefs and dyadic belief incongruence.

The aims of Paper 2 were to examine the factors that may contribute to significant other EE within this sample by examining significant other illness beliefs, and the role of dyadic belief incongruence. The sample used in Paper 2 was the same as that reported in Paper 1.

The findings reported in Paper 2 identified that significant others rated as high-EE attributed significantly more symptoms to the condition and held significantly more negative illness models than those rated as low-EE. Beliefs about the perceived negative consequences for themselves and the patient, and emotional representations, significantly differentiated between these high- and low-EE groups. With respect to dyadic belief incongruence, significant differences were observed on the patient consequences and emotional representation subscales; the results revealed that low-EE significant others tended to report more optimistic beliefs relative to the patient, whilst high-EE significant others' illness belief scores were highly congruent with patient scores. Furthermore, overall differences in illness beliefs did not relate to significant other EE rating.

The results of Paper 2 suggest that significant other beliefs about CFS/ME are important for understanding the presence of high-EE. In particular, the findings reveal that perceiving a high number of symptoms associated with the condition, negative consequences and a negative emotional impact associated with CFS/ME are highly

important for high-EE; these beliefs do not simply reflect the level of symptom severity experienced by patients within these dyads. However, previous literature had suggested that significant other belief minimization may be associated with patient delegitimation and consequently poorer outcomes; in contrast, the current findings suggested that optimistic beliefs about CFS/ME were associated with low-EE, which as shown in Paper 1, was associated with better patient outcomes longitudinally.

6.1.4 Paper 3: Significant other behavioural responses and patient CFS/ME symptom fluctuations in the context of daily life: An experience sampling (ESM) study.

Paper 3 was included within the current body of work to examine on a momentary basis and in a real life context, the associations between those significant other responses previously identified as important in the cross-sectional literature and patient outcomes. The methodology was able to assess the temporal associations between these variables. In line with Paper 1, negative and solicitous significant other responses were investigated separately. Furthermore, both significant other-reported and patient-perceived responses were examined. The sample consisted largely of a sub-sample of those dyads who had participated in Study 1.

Multi-level model analyses revealed that negative significant other responses were associated with increased patient symptom severity and distress at the same momentary assessment. These associations were observed for significant other-reported and patient-perceived negative responses. Mediation analyses indicated that, as predicted, increased distress partially mediated the relationship between perceived negative responses and symptom severity occurring at the same time point. When examining significant other-reported solicitous responses, no significant associations with patient outcomes were identified. However, patient-perceived solicitous responses were

associated with increased activity limitation at the same assessment, in addition to reports of reduced disability. Lagged analyses revealed that the effect of significant other responses on patient outcomes was largely transitory; only significant other-reported negative responses were associated with patient outcomes at the subsequent assessment. These analyses revealed a reduction in symptom severity, potentially reflecting a return to the symptom severity level experienced prior to the perception of the negative response.

The results of Paper 3 suggest a momentary association between negative significant other responses and symptom severity, which is at least, partially mediated by an increase in patient distress. The results also reveal an association with disability in the opposite direction to that predicted; it is possible that patients perceive their significant other as more solicitous (e.g. helpful) when they are able to engage in more activities on a day-to-day basis. However, the analyses highlight an association between solicitous responses and increased activity limitation; this mechanism may account for the association between solicitous responses and increased disability observed in previous cross-sectional data. The conclusions made from Paper 3 are limited by the methodological constraints, namely that causal inferences about the direction of the relationships cannot be made.

6.2 General discussion

The findings outlined above demonstrate that significant other responses towards patients experiencing CFS/ME are important for patient illness outcomes. From the systematic review, it was proposed that there was evidence to suggest two separate interpersonal mechanisms that impact upon patient outcomes in different ways; the previous evidence for these proposed mechanisms and their correlates were somewhat limited.

The current body of work extends the previous cross-sectional research examining negative significant other responses (Romano, et al., 2009; Schmalzing, et al., 2000; K. White, et al., 2006), and contributes to an understanding of the psychosocial processes associated with high-EE; these findings indicate that significant other negative responses, such as anger or frustration at the patient, are meaningfully associated with a CFI high-EE rating assigned to significant others on the basis of critical comments. The consistent findings presented in both Papers 1 and 3 suggest that negative significant other responses are associated with increased patient fatigue severity, and that this relationship is mediated by the presence of increased depressive symptoms experienced by patients within these dyads. This is an important finding clinically; increased patient depression has been shown to predict poorer patient outcomes following specialist therapeutic interventions (Bentall, et al., 2002; Wearden, et al., 2012). Furthermore, the longitudinal analyses reported in Paper 1 reveal that depression was a significant predictor of all patient outcomes at follow-up; reducing the critical aspects of significant other EE would appear to be a beneficial target with respect to improving long-term patient outcomes.

The momentary analyses conducted within the context of daily life reveal that the effects of negative responses are short-lived, and associated with transitory increases in symptom experiences which do not extend to the following momentary assessment. In comparison, high-EE as assessed by critical comments made by significant others in the Camberwell Family Interview was predictive of poorer patient outcomes longitudinally, over a six-month period. Leff & Vaughn (1985) described the dichotomous EE-rating as a trait-like measure; more recent conceptualisations of EE have proposed that it is perhaps more useful to consider EE as a relational variable reflecting interactions of both stress and vulnerability on behalf of the patient and significant other (Hooley & Gotlib, 2000). In this sense, EE may therefore include both stable and dynamic

significant other characteristics (Hooley, 2007). The extent to which significant others engage in responses driven by high criticism (such as negative responses) may therefore vary, at times the responses may be reactive and dependent on patient factors such as symptom severity, whilst at other times the responses may be triggered by underlying beliefs and attitudes which may remain fairly stable over time (Hooley, Rosen, & Richters, 1995). This may therefore account for the observed associations between responses and outcomes over very short and longer periods of time.

Understanding of the mechanisms associated with highly critical EE has been more fully understood within the wider EE literature (Hooley & Gotlib, 2000), however, the high prevalence of EOI identified within the current sample suggests that it is imperative to understand these processes further, if our understanding of the impact of interpersonal processes is to be advanced in relation to CFS/ME patient outcomes. The data presented within study 1 suggests that EOI is not fully represented by, or equivalent to, solicitous responses; the previous cross-sectional literature has identified consistent links between solicitous-like responses and increased patient disability and fatigue (Brooks, et al., 2012; Romano, et al., 2009; Schmaling, et al., 2000). No cross-sectional associations were identified in association with EOI, and at follow-up, high EOI predicted increased fatigue severity only. Whilst there is some degree of overlap between those responses relevant for both constructs, EOI as a global scale includes other types of relevant behaviours and attitudes which do not correspond with solicitousness, such as, intrusive overprotection, exaggerated emotional responses and emotional distress. It is possible that these factors may be less relevant for CFS/ME outcomes than for other disorders, and such differences may account for the lack of meaningful associations identified here. Alternatively, it is possible that it may be more appropriate to decompose EOI into these two types of responses; that is, those which

are perceived as facilitative or helpful, and those which represent the more extreme aspects of EOI, and to examine these separately, in association with patient outcomes.

However, the items included within the momentary analyses did not reflect the extreme behaviours which may typically be characteristic of higher levels of EOI. Instead the items included behaviours which overlap between solicitous responses and EOI; the rationale for doing so was to increase variability in the responses across the sampling period. This allows for fluctuations in responses to be observed (Kimhy, et al., 2012), and increases statistical power (Bolger & Laurenceau, 2013). However, the momentary data suggests that some of those responses conceptualized as solicitous may be experienced as supportive or facilitative by patients; the association with reduced disability was in the opposite direction to the cross-sectional literature (Brooks, et al., 2012; Romano, et al., 2009; Schmalings, et al., 2000). Whilst this may relate to methodological issues surrounding comparisons of cross-sectional and momentary reports of constructs (Palmier-Claus, et al., 2011), it may also suggest that an important line of enquiry might be to differentiate empirically those response styles which are experienced as supportive and beneficial for patient outcomes, from those responses which are associated with poorer patient outcomes. Furthermore, since low levels of significant other support have been reported in association with poorer patient outcomes (Dickson, et al., 2007; Goodwin, 2000), it would be interesting to examine if responses perceived as supportive correspond with the positive EE subscales. Two subscales coded during the CFI examine positive aspects of the patient-significant other relationship; these are positive comments and warmth. Like critical comments, positive comments are scored as frequency counts. However, in contrast to critical comments, the content of positive comments must include evidence for praise, approval or appreciation of the behaviour or personality of the individual. In addition, evidence contributing to the warmth subscale includes sympathetic or empathetic statements,

evidence of interest in the person, including enjoyment of joint activities, and tonal warmth; negative evidence suggesting a lack of warmth can also be considered within the final rating (Leff & Vaughn, 1985).

As previously noted, a large proportion of significant others who received an overall high-EE rating did so on the basis of evidence for EOI; many of these presented with emotional distress at interview when discussing the impact of the condition. The importance of significant other difficulties was also confirmed by examining the illness beliefs associated with high-EE; these findings identify that in particular, perceived negative consequences and emotional representations associated with CFS/ME are important for determining high-EE. Targeting these particular significant other CFS/ME illness beliefs may be important in reducing high-EE, and potentially improving significant other outcomes. The evidence outlined within the literature suggests that significant others may experience negative consequences as a result of the condition (Ax, et al., 2002; Kelly, et al., 1999); however, the analyses presented within Paper 2 suggest that the beliefs held by high-EE significant other are not the result of higher levels of patient fatigue severity within those dyads. These findings therefore suggest that it is the significant other perceptions of the condition which are important for the presence of high-EE. Previous research has identified that significant other coping strategies may be influenced by significant other gender and relationship to the patient (Ax, 1999), the current findings also suggested that this was the case; mothers were significantly more likely to be rated as high-EOI, and mixed high-EE (that is, on the basis of evidence for both EOI and critical comments) than partners, who were significantly more likely to be male.

6.3 Strengths and Limitations

Considering the chapters presented within this thesis as a collective body of work, there are a number of strengths, and limitations, which must be taken into account when evaluating the findings.

A particular strength of the current work is the multi-method approach that has been employed throughout the thesis, incorporating a systematic review, cross-sectional, longitudinal, and momentary methods to assess the associations between significant other factors and patient outcomes in CFS/ME; the advantage of which arises from the combination of the individual strengths of these methods. The systematic review highlighted the potential avenues for future lines of enquiry and the methodological limitations of the existing literature; these conclusions helped inform the programme of study outlined within this thesis. The cross-sectional methods utilised in Papers 1 and 2 allowed the concurrent relationships between significant other beliefs and significant other EE (Paper 2), and significant other EE and patient outcomes (Paper 1) to be identified. In addition, the longitudinal aspect of Paper 1 allowed the impact of significant other factors to be assessed over time, to determine if temporal relationships existed between previously observed EE status and later reports of patient functioning. The experience sampling methodology offered a number of methodological advantages; dyadic interactions were captured within a naturalistic setting and it was possible to explore a number of main effects, including patient changes in outcomes following contact with the significant other.

Furthermore, significant other factors were examined from both a patient and significant other perspective throughout the papers presented within this thesis. This was advantageous in momentary analyses as the method allowed significant other responses occurring within the same moment in time to be examined separately (Paper

3); the relationship between responses and outcomes was therefore examined from the perspective of the individual engaging in the response (i.e. the significant other), as well as the individual experiencing the response (i.e. the patient). This is important in reducing common method variance commonly observed within the previous literature, whereby patient outcomes and significant other variables are both determined by patient self-report. In addition, this issue was addressed in Paper 2 by including significant other beliefs that were not derived from the CFI; the utilisation of the IPQ in comparison to other methods (such as attributional coding) ensured that the source of significant other beliefs was different to the source of the EE rating.

However, there are also limitations which must be considered before drawing conclusions from the current data. Despite employing a range of methods to examine these associations of interest, the current analyses do not enable any conclusions about causality to be made. Furthermore, all variables measuring significant other factors or patient outcomes presented throughout the thesis rely solely on participant self-report, albeit elicited through various methods (such as interview, questionnaire, and computerised ESM protocols). Although these limitations are likely to be common to much of the research conducted within this area, it is possible that techniques such as ESM could also include objective measures of outcomes, although this may not be possible for subjective experiences such as fatigue or pain. Observational studies may also be useful in extending the findings outlined here.

Finally, issues related to the sample recruited for the current studies need to be addressed. All patients were required to have received a specialist diagnosis of CFS/ME, in addition to meeting a study checklist to be eligible for inclusion. However, the illness duration reported by a large proportion of participants extended to a period of many years. Given that the sample therefore consisted of patients with established CFS/ME, the change in outcomes between baseline and follow-up may have been

expected to be minimal; in this event it may have been difficult to demonstrate any longitudinal effects associated with significant other EE. Equally, as the majority of participants were recruited at the point of induction to specialist treatment programs, this may also have impacted upon anticipated longitudinal associations by increasing the likelihood of change across the follow-up period. Data published in conjunction with the National Outcomes Database (NOD) suggest that longitudinal improvements in fatigue are observed following contact with specialist NHS services (Crawley, et al., 2013), despite typically reporting long illness durations (Collin, et al., 2011). The change values reported here are comparable to those previously identified (Crawley, et al., 2013) despite different methods of calculation. Crawley et al., (2013) subtracted the sample mean at follow-up from the sample mean at baseline; within the current study patient scores at follow-up were subtracted from the baseline score on an individual patient basis and a mean calculated for the overall change variable. Variability in the primary patient outcomes was observed, both across the sample as a whole, and when examining dichotomous EE subgroups within Study 1. The longitudinal analyses presented within Paper 1 are however, limited by a lack detailed information about treatment received at follow-up; it was not possible to ascertain the extent of engagement patients had had with specialist clinicians by the study follow-up, nor the extent to which they had complied with the treatment programs. Therefore, potential treatment confounds were uncontrolled for in these analyses. Yet, despite these potential confounds, the significant longitudinal association with poorer patient outcomes suggests that the effects associated with significant other high-EE are genuine.

Recruitment of patient groups can be challenging particularly when seeking to recruit individuals within dyads; it is possible that the low rates of critical comments observed within the sample in particular may be the result of a self-selection bias occurring at

recruitment. Only 22% of those patients approached within the specialist clinics consented to taking part in Study 1, and of those participants, 42% completed both Study 1 and Study 2. It is possible therefore that the current sample reflect individuals who were highly motivated to participate in psychological research. In addition, in each study the target sample size was not quite met; questions surrounding sufficient statistical power are therefore evident, particularly within the patient follow-up in Study 1. Issues of statistical power within the current sample are exacerbated by the heterogeneous nature of the significant other sample; it is possible that interpersonal process may be different in different relationship types. The collection of additional patient information at follow-up, such as the amount of treatment received or level of engagement with services would have also been beneficial in determining improvement controlling for the effect of treatment.

Finally, the generalizability of the findings to the wider chronic fatigue syndrome population must be considered. Although the samples recruited for both Studies 1 and 2 demonstrate similar demographic characteristics to the wider population in terms of mean age of onset and reported illness duration, the proportion of female participants within the current studies is inflated in comparison to demographic data, whereby it is estimated that approximately 75% of patients with CFS/ME are female (Cairns & Hotopf, 2005). However, the recruitment of female participants observed within the current studies is highly comparable to the sampling rates reported within other studies examining significant other factors in CFS/ME (such as Blazquez, et al., 2012; Goodwin, 1997; Heijmans, et al., 1999; Romano, et al., 2009); the findings outlined within the thesis would therefore appear to be generalizable to the specific literature of interest.

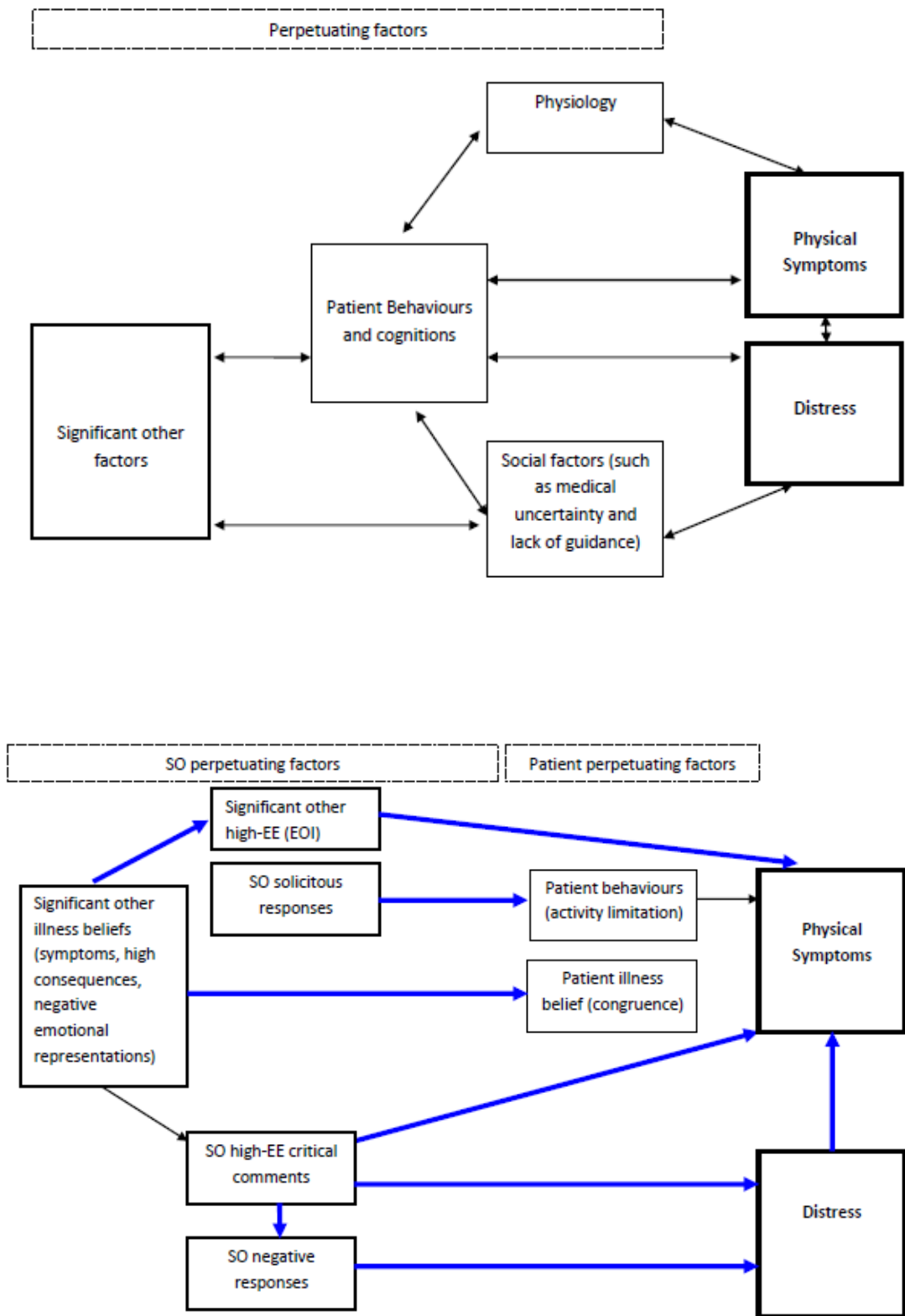
6.4 Implications

6.4.1 Informing theoretical models of chronic fatigue syndrome

Cognitive behavioural models of CFS/ME outline that social factors may be an important perpetuating factor in illness maintenance; however, this currently lacks specificity in terms of the factors that this may include. The empirical work presented within this thesis examined significant other factors as specific potential perpetuating factors in the maintenance of CFS/ME; the hypothesised and observed associations are presented in Figure 3. In addition, the findings of the thesis also address a current limitation of the cognitive behavioural model; the associations between significant other factors are systematically examined, in addition to the associations with patient factors known to be important in symptom maintenance (i.e. patient beliefs and behaviours).

The findings outlined suggest that the beliefs associated with high-EE, particularly high-EOI appear to be highly congruent to those held by patients; the expression of high-EOI was found to be associated with poorer long-term patient fatigue severity. In addition, the evidence obtained from the ESM study indicated that patient behaviours (i.e. resting) are also associated with significant other solicitous responses at a momentary level. Finally, significant other criticism and negative responses were identified as important for patient illness outcomes as a result of increasing patient distress, or depressive symptoms. These findings point to specific ways in which significant other factors may be impacting on symptom perpetuation, although additional work is required to develop the theoretical model further.

Figure 3: Hypothesized extension to the cognitive behavioural model for CFS/ME (top) and cognitive behavioural model including findings outlined within this thesis (bottom)



6.4.2 Significant other intervention development

Furthermore, the evidence suggests that the future development of significant other-focussed interventions may be beneficial for both patient and significant other outcomes. Previous therapeutic interventions providing family-focussed CBT for adolescents with CFS/ME have found it be helpful in improving patient outcomes over relatively short follow-up periods (Chalder, Deary, Husain, & Walwyn, 2010; Chalder, Tong, & Deary, 2002). Interestingly, the authors report that these families were presented with a treatment manual, and furthermore, were provided with the support to assist their child through the rehabilitation programme (Chalder, et al., 2010; Chalder, et al., 2002).

No such interventions have been undertaken with adults experiencing CFS/ME, however, several interventions utilising the EE construct have previously been developed for families of patients experiencing psychosis. Evidence suggests that family interventions are effective at reducing patient relapse and hospitalisations, in addition to other beneficial outcomes such as improved patient social adjustment and significant other EE reduction (Pfammatter, Junghan, & Brenner, 2006; Pharoah, Mari, Rathbone, & Wong, 2010). Furthermore, family interventions may also be efficacious in improving significant other outcomes; it has been suggested that the focus of interventions should be on reducing distress and improving well-being for all family members (Lobban et al., 2013). Increasing knowledge of psychosis, targeting family appraisals about the impact of the illness and caring for the patient, in addition to increasing coping resources have been highlighted as important aspects of these psycho-educational interventions (Addington, McCleery, & Addington, 2005; Raune, Kuipers, & Bebbington, 2004; Sin, Henderson, Pinfold, & Norman, 2013). Given that the findings reported in Paper 2 suggests that significant others rated as high-EE within the current population also perceive higher CFS/ME related symptoms, greater

consequences and emotional representations, there is reason to suggest that family interventions based upon those found in the psychosis literature may also be beneficial in CFS/ME.

Advances in health technology have led to the recent development of modular, online self-help interventions for relatives of people with psychosis (Lobban et al., 2011; Sin, et al., 2013). The flexible nature of such interventions may be advantageous in that modification of the content based upon the patient-significant other relationship type could be possible, and the implementation may require less professional input than other forms of intervention (Lobban, et al., 2011; Lobban, et al., 2013; Sin, et al., 2013); this may help overcome some of the difficulties associated with integrating family interventions into standard service provision (Kuipers, 2006). In addition, further recent evidence suggests that online interventions may also be beneficial for individuals experiencing physical symptoms; online CBT-based interventions have shown to be efficacious for improving fatigue outcomes for patients experiencing various conditions such as multiple sclerosis or cancer (Moss-Morris et al., 2013; Ritterband et al., 2012).

These interventions potentially provide a framework to guide the development of significant other interventions in CFS/ME. Currently, presentation of explanatory models for CFS/ME form introductory aspects of patient therapeutic programmes, providing the rationale for collaborative treatment plans to be developed (Wearden, et al., 2010); these manuals may also usefully inform the development of significant other intervention components. As significant other high-EE was found to be predictive of poorer longitudinal patient outcomes, it is possible that a reduction in significant other high-EE or promotion of low-EE may be also beneficial for patient illness outcomes. In addition to the longitudinal associations, the results of the ESM study also identify that significant other responses are important for symptom fluctuations and the day-to-day

experience of CFS/ME. Further research would be necessary to clarify which responses are facilitative and which are detrimental to patient outcomes.

6.5 Future work

Whilst the current findings have contributed to our understanding of the role of interpersonal processes in the perpetuation of CFS/ME, a number of areas have been identified where further research and clarification of significant other factors would be beneficial. Firstly, the assumption that the principle EE subscales and significant other behavioural responses are linked was not statistically assessed within this thesis. It would be advantageous to empirically assess these relationships, both within the cross-sectional data, and potentially in the momentary analyses; this work could be further developed by examining the moderating effect that significant other EE status may have on dyadic interactions within the context of daily life.

Furthermore, examination of the responses associated with EOI may be particularly valuable to investigate further; the relationships between EOI, solicitous responses, and patient outcomes appear to be more complex than initially hypothesised. It is possible that it might also be necessary to modify the EOI concept in the context of EOI, given the high proportion of significant others achieving a high-EE rating on the basis of EOI only. In order to understand the way in which EOI may impact upon patient outcomes more fully, it is imperative to develop an understanding of the beliefs and responses associated with a high-EOI classification. Building upon the current work examining the general illness models associated with overall high-EE, future work might usefully employ alternative methodologies, such as an attributional framework (Munton, Silvester, Stratton, & Hanks, 1998; Stratton, et al., 1988) for examining more specific beliefs associated with high levels of criticism and EOI, in line with much of the wider EE literature (Barrowclough & Hooley, 2003). In addition, previous research within

CFS/ME populations has suggested that significant other spontaneous causal attributions for symptom events may be linked with specific significant other behavioural response styles (Brooks, et al., 2012). Therefore, further examination of these processes could help inform the particular correlates of the proposed interpersonal mechanism identified within the previous literature linking solicitous responses with poorer patient outcomes (Brooks, et al., 2012; Romano, et al., 2009; Schmaling, et al., 2000).

Those subscales assessing the positive aspects of EE, that is, warmth and positive comments have largely been overlooked within the wider literature. However, the beneficial effect of high levels of warmth in the absence of high-EE was observed in schizophrenia early in the development of the EE construct (Brown, et al., 1972). More recent focus on positive EE in mental health conditions, and warmth in particular, has shown that high levels within the family environment can have a protective effect for patients (Lopez et al., 2004), and potential predictive validity in relation to patient improvements following family interventions (Le Grange, Hoste, Lock, & Bryson, 2011). It is possible, given the negative impact of delegitimizing interactions with significant others (Dickson, et al., 2007), that warmth, or lack thereof, may also be predictive of outcomes within this CFS/ME patient group.

The literature examining the associations between EE and patient outcomes in schizophrenia have focussed predominantly on high-EE as a predictor for poorer outcomes, such as symptom relapse (Bebbington & Kuipers, 1994; Butzlaff & Hooley, 1998), however, low-EE can also be conceptualised as predictive of better patient outcomes (Lopez, et al., 2004); it has recently been suggested that it is equally important to understand the processes associated with low-EE, particularly in the development of family based interventions (Treanor, Lobban, & Barrowclough, 2013). The findings presented in Paper 2 examine the illness beliefs associated with low-EE;

however, this could be further developed by examining the responses typical of interactions in low-EE dyads, to identify those responses which may be more adaptive for significant other and patient outcomes.

Future work incorporating objective measures of significant other responses or patient outcomes may be beneficial, as outlined previously with reference to the current methodological limitations. This may include observational data of dyadic interactions, to examine if significant other observable responses meaningfully correspond with their EE rating, for example, by demonstrating more negative verbal and non-verbal behaviours, and less positive behaviours associated with high-EE, as previously observed in other patient groups (Hooley, 1986; Miklowitz, et al., 1995). Furthermore, development of ESM techniques to include additional ambulatory assessments is a promising avenue for future research within this area. Whilst this has been done previously with reference to measures of patient physical activity in CFS/ME (Evering, et al., 2011), novel techniques are also being developed to assess social factors in relation to patient health outcomes (Mehl, Robbins, & Deters, 2012). Advances in technology have resulted in the development of electronic devices able to record naturally occurring interactions, offering the potential to passively capture interpersonal processes (M. L. Robbins et al., 2011). These methods may address some the biases inherent in self-reports of sensitive information such as significant other responses, and if added to standard ESM diary techniques, may provide further powerful insights in to the role of dyadic interactions, perceived responses, and patient outcomes.

Finally, as outlined previously, the results of Paper 1 suggest that there may be differences in the distribution of high-EE within different significant other subgroups in CFS/ME samples. Further exploration of these issues with larger sample sizes would be instructive in future investigations.

6.6 Conclusions

The work presented here demonstrates novel techniques for examining significant other factors within a CFS/ME population. A clear association for the interpersonal processes associated with high criticism has been documented, building upon the existing CFS/ME literature, and in line with the wider EE knowledge base. What are currently less clear, are the mechanisms through which EOI and solicitous responses impact upon patient outcomes; and indeed if these are representing the same underlying interpersonal processes. These unanswered questions provide the potential avenues for future research. The results suggest that significant other factors are important in the perpetuation of patient CFS/ME, and furthermore have highlighted several significant other factors that are potential targets for future intervention development.

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Appendices

Appendix 1 – NHS ethical approval letter for Study 1 (11/NW/0198)


National Research Ethics Service
NRES Committee North West - Liverpool East
North West REC Centre
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ
Telephone: 0161 6257835

31 May 2011

Miss Rebecca Band
Room H22, Coupland Building
School of Psychological Sciences
University of Manchester
M13 9PL

Dear Miss Band

Study title: The impact of significant others' responses to illness upon patient outcomes and the maintenance of symptoms in chronic fatigue syndrome (also known as myalgic encephalomyelitis; CFS/ME)

REC reference: 11/NW/0198

Thank you for your letter of 12 May 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

This Research Ethics Committee is an advisory committee to the North West Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England

Appendix 2- Participant Information Sheet (PIS) for

Study 1; patient version



Participant Information Sheet (PIS)

Significant others and patient outcomes in CFS/ME

We would like to invite you to take part in a research study. Before you decide you need to understand why this research is being done and what it would involve for you. Please take the time to read the following information carefully and discuss this with others if you wish. Please ask us if there is anything that is unclear or that you would like more information about. Take time to decide whether or not you wish to take part.

What is the aim of the study?

This study aims to investigate the role that close interpersonal relationships might have for people with CFS/ME. We are interested at looking at the emotions, beliefs and behaviours of CFS/ME patients and individuals close to them (referred to as significant others), and differences in patient symptom patterns.

Why have I been invited?

We are inviting you to take part in this study if you have a diagnosis of CFS/ME. Entry into the study will require you to nominate a significant other. Initially, you will be asked to take part in a very brief telephone interview to find out if you are eligible for the study. A total of 60 couples (patient plus significant other) will take part in the study.

Do I have to take part?

No you do not have to take part. It is completely up to you to decide, but if you do we will then ask you to sign a consent form to show that you have read the information sheet and have agreed to take part. If you do decide to take part but change your mind later you are free to withdraw at any time, without this having any effect on your current or future treatment, and you do not need to give us a reason.

What will participation involve?

You will first take part in a short telephone interview with the researcher to find out if you are eligible for the study. If you are eligible and agree to participate then the study will be split into 3 parts:

- After the telephone conversation, you will be sent a research pack by email or post. This will contain a number of questions about your CFS/ME. You can fill this in at a pace that is convenient to you before the second part of the research.
- Part 2 of the study will involve the chief researcher coming to interview you about your illness and your relationship with your significant other. The interview will be arranged during the initial telephone interview, and can happen at a time and a place to best suit you. The interview will last approximately 30-45 minutes, and will be audio-taped for future transcription and analysis. Audio-tapes and transcripts will be anonymised. Both will be securely stored and password protected. Data from

questionnaires will be anonymised on a secure database. Study data will be retained for up to five years after the end of the study. Identifiable data will be destroyed as soon as possible. However, with your permission, the researcher will securely store your personal details to enable her to contact you about future studies about CFS/ME that you might be interested in taking part in. This is not obligatory and declining to do so will not affect your participation within this study in any way.

- The third part of the study will take approximately place 6 months after the first part of the research. A second research pack will be sent to you, asking you about your CFS/ME at that time. You will be asked to complete the questionnaires and return them to the researcher.

-

Will anyone else know that I am taking part in this study?

The whereabouts of the researcher, when out of the office interviewing, is made known to a member of staff at the University of Manchester in accordance with its lone researcher policy.

What are the possible risks of the study and what will be done to ensure confidentiality?

There is the possibility that you may find some of the questions in this study uncomfortable or upsetting. If this is the case then you are free to leave any of these questions unanswered and you are free to end your participation any time. All information which is collected about you, or that you provide in relation to your significant other, during the course of this research will be kept strictly confidential. It is important for you to be assured that we will not share any of your answers with your significant other, and neither will we tell you what they have said in their questionnaires or interview. Any information about you which we collect will have your personal information such as your name and address removed so that you cannot be recognised. No information collected as part of the study will be shared with your GP unless you say something that makes us believe you might harm yourself or others. Completed questionnaires, audiotapes and transcripts of audiotapes will all be kept in secured filing cabinets at the University of Manchester and will only be seen by the members of the research team. They will be destroyed 5 years after the end of the study.

What are the benefits of this study?

There may be no direct benefit to you as a result of participating within this study, although it will allow you the opportunity to discuss your personal experiences of CFS/ME. It is hoped that this study will provide a better understanding of the impact that close interpersonal relationships can have for patients with CFS/ME.

What will happen if I don't want to carry on with the study?

You can withdraw from the study completely at any time and this will not affect your current or future treatment or any dealing with the CFS/ME service. You would not need to give reasons for your withdrawal.

What if I have any questions?

If you have any questions about any aspect of this study, you should speak to the researchers who will do their best to answer your questions. You can contact the researcher on 0161 3060444 or by email at Rebecca.band-2@postgrad.manchester.ac.uk. You may also want to talk to your healthcare team or family about the study.

What if there is a problem or I want to complain about this study?

If there is a problem, you may contact the researcher in the first instance. All concerns will be dealt with promptly, and information will be provided by telephone or in writing to inform you of how the problem has been addressed. If the researcher is unable to resolve your concern or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on 0161 2757583 or 0161 2758093 or by email to research-governance@manchester.ac.uk. In the event that you may wish to make a formal complaint, you may wish to contact the NHS patient advice and liaison service (PALS). Contact telephone numbers for local PALS offices can be found at www.pals.nhs.uk.

Will I be able to find out about what this study has found?

Hopefully, this research will later be published in a scientific journal. The lead researcher will send all of the people who took part a summary of the results, and if they want, a copy of the final published article.

Thank you very much for reading this. If you would like any further information or have any questions, please contact the chief investigator of this project:

Rebecca Band
PhD Student
The University of Manchester
Email: Rebecca.band-2@postgrad.manchester.ac.uk
Telephone: 01613060444

Appendix 3 – NHS ethical approval letter for Study 2 (11/NW/0495)



National Research Ethics Service

NRES Committee North West - Greater Manchester West

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7815

11 August 2011

Miss Rebecca Band
Room H22, Coupland Building
School of Psychological Sciences
University of Manchester
M13 9PL

Dear Miss Band

Full title of study: The impact of daily interactions on fluctuations in patient symptom severity and disability: An experience sampling methodology (ESM) investigation in chronic fatigue syndrome (CFS/ME)

REC reference number: 11/NW/0495

Thank you for your email of 10 August 2011. I can confirm the REC has received the documents listed below as evidence of compliance with the approval conditions detailed in our letter dated 10 August 2011. Please note these documents are for information only and have not been reviewed by the committee.

I can confirm that the additional conditions have been met.

Documents received

The documents received were as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering Letter		10 August 2011
Participant Consent Form: Patient Version	2	10 August 2011
Participant Consent Form: Significant Other Version	2	10 August 2011
Participant Information Sheet: Patient Version	2	10 August 2011
Participant Information Sheet: Significant Other Version	2	10 August 2011
Questionnaire: Patient ESM Items	2	10 August 2011
Questionnaire: Significant Other ESM Items	2	10 August 2011

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

This Research Ethics Committee is an advisory committee to the North West Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England

Participant Information Sheet (PIS)

Daily interactions and symptom fluctuations in CFS/ME

We would like to invite you to take part in a research study. Before you decide you need to understand why this research is being done and what it would involve for you. Please take the time to read the following information carefully and discuss this with others if you wish. Please ask us if there is anything that is unclear or that you would like more information about. Take time to decide whether or not you wish to take part.

What is the aim of the study?

This study aims to investigate the factors that may impact upon short term symptom fluctuations in CFS/ME. We are interested at looking at the daily activities of people with CFS/ME and individuals close to them (referred to as significant others). We will be looking at several aspects of daily life for both participants, which include activities, social interactions, mood and changes in patient symptom severity and disability.

Why have I been invited?

We are inviting you to take part in this study if you have a diagnosis of CFS/ME. Entry into the study will require you to nominate a significant other (i.e. a friend/relative). A total of 30 couples (patient plus significant other) will take part in the study.

Do I have to take part?

No you do not have to take part. It is completely up to you to decide, but if you do we will then ask you to sign a consent form to show that you have read the information sheet and have agreed to take part. If you do decide to take part but change your mind later you are free to withdraw at any time, without this having any effect on your current or future treatment, and you do not need to give us a reason.

What will participation involve?

First contact with the researcher will be made via telephone to discuss the study. If you are eligible and agree to participate then the study will be split into 2 parts:

- A briefing session will be arranged during the telephone conversation. During this meeting you will be given a short set of questions to fill in about your CFS/ME. The procedure for studying the daily interactions and activities will be fully explained to you, and you will also be given study equipment. You will have the opportunity to ask any outstanding questions that you might have.
- Part 2 of the study will last for six days and will start the day after both you and your significant other have had a briefing session. You will be asked questions about your activities, interactions, mood and symptoms at ten random points between 7.30am and 10.30pm for the six days. Your significant other will also be asked to answer similar questions at the same time point, but it is important that both participants

answer independently from each other. All data will be anonymised on a secure database. Study data will be retained for up to five years after the end of the study. Identifiable data will be destroyed as soon as possible.

- At the end of the six days, the researcher will visit you again to collect all equipment and to ask you about your experience of the study.

Will anyone else know that I am taking part in this study?

The whereabouts of the researcher, when out of the office during visits, is made known to a member of staff at the University of Manchester in accordance with its lone researcher policy.

What are the possible risks of the study and what will be done to ensure confidentiality?

There is the possibility that you may find some of the questions in this study uncomfortable or upsetting. If this is the case then you are free to leave any of these questions unanswered and you are free to end your participation any time. All information which is collected about you, or that you provide in relation to your significant other, during the course of this research will be kept strictly confidential. It is important for you to be assured that we will not share any of your answers with your significant other, and neither will we tell you what they have said in their responses. Any information about you which we collect will have your personal information such as your name and address removed so that you cannot be recognised. No information collected as part of the study will be shared with your GP. However, if something is disclosed that indicates there is a risk of harm to you or somebody else then we will have to break confidentiality and inform the appropriate authority. Completed questionnaires, and study data will all be kept in secured filing cabinets, or password protected electronic storage at the University of Manchester and will only be seen by the members of the research team. They will be destroyed 5 years after the end of the study.

What are the benefits of this study?

There may be no direct benefit to you as a result of participating within this study. However, it is hoped that the research will result in a greater understanding of the day to day clinical experience of CFS/ME, and the different factors which impact upon symptom fluctuations in CFS/ME.

What will happen if I don't want to carry on with the study?

You can withdraw from the study completely at any time and this will not affect your current or future treatment or any dealing with the CFS/ME service. You would not need to give reasons for your withdrawal.

What if I have any questions?

If you have any questions about any aspect of this study, you should speak to the researchers who will do their best to answer your questions. You can contact the researcher on 0161 3060444 or by email at Rebecca.band-2@postgrad.manchester.ac.uk. You may also want to talk to your healthcare team or family about the study.

What if there is a problem or I want to complain about this study?

If there is a problem, you may contact the researcher in the first instance. All concerns will be dealt with promptly, and information will be provided by telephone or in writing to inform you of how the problem has been addressed. If the researcher is unable to resolve your concern or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on 0161 2757583 or 0161 2758093 or by email to research-governance@manchester.ac.uk.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against The University of Manchester or NHS Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you. In the event that you may wish to make a formal complaint, you may wish to contact the NHS patient advice and liaison service (PALS). Contact telephone numbers for local PALS offices can be found at www.pals.nhs.uk.

Will I be able to find out about what this study has found?

Hopefully, this research will later be published in a scientific journal. The lead researcher will send all of the people who took part a summary of the results, and if they want, a copy of the final published article.

Thank you very much for reading this. If you would like any further information or have any questions, please contact the chief investigator of this project:

Rebecca Band
PhD Student
The University of Manchester
Email: Rebecca.band-2@postgrad.manchester.ac.uk
Telephone: 01613060444

Appendix 5 – Patient study clinical checklist (screening)

Criteria	Yes	No
Is your fatigue (tiredness, weariness) your main symptom?	<input type="checkbox"/>	<input type="checkbox"/>
Can your fatigue be distinguished from low mood, lack of interest and sleepiness?	<input type="checkbox"/>	<input type="checkbox"/>
Have you had this fatigue all your life, as far as you can remember?	<input type="checkbox"/>	<input type="checkbox"/>
Did your fatigue start with a definite onset (which may be gradual)?	<input type="checkbox"/>	<input type="checkbox"/>
Is your fatigue a clear change from how you were previously?	<input type="checkbox"/>	<input type="checkbox"/>
Is your fatigue out of proportion to what you would expect as normal for your level of exertion?	<input type="checkbox"/>	<input type="checkbox"/>
Does your fatigue restrict you from performing any activities, for example, occupational, social, leisure, self-care?	<input type="checkbox"/>	<input type="checkbox"/>
Does your illness affect both your physical ability (lack of energy / strength) and mental functioning (lack of motivation & alertness - thinking, concentrating, talking, reading or remembering)	<input type="checkbox"/>	<input type="checkbox"/>
Have you been fatigued for the last 6 months?	<input type="checkbox"/>	<input type="checkbox"/>
During this time was your fatigue present for more than half of the time?	<input type="checkbox"/>	<input type="checkbox"/>
Medical exclusions	Checked	Not checked
Do you have any medical conditions that might be responsible for your chronic fatigue (list if any)	<input type="checkbox"/>	<input type="checkbox"/>

All of the white boxes (above) should be ticked, and none of the grey boxes, for the participant to meet the Oxford criteria.

Oxford criteria met?	Met	Not met
Meets all of the inclusion criteria and none of the exclusion criteria for CFS	<input type="checkbox"/>	<input type="checkbox"/>
Presence of a significant other	<input type="checkbox"/>	<input type="checkbox"/>

Appendix 6 – Patient outcome measures for Study 1

CFS/ME related questions

Chalder fatigue scale

We would like to know whether you have been having problems with feeling tired, weak or lacking in energy in the last month. Please answer each question by ticking the answer which you think most nearly applies to you. **If you have been feeling tired for a long time, we want you to compare yourself to how you felt when you were last well.**

	Less than usual	No more than usual	More than usual	Much more than usual
Do you have problems with tiredness?				
Do you need to rest more?				
Do you feel sleepy or drowsy?				
Do you have problems starting things?				
	Better than usual	No more than usual	More than usual	Much more than usual
Do you lack energy?				
Do you have less strength in your muscles?				
	Less than usual	No more than usual	More than usual	Much more than usual
Do you feel weak?				
Do you have difficulty concentrating?				
Do you make slips of the tongue when speaking?				
Do you find it more difficult to find the correct word?				
	Better than usual	No more than usual	More than usual	Much worse than usual
How is your memory?				

SF-36:

In general would you say your health is:

Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor ☐

Compared to one year ago, how would you rate your health in general now?

Much better ☐ Somewhat better ☐ About the same ☐
Somewhat worse ☐ Much worse ☐

The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much? We are interested in how you have been in the last month.

Please tick one box on each line

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports			
Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf			
Lifting or carrying groceries			
Climbing several flights of stairs			
Climbing one flight of stairs			
Bending, kneeling or stooping			
Walking more than a mile			
Walking several hundred yards			
Walking 100 yards			
Bathing or dressing yourself			

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your **PHYSICAL health**?

	Yes	No
Cut down on the amount of time you spend on work or other activities		
Accomplished less than you would like		
Were limited in this kind of work or other activities		
Had difficulty performing the work or other activities (e.g. it took extra effort)		

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any **EMOTIONAL problems** (such as feeling depressed or anxious)?

	Yes	No
Cut down on the amount of time you spend on work or other activities		
Accomplished less than you would like		
Didn't do work or other activities as carefully as usual		

During the past 4 weeks to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

- Not at all ☐
 Slightly ☐
 Moderately ☐
 Quite a bit ☐
 Extremely ☐

How much bodily pain have you had during the past 4 weeks?

- None ☐
 Very Mild ☐
 Mild ☐
 Moderate ☐
 Severe ☐
 Very Severe ☐

During the past 4 weeks, how much did pain interfere with your normal work (including outside the home and housework)?

- Not at all ☐
- A little bit ☐
- Moderately ☐
- Quite a bit ☐
- Extremely ☐

WSAS: People's problems sometimes affect their ability to do certain day-to-day tasks in their lives. To rate your problems look at each section and determine on the scale provided how much your problem impairs your ability to carry out the activity.

1. Work – if you are retired or choose not to have a job for reasons unrelated to your problem, please tick here

- 0 ☐ 2 3 4 5 6 7 8
- Not at all Slightly Definitely Markedly Very severely
- I cannot work

2. Home management – cleaning, tidying, shopping, cooking, looking after home/children, paying bills etc

- 0 1 2 3 4 5 6 7 8
- Not at all Slightly Definitely Markedly Very severely

3. Social leisure activities – with other people, e.g. parties, pubs, outings, entertaining etc

- 0 1 2 3 4 5 6 7 8
- Not at all Slightly Definitely Markedly Very severely

4. Private leisure activities – done alone, e.g. reading, gardening, sewing, hobbies, walking etc

- 0 1 2 3 4 5 6 7 8
- Not at all Slightly Definitely Markedly Very severely

5. Family and relationships – form and maintain close relationships with others including the people that I live with

- 0 1 2 3 4 5 6 7 8
- Not at all Slightly Definitely Markedly Very severely

HADS: Please read each item and tick the box which comes closest to how you have been feeling during the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

1. I feel tense or wound up:

- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

2. I still enjoy the things I used to enjoy:

- Definitely as much ☐
- Not quite as much ☐
- Only a little ☐
- Hardly at all ☐

3. I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

4. I can laugh and see the funny side of things:

- As much as I always could ☐
- Not quite as much now ☐
- Definitely not so much now ☐
- Not at all ☐

5. Worrying thoughts go through my mind:

- A great deal of the time ☐
- A lot of the time ☐
- From time to time but not too often ☐
- Only occasionally ☐

6. I feel cheerful:

- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

7. I can sit at ease and feel relaxed:

- Definitely ☐
- Usually ☐
- Not often ☐
- Not very often ☐

8. I feel as if I am slowed down:

- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

9. I get a sort of frightened feeling like butterflies in my stomach:

- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

10. I have lost interest in my appearance:

- Definitely ☐
- I don't take as much care as I should ☐
- I may not take quite as much care as ever ☐
- I take just as much care as ever ☐

11. I feel restless as if I have to be on the move:

- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

12. I look forward with enjoyment to things:

- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

13. I get sudden feelings of panic:

- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

14. I can enjoy a good book or radio or TV programme:

- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

VAS-F, Your level of energy and fatigue: You are asked to place an "X" through these lines to indicate how you are feeling **RIGHT NOW**

- | | | |
|--|-------|--|
| Not at all tired | _____ | Extremely tired |
| Not at all sleepy | _____ | Extremely sleepy |
| Not at all drowsy | _____ | Extremely drowsy |
| Not at all fatigued | _____ | Extremely fatigued |
| Not at all worn out | _____ | Extremely worn out |
| Not at all energetic | _____ | Extremely energetic |
| Not at all active | _____ | Extremely active |
| Not at all vigorous | _____ | Extremely vigorous |
| Not at all efficient | _____ | Extremely efficient |
| Not at all lively | _____ | Extremely lively |
| Not at all exhausted | _____ | Totally exhausted |
| Keeping my eyes open is no effort at all | _____ | Keeping my eyes open is a tremendous chore |
| Moving my body is no effort at all | _____ | Moving my body is a tremendous chore |
| Concentrating is no effort at all | _____ | Concentrating is a tremendous chore |
| Carrying on a conversation is no effort at all | _____ | Carrying on a conversation is a tremendous chore |
| I have absolutely no desire to close my eyes | _____ | I have a tremendous desire to close my eyes |
| I have absolutely no desire to lie down | _____ | I have a tremendous desire to lie down |

Appendix 7 – Modified Camberwell Family Interview (CFI) schedule for CFS/ME

Camberwell Family Interview schedule – adapted for CFS/ME

Date of interview:

Interviewer:

Tape number:

INITIAL QUESTION: to establish terminology to be used throughout the interview

Do you prefer to use the term CFS or ME?

1. BACKGROUND INFORMATION

Composition of household (i.e. sharing same cooking facilities)

Total number of members of household, their age, relationship to the patient and occupational status

Hours face to face contact with patient

History of relationship

How long have you known.....?

How long have you been partners?

When did you first start living together?

Since you first started living together, have there been any periods when you have lived apart?

Other relationships

Has anyone else in the family ever had a diagnosis of CFS/ME in the past?

Are there any members of the family who do not live with you but who either visit you often or are important influences in your life? e.g. parents, grandparents, adult children, stepchildren

Section A

CFS HISTORY – onset

I should like to begin by asking you when(*patient's*) troubles first began?

IMPORTANT TO NOTE WHETHER SO KNEW PATIENT AT ONSET OF CFS. If not, omit or modify questions below on illness onset.

Illness onset

When did you first notice that something was wrong with him/her?
Would you say the onset was sudden or quite gradual?

Probes

What was [p] behavior like at this time?
What happened then?
How long has this been going on?

Do you have any idea what might have caused the illness onset?

Was there any difficulty in deciding what was wrong?

When was the diagnosis of CFS/ME first made?

Who made the diagnosis of CFS?

Reactions to diagnosis of: patient
 interviewee
 other members of the family

If SO met patient after he/she already had CFS/ME:

What did you think whentold you he/she had CFS?
How did you react?

Do you think there is any difference between a diagnosis of CFS and ME?

CFS HISTORY– between onset and present

Who has been responsible for the medical care (GP, hospital consultant, clinic)?
What course has the CFS taken?
Have there been any periods when the CFS/ME has been more or less difficult to contend with?

CFS CURRENT STATUS

I'd now like to ask you how [p]'s CFS/ME has been recently, perhaps thinking about the last three months in particular.

SO over the past 3 months, have there been any particular CFS related problems? (*probes for detail, probes to keep within 3 month period*)

Probes

When did it begin to get worse?
What happened?
How long has this been going on?

Family time budget (last 3 months)

I would like to get a picture of how (patient) usually spends a day?

On a typical weekday: What time would s/he ... (see behaviours below)
 How would s/he... (see behaviours below)
 Who would be there?

Behaviours: Get up
 Have breakfast

Leave for work/ spend the morning
Have lunch
Spend the afternoon
Return from work/ have tea
Spend the evening
Go to bed

How about weekends?

Now I'd like to ask you some more general questions about how you get along. I'm going to ask you about some problems which some people have which you may or may not have experienced.

Irritability

One of the ways in which having a long standing medical condition can affect some people is to make them more irritable. By this, I mean snappy or more likely to 'fly off the handle' at things which would not normally worry them.

How often has [p] been irritable?
How often would this sort of thing occur
How often has [p] been like this with (each household member)

Can you describe what happened?
When did this last occur?

What (other) sort of things make him/her irritable?
When does [p] get irritable? Have there been any times when it was worse?
Did this usually occur at any particular time of day?

How do you (other members of the household) react?
Can you control or cope with the irritability at all?... How?... To what extent?
Do you think that [p] should be more able to control his/ her irritability?

CHECK FOR IRRITABILITY BETWEEN

Patient and partner
(‘All couples feel irritable with each other from time to time’)
Patient and each other member of household

Has irritability changed since s/he developed CFS?
Has it changed recently?

Quarrels and arguments

Most families have quarrels and arguments from time to time. Apart from the sort of irritability we have been talking about has [p] recently had any rows or quarrels with you or anyone else in the family?

When did it occur? What happened?
How long did the disagreement last? What sort of things did you say to each other?

Did you shout at each other?

Do you have periods of not speaking following a disagreement? Has there ever been an atmosphere in the house after a row or quarrel?

Have you ever parted because of a quarrel - even overnight?

CHECK FOR ROWS AND QUARRELS BETWEEN

Patient and SO

Patient and other household members

Has anyone in the family ever expressed concern that arguing or quarrelling might make [p]'s CFS/ME worse?

Nagging

Apart from the irritability you have mentioned do you ever nag or grumble at ____ (patient)?

What sort of things do you complain about?

What do you say?

How often has this occurred in the last 3 months?

Section B

I would like to ask some questions about the way [p] may have been affected by CFS/ME, and about some problems which people sometimes have. Of course, not all of these may apply to [p], but I'd like to run through these quickly and perhaps you could tell me whether or not [p] has been like this, especially over the past three months.

Lacking in energy?	Tiredness (what has ____ fatigue been like recently?) Tires easily How feels after rest/ exercise Slowness (has s/he seemed particularly slow doing things?) Has s/he stopped doing anything?
--------------------	---

Sleep	What has 's sleep been like? (amount) Has [p] had difficulty in getting off? Has the [p] been waking up very early? (onset, mid or early waking, dreams, getting up, when)
-------	--

Appetite	What has [p]'s appetite been like? Has [p] had any intolerance to any type of food? Intolerance to alcohol/ tea/ coffee
----------	---

Bodily complaints	Has [p] complained of any headaches or dizziness? Has [p] complained of any pains? (Muscular/ joint?) (where?) Sore throats Sensitivity to noise/ light Nausea Bowel problems (diarrhoea, constipation) Any others?
-------------------	---

Probes: How often? Severity?

Withdrawal	Has s/he kept to him/ herself a lot? Or refused to meet people? Has s/he tended to avoid in the household? What about friends or relatives?
------------	--

	Has s/he had times of being less talkative?
Probes:	Does this mean can't go out? Limiting in any way?
Memory	Has s/he had any marked difficulties with memory? Such as problems remembering anything Does s/he ever seem confused? Problems with word loss Concentration problems
Fears	Has s/he experienced any unusual fears? Fears of exercise, relapse, going out Any other fears? Does s/he talk about these fears? (how often, to whom?)
Anxiety	Periods of anxiety or panic Did the anxiety or panic occur at any special time?
Worry	Worrying about a lot of things? Such as about you or anyone else? (Family/ family relationships?) ...or about other things such as relationships with friends, work (Social relationships, Work/ career, Financial matters) Health – worries about course of illness, treatment What makes you think s/he is worrying about this? Has s/he talked about it, how often, to whom?
Misery	Depressed, tearful, sad What makes you think she was depressed/miserable? Did s/he complain? When did it happen? Can you describe what happened? Has s/he blames herself for things that don't seem important? Has s/he said life is not worth living? How would you tend to react to that?
Obsessions	Been unusually finicky or fussy about anything? Has s/he had routines of doing thing only in a certain way even if it seems silly? Rituals associated with CFS treatment regime
Personal care and habits	Look after him/her self alright? Clean and tidy?

MANAGEMENT

Does [p] follow a treatment plan for their CFS? (*check understanding not just Dr led treatment plans, also including alternative/ self administered etc.*)

Can you tell me what [p]'s treatment regime is?

Who provided this treatment plan (consultant, GP, self administered)?

Does [p] always stick to this treatment plan?

Are there any particular factors which stop [p] sticking to their treatment plan?

Has this treatment plan always been the same?

What treatment has [p] used in the past?

Has [p] tried any other methods of treatment in the past?

Are you happy with [p]'s current treatment plan?

Overall, how well do you think [p] handles his/ her CFS/ME? Is there anything he or she could do to manage better?

The impact of the family on patient's self-management

Does [p] look after his or her CFS/ME alone, or are other members of the family involved in anyway?

Are there any ways in which you (other family members) help [p]'s management of his/ her CFS/ME?

Do you think there are any things you (Other family members) do which get in the way of [p]'s management of his/ her CFS/ME?

Do **you** (does anyone else) help the patient with

Medication

Diet

Exercise

Sleep hygiene

Going to medical appointments (GP, hospital, clinic) with the patient

Does anything any member of the family does interfere with [p]'s ability to manage his/ her CFS/ME?

Do you ever alter your (the family's) routine to fit in with [p]'s CFS/ME care routine?

How has the family's lifestyle changed or adapted in anyway due to [p]'s CFS/ME?

Probes: How do you feel about that?/ How does that make you feel?/ Does that ever make you feel on edge?

TWO KEY QUESTIONS

What difference has [p]'s CFS/ME made to you? (and the family as a whole)

From your own point of view, what has been the worst aspect of [p]'s CFS/ME?

Marital relationships

How do you spend the evenings together when you are at home?

How much chance do you get to go out together?

Are there any things which you anddo together in the evening and at weekends? (watching TV, sitting and chatting, playing games, hobbies etc.)

In general, how would you say you get along together?

Do you usually know whenis feeling moody or upset, or whenis feeling pleased?

Do you thinkknows when you are feeling upset or pleased?

Over the past year, have you been apart for any reason (visiting relatives, work, holidays etc.)? How long was this for, how did you feel about it?

In what way do you tend to get on each other's nerves?

Relationship with other family members e.g. children

How much time does.....spend with the children?
Has his/ her role as a parent changed as a result of the CFS, or is his/ her ability to deal with the children affected by CFS?
How do the children react to the CFS?
Do you agree/ disagree over child management?

Affection, Warmth, Interest

Has the affectionhas shown towards you changed at all recently?
Has it changed since the CFS began (if relevant)?
In what way?

What about interest in you, isinterested in the things you do? Does s/he show much interest?

Are you satisfied with the affection an interest s/he shows in you?

Probes (if necessary)

How would you like things to be different?
How do you feel about the change?
Does this bother you much?

Has the way you feel aboutchanged at all since the CFS/ME began? Or recently?
In what way?

If yes: How would you like things to be different?
Or: How do you feel about the change does it bother you?

Social relationships

Would you say that [p] is a friendly person?

Does[p] currently spend much time mixing with people outside the family?
How does this compare to before [p] had CFS/ME?

Does[p] currently have hobbies/ interests which take him/ her outside the home?
How does this compare to before[p]had CFS/ME?

Do you think that having CFS has affected [p]'s social life?
Do you think that any aspect of his/ her social life could affect his/ her CFS?

HOUSEHOLD TASKS

I'd like to ask you a bit about how you share out the various jobs that have to be done in the family.

Who generally does the following:

Shopping for food and cooking
Cleaning, tidying etc.
Hoovering
Laundry
Ironing
Decorating

Gardening
Windows
Childcare jobs

If relevant: Has the amount has done in the house changed since the CFS began?

In general, are you satisfied with the way things are done at home?

Are you satisfied with the way jobs are shared out?

How do you feel about that now?

FINANCES AND MONEY

What have been the effects of’s CFS on his/ her employment status? (quit work, cut down hours, changed job)

Have there been any financial implications for the household of’s CFS?

Has there been any change in how well your husband/wife has dealt with his/her money?

Has there been any impact of’s CFS on your employment?

IMPACT OF CFS ON PATIENT’S LIFE

Are there any activities which YOU have been unable to do or which have been affected by’s CFS?

Although’s CFS has clearly had a negative impact on a number of areas of his/ her life, can you think of any way in which may have benefited because of his/ her illness?

Do you think there is any way in which you have benefited from having CFS?

Are there any of’s activities which have been affected by his/ her having CFS?

e.g. doing things around the house
 shopping
 going out socially
 going away on holiday
 work
 mobility, walking
 sports
 leisure activities

Is there anything else?

(Try to get an idea of how much each activity is affected on an informal 5 point scale: not at all, a little, a moderate amount, a lot, unable to do activity)

Appendix 8 – Guidance for rating critical comments within the CFS/ME sample

A critical comment will be defined in the same way as outlined within the EE training manual as *“a statement which, by in the manner in which it is expressed, constitutes an unfavourable comment upon the behaviour or the personality of the person to whom it refers”* (Leff & Vaughn, 1985). Additionally, all of the standard rating criteria will be used to extract critical comments from CFI interviews conducted within this sample. Remarks will be rated as critical if they show sufficient critical content (more intense or obvious dislike or disapproval of behaviour) or variations in critical vocal tone.

However, a number of issues arise when attempting to define critical comments from CFS/ME family members. In CFS/ME the behaviours associated with the symptoms and the responses that these elicit from relatives are very different in their content and may be less clear cut than in the traditional EE patient samples. Critical statements are typically expressed in a less emphatic or intense manner in comparison to other patient samples, and may be verbalised in a less direct manner. For example, the criticism of the individual or their behaviour may be implied within the utterance, and additionally, typical critical statements such as ‘it annoys me’, ‘I got angry’ occur less frequently and less explicitly within this sample. Critical remarks often refer to the prominent and disabling aspects of the disorder (such as illness management, fatigue, cognitive and emotional problems, inability to work) and the consequences of these symptoms more commonly than directly criticising the patient behaviours or personality characteristics.

Therefore, all utterances which ‘feel’ critical or in which there may be dissatisfied content or tone should be extracted for rating. These utterances will then be coded as ‘borderline’ or ‘dissatisfied’ remarks.

Guidance for determining borderline and dissatisfied comments

Borderline statements: Those statements which ‘feel’ as though they are potentially critical, but fail to meet the standard criteria for criticism, on either tone or the content of the remark should be extracted and rated as borderline critical comments.

Statements rateable for dissatisfaction: those statements in which the relative expresses some dissatisfaction or regret concerning the behaviour, or a desire for thing to be different, without explicitly blaming the patient should be extracted and rated as dissatisfaction comments.

Examples of critical, borderline and dissatisfied comments within the CFS/ME sample


1. **Critical comment:** “I understand why she's getting irritable and I do, I think she could do more to control the Chronic Fatigue which would control the mood swings, that's my personal opinion. I think, you know, that there's things that really really frustrate me and I think 'you know what, you don't help yourself at times'. This is what we argue about, that is the majority of arguments because when she is feeling better, that's when I lose me temper because it's like you obviously don't value your quality of life because when you feel better, that's it you're off and it's like a viscous circle,

you know what I mean so...so the questions do you think she could control it, it's just a viscous circle so no, I think she could make more effort to control the ME rather than the, and then I think it would all slot into place"

2. **Borderline comment:** "she fights against it, she urm, she's still, she won't stop doing things. I'll give you an example right, the Christmas tree that you're sat next to, she HAD to do it, even though it took her probably two days to do it, I wasn't allowed to do it, 'no, I'll do it, I'll do it' so she's still exactly the same, she doesn't take help easily, she doesn't, she wants to do everything herself, which is a bit of a come down for somebody in her position I guess, but that's what she wants to do"
3. **Dissatisfaction only:** "the only thing that tends to get on my nerves about him is he won't get as much help as he needs, just very stubborn and there are times when he's very tired and he won't admit it because he wants to protect me".

Appendix 9 – IPQ-R and CBRQ: Patient version

1 Page		Significant others and patient outcomes in CFS				
IPQ-R We are interested in your own personal views of how you now see your current CFS/ME. Please indicate how much you agree or disagree with the following statements about your CFS/ME by ticking the appropriate box.						
	VIEWS ABOUT YOUR CFS/ME	STRONGLY DISGREE	DISAGREE	NEITHER DISAGREE NOR AGREE	AGREE	STRONGLY AGREE
IP1*	My CFS/ME will last a short time					
IP2	My CFS/ME is likely to be permanent rather than temporary					
IP3	My CFS/ME will last for a long time					
IP4*	This CFS/ME will pass quickly					
IP5	I expect to have this CFS/ME for the rest of my life					
IP6	My CFS/ME is a serious condition					
IP7	My CFS/ME has major consequences on my life					
IP8*	My CFS/ME does not have much effect on my life					
IP9	My CFS/ME strongly affects the way others see me					
IP10	My CFS/ME has serious financial consequences					
IP11	My CFS/ME causes difficulties for those who are close to me					
IP12	There is a lot which I can do to control my symptoms					
IP13	What I do can determine whether my CFS/ME gets better or worse					
IP14	The course of my CFS/ME depends on me					
IP15*	Nothing I do will affect my CFS/ME					
IP16	I have the power to influence my CFS/ME					
IP17*	My actions will have no affect on the outcome of my CFS/ME					
IP18*	My CFS/ME will improve in time					
IP19*	There is very little that can be done to improve my CFS/ME					
IP20	My treatment will be effective					



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	in curing my CFS/ME					
IP21	The negative effects of my CFS/ME can be prevented (avoided) by my treatment					
IP22	My treatment can control my CFS/ME					
IP23 *	There is nothing which can help my condition					
IP24 *	The symptoms of my condition are puzzling to me					
IP25 *	My CFS/ME is a mystery to me					
IP26 *	I don't understand my CFS/ME					
	VIEWS ABOUT YOUR CFS/ME	STRONGLY DISGREE	DISAGREE	NEITHER DISAGREE NOR AGREE	AGREE	STRONGLY AGREE
IP27 *	My CFS/ME doesn't make any sense to me					
IP28	I have a clear picture or understanding of my condition					
IP29	The symptoms of my CFS/ME change a great deal from day to day					
IP30	My symptoms come and go in cycles					
IP31	My CFS/ME is very unpredictable					
IP32	I go through cycles in which my CFS/ME gets better and worse.					
IP33	I get depressed when I think about my CFS/ME					
IP34	When I think about my CFS/ME I get upset					
IP35	My CFS/ME makes me feel angry					
IP36 *	My CFS/ME does not worry me					
IP37	Having this CFS/ME makes me feel anxious					
IP38	My CFS/ME makes me feel afraid					

Causes of my CFS/ME

We are interested in what you consider may have been the cause of your CFS/ME. As people are very different, there is no correct answer for this question. We are most interested in your own views about the factors that caused your CFS/ME rather than what others including doctors or family may have suggested to you. Below is a list of possible causes for your CFS/ME. Please indicate how much you agree or disagree that they were causes for you by ticking the appropriate box.

	POSSIBLE CAUSES	STRONGLY DISGREE	DISAGREE	NEITHER DISAGREE NOR AGREE	AGREE	STRONGLY AGREE
C1	Stress or worry					
C2	Hereditary - it runs in my family					
C3	A Germ or virus					
C4	Diet or eating habits					
C5	Chance or bad luck					
C6	Poor medical care in my past					
C7	Pollution in the environment					
C8	My own behaviour					
C9	My mental attitude e.g. thinking about life negatively					
C10	Family problems or worries					
C11 *	Overwork					
C12 *	My emotional state e.g. feeling down, lonely, anxious, empty					
C13 *	Ageing					
C14 *	Alcohol					
C15 *	Smoking					
C16 *	Accident or injury					
C17 *	My personality					
C18 *	Altered immunity					

In the table below, please list in rank-order the three most important factors that you now believe caused YOUR CFS/ME. You may use any of the items from the box above, or you may have additional ideas of your own.

The most important causes for me:

1. _____
2. _____
3. _____



The University of Manchester

Version 1

18/03/11

CBRQ:

Your views about your symptoms Listed are a number of symptoms that you may have experienced since your illness. Read the instructions at the top of each column carefully as they ask you different questions in relation to your symptoms

	Please tick the box in this column if you have experienced the symptom SINCE your illness began	Tick ONE of the columns below for each symptom by choosing what you think the symptom is <u>MOST related to</u>		
		<i>This symptom is related to my illness</i>	<i>This symptom is related to stress</i>	<i>This symptom is related to reduced activity</i>
Pain				
Sore throat				
Nausea				
Breathlessness				
Flushed face				
Weight change				
Fatigue				
Shakiness				
Swollen glands				
Stiff or sore joints/muscles				
Loss of coordination				
Depressed mood				
Body tension				
Light sensitivity				
Restlessness				
Sore eyes				
Pounding heart				
Irritability				
Headaches				
Upset stomach				
Sleep difficulties				
Increased sweating				
Dizziness				
Tight chest				
Loss of strength				
Loss of interest				
Concentration/memory problems				

Appendix 10 – IPQ-R and CBRQ: Significant other version

CBRQ:

Your views about your significant other's symptoms

Listed are a number of symptoms that your significant other may have experienced since their illness. Read the instructions at the top of each column carefully as they ask you different questions in relation to their symptoms

	Please tick the box in this column if they have experienced the symptom SINCE their illness began	Tick ONE of the columns below for each symptom by choosing what you think the symptom is <u>MOST related to</u>		
		<i>This symptom is related to their illness</i>	<i>This symptom is related to stress</i>	<i>This symptom is related to reduced activity</i>
Pain				
Sore throat				
Nausea				
Breathlessness				
Flushed face				
Weight change				
Fatigue				
Shakiness				
Swollen glands				
Stiff or sore joints/muscles				
Loss of coordination				
Depressed mood				
Body tension				
Light sensitivity				
Restlessness				
Sore eyes				
Pounding heart				
Irritability				
Headaches				
Upset stomach				
Sleep difficulties				
Increased sweating				
Dizziness				
Tight chest				
Loss of strength				
Loss of interest				
Concentration/memory problems				

IPQ-R-SO CFS/ME: Your views about your relatives CFS/ME

We are interested in your own personal views of how you now see your relatives current CFS/ME.

Please indicate how much you agree or disagree with the following statements about your relative's CFS/ME by ticking the appropriate box.

	VIEWES ABOUT THEIR CFS/ME	STRONGLY DISGREE	DISAGREE	NEITHER DISAGREE NOR AGREE	AGREE	STRONGLY AGREE
IP1	Their CFS/ME will last a short					

	time					
IP2	Their CFS/ME is likely to be permanent rather than temporary					
IP3	Their CFS/ME will last for a long time					
IP4*	Their CFS/ME will pass quickly					
IP5*	I expect them to have this CFS/ME for the rest of their life					
IP6	Their CFS/ME is a serious condition					
IP7	Their CFS/ME has major consequences on their life					
IP8*	Their CFS/ME does not have much effect on their life					
IP9	Their CFS/ME strongly affects the way others see them					
IP10	Their CFS/ME has serious financial consequences for them					
IP11	Their CFS/ME causes difficulties for those who are close to them					
IP12	There are some things they can do to control their symptoms					
IP13	To some extent what they do can determine whether their CFS/ME gets better or worse					
IP14	The course of their CFS/ME depends on them					
IP15 *	Nothing they do will affect their CFS/ME					
IP16	They have the power to influence their CFS/ME					
IP17 *	Their actions will have no effect on the outcome of their CFS/ME					
IP18 *	Their CFS/ME will improve in time					
IP19 *	There is very little that can be done to improve my relatives CFS/ME					
IP20	Their treatment will be effective in curing their CFS/ME					
IP21	The negative effects of their CFS/ME can be prevented or avoided by their treatment					
IP22	Their treatment can control their CFS/ME					
IP23	There is nothing which can					

*	help their condition					
IP24	The symptoms of their condition are puzzling to me					
IP25	Their CFS/ME is a mystery to me					
IP26	I don't understand their CFS/ME					
IP27	Their CFS/ME doesn't make any sense to me					
IP28 *	I have a clear picture or understanding of their CFS/ME					
IP29	The symptoms of their CFS/ME change a great deal from day to day					
IP30	Their symptoms come and go in cycles					
IP31	Their CFS/ME is very unpredictable					
IP32	They go through cycles in which their CFS/ME gets better and worse.					
IP33	I get depressed when I think about their CFS/ME					
IP34	When I think about their CFS/ME I feel upset					
IP35	Their CFS/ME makes me feel angry					
IP36 *	Their CFS/ME does not worry me					
IP37	Their CFS/ME makes me feel anxious					
IP38	Their CFS/ME makes me feel afraid					
IP39	There are some things that I can do to control their symptoms					
IP40	To some extent, what I do can determine whether their CFS/ME gets better or worse					
IP41 *	Nothing I do will affect their CFS/ME at all					
IP42 *	My actions will have no effect on the outcome of their CFS/ME					
IP43	If I tried harder I could control their symptoms					
IP44	I could do more to help them					
IP45	If I were a stronger person they would get better					
IP46 *	Their CFS/ME does not have much effect on my life					
IP47	Their CFS/ME has financial					

	consequences for me					
IP48	Their CFS/ME makes it more difficult for me to do day to day things					
IP49	I don't get on as well with our family since their CFS/ME					
IP50	Their CFS/ME has messed up my social life					
IP51	Their CFS/ME means I am valued less by other people					
IP52	Their CFS/ME makes working very difficult for me					
IP53	I have lost important relationships as a result of their CFS/ME					
IP54 *	Their CFS/ME has had some positive effects on my life					

We are interested in what you consider may have been the cause of your relatives CFS/ME. As people are very different, there is no correct answer for this question. We are most interested in your own views about the factors that caused your relatives CFS/ME rather than what others including doctors or family may have suggested to you. Below is a list of possible causes for your CFS/ME. Please indicate how much you agree or disagree that they were causes for your relative by ticking the appropriate box.

	POSSIBLE CAUSES	STRONGLY DISAGREE	DISAGREE	NEITHER DISAGREE NOR AGREE	AGREE	STRONGLY AGREE
C1	Stress or worry					
C2	Heredity - it runs in the family					
C3	A germ or virus					
C4	Diet or eating habits					
C5	Chance or bad luck					
C6	Poor medical care in their past					
C7	Pollution in the environment					
C8	Their own behaviour					
C9	Their mental attitude e.g. thinking about life negatively					
C10	Family problems or worries					
C11*	Overwork					
C12*	Their emotional state e.g. feeling down, lonely, anxious, empty					
C13*	Ageing					
C14*	Alcohol					
C15*	Smoking					
C16*	Accident or injury					
C17*	Their personality					
C18*	Altered immunity					

In the table below, please list in rank-order the three most important factors that you now believe caused YOUR RELATIVES CFS/ME. You may use any of the items from the box above, or you may have additional ideas of your own.

The most important causes for my relatives CFS/ME:

1. _____
2. _____
3. _____

Appendix 11 – ESM items for patients and significant others

Patient version

1. Before the beep went off I was feeling sad
2. Before the beep went off I was feeling excited
3. Before the beep went off I was feeling annoyed
4. Before the beep went off I was feeling happy
5. Before the beep went off I was feeling irritated
6. Before the beep went off I was feeling satisfied
7. Before the beep went off I was feeling distressed
8. Before the beep went off I was feeling relaxed
9. Before the beep went off I was feeling lonely
10. Before the beep went off I was feeling anxious
11. Before the beep went off I was feeling cheerful
12. Before the beep went off I was feeling guilty

13. Right now I feel weak
14. Right now I feel active
15. Right now I feel tired
16. Right now I feel well
17. Right now I am experiencing mental fog
18. Right now I am experiencing pain
19. Right now I am sleepy

20. Before the beep went off I was resting to control my symptoms
21. Before the beep went off I was rushing to get things done whilst I feel able
22. Before the beep went off I was avoiding activities that might make my symptoms worse
23. Before the beep went off I was doing things whilst I can

24. Thinking about what I was doing just before the beep went off, this activity is enjoyable
25. This activity is difficult/ challenging
26. This activity reduced my stress
27. I would rather be doing something else

28. Just before the beep went off I was alone
29. Just before the beep went off I was with the other participant (*if the answer is 'no' the following question will be 43)*)

30. We were talking or doing something together
31. I like this person
32. I feel comfortable with this person
33. I would rather be alone

34. Thinking about the other participant, before the beep went off this person was nagging me
35. Before the beep went off this person was leaving me alone
36. Before the beep went off this person was doing things for me
37. Before the beep went off this person was irritated with me
38. Before the beep went off this person was looking after me
39. Before the beep went off this person was pushing me to do things

40. Before the beep went off this person was helping me
41. Before the beep went off this person was checking up on me
42. Being with this person is
43. Just before the beep went off I was with/ also with someone else:
44. **Thinking about the time elapsed between the current and previous beep I have been with the other participant** *(if the answer is 'no' the following question will be 57)*
45. We have been together
46. We have been talking or doing something together
47. **Thinking about the time elapsed between the current and previous beep, the other participant was nagging me**
48. **During this time period this person was leaving me alone**
49. **During this time period this person was doing things for me**
50. **During this time period this person was irritated with me**
51. **During this time period this person was looking after me**
52. **During this time period this person was pushing me to do things**
53. **During this time period this person was helping me**
54. **During this time period this person was checking up on me**
55. Being with this person is
56. Since the last beep I have been with other people:
57. Since the last beep went off I was able to leave the house
58. Since the last beep went off I was able to do household tasks
59. Since the last beep went off I was able to socialise with other people
60. Since the last beep went off I was able to enjoy leisure activities
61. Since the last beep went off I was able to work
62. Since the last beep I have been generally active
63. Thinking about the most important event that has happened to me since the last beep went off, it was
64. This beep disturbed me

Significant other version

1. Before the beep went off I was feeling sad
2. Before the beep went off I was feeling excited
3. Before the beep went off I was feeling annoyed
4. Before the beep went off I was feeling happy
5. Before the beep went off I was feeling irritated
6. Before the beep went off I was feeling satisfied
7. Before the beep went off I was feeling distressed
8. Before the beep went off I was feeling relaxed
9. Before the beep went off I was feeling lonely
10. Before the beep went off I was feeling anxious
11. Before the beep went off I was feeling cheerful
12. Before the beep went off I was feeling guilty

13. Thinking about what I was doing just before the beep went off, this activity is enjoyable
14. This activity is difficult/ challenging
15. This activity reduced my stress
16. I would rather be doing something else

17. Just before the beep went off I was alone
18. Just before the beep went off I was with the other participant (if the answer is 'no' the following question will be 32)

19. We were talking or doing something together
20. I like this person
21. I feel comfortable with this person
22. I would rather be alone

23. Thinking about the other participant, before the beep went off I was nagging him/her
24. Before the beep went off I was leaving him/her alone
25. Before the beep went off I was doing things for him/her
26. Before the beep went off I was irritated with him/her
27. Before the beep went off I was looking after him/her
28. Before the beep went off I was pushing him/her to do things
29. Before the beep went off I was helping him/her
30. Before the beep went off I was checking up on him/her

31. Being with this person is

32. Just before the beep went off I was with/ also with someone else
33. **Thinking about the time elapsed between the current and previous beep I have been with the other participant** (if the answer is 'no' the following question will be 45)

34. We have been together
35. We have been talking or doing something together

36. **Thinking about the time elapsed between the current and previous beep, I was nagging him/her**
37. **During this time period I was leaving him/her alone**
38. **During this time period I was doing things for him/her**
39. **During this time period I was irritated with him/her**
40. **During this time period I was looking after him/her**
41. **During this time period I was pushing him/her to do things**
42. **During this time period I was helping him/her**
43. **During this time period I was checking up on him/her**

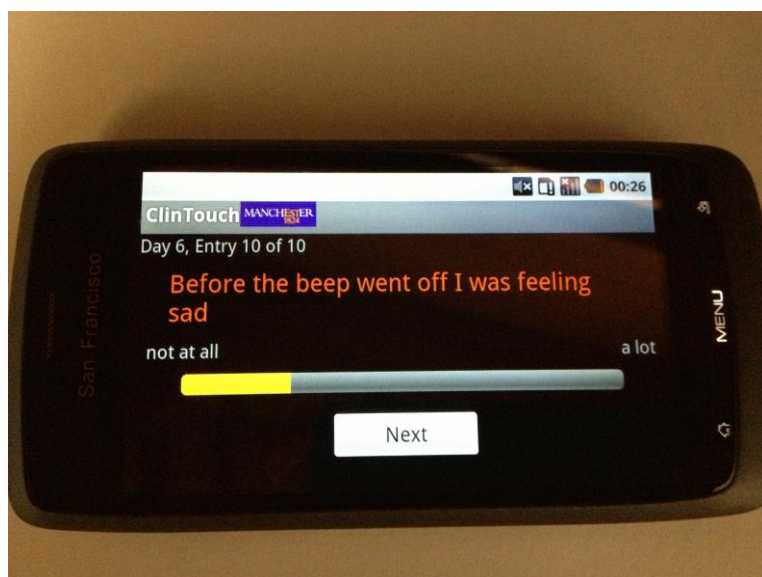
44. Being with this person is

45. Since the last beep I have been with other people:
Thinking about the most important event that has happened to me since the last beep went off, it was

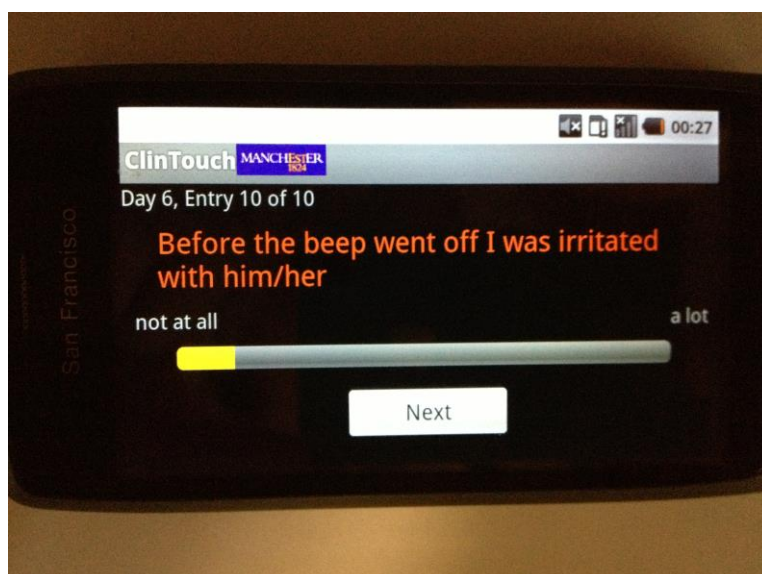
46. This beep disturbed me

Appendix 12 – Screenshots of the ESM hardware and software

Example of an affect item presented on the San Francisco smartphone:



Example of a significant other response item (significant other version):



Briefing checklist

Daily interactions and symptom fluctuations in CFS/ME

Briefing checklist

Participant ID no: _____

☐ **Introduction**

We want to investigate symptom patterns and fluctuations in the course of daily life. To do so we will use an Android Smartphone, which you will be carrying all the time. It is very important to live your life and do things you normally would do. The phone will emit 10 random beeps throughout the day between 7.30am and 10.30pm. Once you hear a beep, follow the instructions on screen to begin the questions. You do not have to get up earlier than usual to hear all the beeps, but when you are awake you will have to carry the phone with you. Please fill in the questions on the phone immediately after hearing the beep. You and your relative will both be filling out questions on the phones at the same time and answering similar questions. It is important that you answer truthfully; your relative will not be able to see your answers.

☐ **Explain briefly the purpose of the study**

- ☐ The purpose is to investigate the daily experiences of CFS/ME and potential factors that might impact upon symptom fluctuations
- ☐ Use the San Francisco Smartphone – please carry this all the time
- ☐ Receipt for Smartphone
- ☐ Every time the phone emits a beep you will have to fill out the questions on the phone immediately
- ☐ Spontaneous responses in the moment
- ☐ Filling out independently and keep it private

☐ **Explain how the phone works**

- ☐ Not water resistant
- ☐ Phone must be switched on at all times during the study
- ☐ Phones will need to be charged every three days or so (1 charger per set)
- ☐ Beeps will go off between 7.30am and 10.30pm (it is important to live your everyday life and not to change routines for the study)
- ☐ Phones with a blue sticker will be for the patient with CFS/ME, orange stickers are for SO's
- ☐ Synchronised beeps
- ☐ Demonstrate beep lengths
- ☐ Beep volume and vibration option (set and non-changeable for duration)
- ☐ The programme will open automatically when it is time to answer the question – What the screen will look like. Don't worry about the other functions on the phone.
- ☐ You may press snooze once and the alarm will sound again in 2 minutes. After a period the questions will become locked for that moment and you will not be able to complete them. The following beep should happen automatically even if you have missed previous beeps
- ☐ Beeps can go off after 15 minutes or 2 hours. If you don't hear a beep after 4 hours and you have not been in a noisy place then please contact us (check contact details)

- ☐ Unlock the phone using the silver button at the top and sliding the green circle to the right
- ☐ Any unexpected pages or anything open – press the house icon (bottom left hand corner next to the menu). Any signs that the software has crashed call asap.
- ☐ **Explain the questions and answering format**
 - ☐ Different sections will have questions about your thoughts, experiences and context (e.g. what you are doing, whom you are with) at the moment (just before the beep went off – notice wording)
 - ☐ Demonstrate how to use the touch screen
 - ☐ Demonstrate how to turn the phone around
 - ☐ Different types of questions (rating scale, fixed answer, yes or no).
Demonstrate:
 - ☐ Explain mood rating scale
 - ☐ Explain points on the scale (not at all- moderate – a lot; points in between)
 - ☐ Explain that 'other participant' will always refer to the other person in the study
 - ☐ Every question refers to the moment just before the beep went off except for the 'since the last beep' questions – which are asking for the time period between beeps
 - ☐ Reiterate that the questions are not generally about what people do or feel, but what they were doing just before the beep went off
 - ☐ Explain since the last beep questions (time elapsed between the previous and current beep)
 - ☐ First beep from second day and first beep from first day (explain that these refer to time since last beep on the previous day and time since practice beep, respectively)
 - ☐ Participant trial exercise
- ☐ **Concluding briefing session**
 - ☐ Ask if they have any questions or concerns
 - ☐ Explain that the programme will start the next day automatically
 - ☐ Show them the contact details again and assure them that they can contact anytime if they have problems
 - ☐ Schedule phone check for day two
 - ☐ Best number to contact them on
 - ☐ Will contact again in a further two days to ensure that all is going well
 - ☐ Once the ESM has finished you will arrange the final meeting to collect the phones and conduct brief (5 minute) interview with the Significant others.

Daily interactions and symptom fluctuations in CFS/ME

ESM feedback questionnaire

Thank you once again for participating in the ESM study. Please let us know your thoughts about, and experiences of the study by filling out the feedback questions below. Feel free to add any additional comments that you may have in the box provided.

1. After hearing an alarm, how long did you leave it before filling in the questions?
 - A) Within one minute.
 - B) 1 - 2 minutes
 - C) 2 - 5 minutes
 - D) 5 - 10 minutes
 - E) 10 - 15 minutes

2. How long did it take you to complete each set of questions once you started?
 - A) Within one minute.
 - B) 1 - 2 minutes
 - C) 2 - 5 minutes
 - D) 5 - 10 minutes
 - E) 10 - 15 minutes

3. Did answering the questions take a lot of work?

<i>Not at all</i>	1	2	3	4	5	6	7	<i>Very much so</i>
-------------------	---	---	---	---	---	---	---	---------------------

4. Were there times when you felt like not answering?

<i>Not at all</i>	1	2	3	4	5	6	7	<i>Very much so</i>
-------------------	---	---	---	---	---	---	---	---------------------

5. Did answering the questions take up a lot of time?

<i>Not at all</i>	1	2	3	4	5	6	7	<i>Very much so</i>
-------------------	---	---	---	---	---	---	---	---------------------

6. Were there times where you had to stop doing something in order to answer the questions?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

7. Was it difficult to keep track of what the questions were asking you?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

8. Were you familiar with using this type of technology?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

9. Was it difficult to keep the device with you or carry it around?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

10. Did you ever lose or forget the device?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

11. Was using the key pad/touch screen difficult to use?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

12. Were there times where you couldn't answer the questions because there wasn't enough signal on the phone?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

13. Do you think other people would find the software easy to use?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

14. Do you think that you could make use of this approach in your everyday life?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

 Very much so

15. Do you think that this approach could help you or other people?

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

Very much so

16. Overall, this experience was stressful

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

Very much so

17. Overall, this experience was challenging

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

Very much so

18. Overall, this experience was pleasing

Not at all

1	2	3	4	5	6	7
---	---	---	---	---	---	---

Very much so

Any other comments about the ESM experience: