

Distinguishing patients with chronic fatigue from those with chronic fatigue syndrome: a diagnostic study in UK primary care

L Darbishire, L Ridsdale and P T Seed

SUMMARY

Background: Chronic fatigue syndrome (CFS) has been defined, but many more patients consult in primary care with chronic fatigue that does not meet the criteria for CFS. General practitioners (GPs) do not generally use the CFS diagnosis, and have some doubt about the validity of CFS as an illness.

Aim: To describe the proportion of patients consulting their GP for fatigue that met the criteria for CFS, and to describe the social, psychological, and physical differences between patients with CFS and those with non-CFS chronic fatigue in primary care.

Design of study: Baseline data from a trial of complex interventions for fatigue in primary care.

Setting: Twenty-two general practices located in London and the South Thames region of the United Kingdom recruited patients to the study between 1999 and 2001.

Method: One hundred and forty-one patients who presented to their GP with unexplained fatigue lasting six months or more as a main symptom were recruited, and the Centers for Disease Control (CDC) case definition was applied to classify CFS.

Results: Approximately two-thirds (69%) of patients had chronic fatigue and not CFS. The duration of fatigue (32 months) and perceived control over fatigue were similar between groups; however, fatigue, functioning, associated symptoms, and psychological distress were more severe in the patients in the CFS group, who also consulted their GP significantly more frequently, were twice as likely to be depressed, and more than twice as likely to be unemployed. About half (CFS = 50%; chronic fatigue = 55%) in each group attributed their fatigue to mainly psychological causes.

Conclusions: In primary care, CFS is a more severe illness than chronic fatigue, but non-CFS chronic fatigue is associated with significant fatigue and is reported at least twice as often. That half of patients, irrespective of CFS status, attribute their fatigue to psychological causes, more than is observed in secondary care, indicates an openness to the psychological therapies provided in that setting. More evidence on the natural history of chronic fatigue and CFS in primary care is required, as are trials of complex interventions. The results may help determine the usefulness of differentiating between chronic fatigue and CFS.

Keywords: chronic fatigue; chronic fatigue syndrome; diagnosis; primary care.

L Darbishire, BSc, MSc, research associate; L Ridsdale, BA, MSc, MD, PhD, FRCP(C), FRCGP, reader in general practice, P T Seed, statistician, Department of General Practice, Guy's, King's College and St Thomas's School of Medicine, London.

Address for correspondence

L Darbishire, Department of General Practice, Guy's King's College and St Thomas's School of Medicine, 5 Lambeth Walk, London, SE11 6SP. E-mail: lucy.darbishire.ac.uk

Submitted: 5 June 2002; Editor's response: 9 October 2002; final acceptance: 27 January 2003.

©British Journal of General Practice, 2003, 53, 441-445.

Introduction

It is estimated that approximately 9% of people experience fatigue of more than six months' duration at any one time.¹ Despite this, data from the 1985 United Kingdom National Morbidity Survey suggest that doctors classify approximately 12 new presentations of 'malaise, fatigue, debility and tiredness' per 1000 patients seen in one year, with total annual consultation rates for fatigue at 18 per 1000.² Two-thirds of patients presenting with chronic fatigue in primary care do not meet criteria for chronic fatigue syndrome (CFS),³ but most published investigations focus on defining, measuring, and managing patients with CFS in specialist settings.⁴ General practitioners (GPs) have not generally taken up and used the classification of CFS, expressing either concern about its validity as an illness,⁵ or scepticism as to its usefulness in the context of primary care.⁶ Without much evidence from trials of treatment for chronic fatigue in primary care, expert groups propose that it should be treated with cognitive and behavioural interventions in this context.^{7,8} Practitioners and investigators may use the findings from this study to help decide on the practical use of applying this specialist diagnosis in primary care.

We recruited into a randomised trial a group of patients presenting to their GP with unexplained chronic fatigue of more than six months' duration, and described this group at baseline by CFS status. The aim of this paper is to describe patients who consulted their GP with chronic fatigue, and to make comparisons between those patients who met the case definition for CFS and those who did not. We explored whether using the diagnosis of CFS is useful in primary care. We thought that applying the CFS case definition might identify a group that not only had more severe illness, but also had more physical causal attributions, which appear to be more resistant to cognitive and behavioural change following therapeutic intervention with counselling and cognitive behavioural therapy.³

Method

Patient recruitment

General practitioners working in 22 practice groups ($n = 128$) recruited patients to the study, with a patient population of 174 000 aged between 16 and 75 years. Between January 1999 and June 2001, using the eligibility criteria shown in Box 1, GPs referred patients who presented to them complaining of fatigue lasting more than six months as a main or important problem. The practices were in London and the South Thames Region of England and included rural, suburban, and metropolitan areas. Following referral by the GP, an appointment was arranged between the patient and a

HOW THIS FITS IN

What do we know?

Expert groups have suggested that chronic fatigue be treated in primary care although there is little research with this group in this setting, with little attention having been paid to patients with chronic fatigue syndrome (CFS).

What does this paper add?

Two-thirds of patients with six months of fatigue in primary care did not conform to criteria for CFS, and despite having less fatigue, functional impairment, depression, anxiety, consultation frequency, and unemployment, non-CFS patients experienced significant fatigue symptoms of a similar duration. Attributions were more likely to be psychological than has been reported in studies performed in specialist settings, and this was irrespective of CFS status.



Clinically evaluated, unexplained, persistent or relapsing chronic fatigue (of at least six months' duration) that is of new or definite onset (has not been lifelong); is not the result of ongoing exertion; is not substantially alleviated by rest; and results in substantial reduction in previous levels of occupational, educational, social or personal activities.

Four or more of the following symptoms are concurrently present for more than six months: impaired memory/concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, new headaches, unrefreshing sleep, post-exertional malaise.

Box 2. Case definition for CFS.⁹

patients scoring lower than 4 being excluded from the study, when the questionnaire was scored bimodally. For subsequent analyses, each item of the fatigue questionnaire was rated on a scale from 0 to 3 and summed, with a maximum possible score of 33. Depression and anxiety were measured using the Hospital Anxiety and Depression Rating Scale (HAD).¹¹ The Work and Social Adjustment Questionnaire (WASA) measured functional impairment during work, home, social, and private activities, each on an eight-point scale,¹² and perceptions about cause were measured with a five-point attribution scale (from 0 = 'my fatigue is psychological' to 5 = 'my fatigue is physical').¹³

The Illness Perceptions Questionnaire (IPQ)¹⁴ assessed the five dimensions of illness beliefs in three sections. Symptom identity consists of 12 commonly experienced symptoms that a patient perceives they experience as part of their illness (dizziness, headaches, nausea, pain, sleep difficulties, sore joints, breathlessness, fatigue, loss of strength, sore eyes, upset stomach, and weight loss). Timeline (i.e. 'my illness will last a long time'), cure/control (i.e. 'there is a lot I can do to improve my illness'), and consequences (i.e. 'my illness has had major consequences on my life') were measured. Each of these dimensions has multiple items, with responses to each item measured on an incremental five-point scale anchored at 'strongly disagree' and 'strongly agree'. The mean of all items within each scale was calculated, with a higher score describing a longer expected time-line, more positive cure/control beliefs, and more reported negative consequences of fatigue. The 'cause' dimension consists of a list of ten independent attributions about cause, each of which relates to internal or external causal beliefs.^{14,15} The percentage of causal statements that each patient either 'agreed' or 'strongly agreed' with was recorded as psychological (stress, my state of mind, my own behaviour, and/or other people), or non-psychological/physical (diet, heredity, poor past medical care, pollution, chance, and/or a germ or virus). Subtracting the percentage of psychological causes endorsed from the percentage of non-psychological causes endorsed, resulted in percentage difference between psychological and physical causes endorsed.

Information from GP notes

Data on past psychiatric diagnosis, current psychotropic medication, and consulting frequency were extracted from the patients' medical records. Consultation frequency was retrieved for the eight-month period prior to recruitment.

GPs included patients:

- aged 16 to 75 years;
- complaining of fatigue as a main or important problem lasting for six months or more;
- with no recent change to any drug regimen; and
- with normal full blood count, erythrocyte sedimentation rate, and thyroid function tests, within the previous six months.

GPs excluded patients:

- with psychotic illness, organic brain syndrome, or substance dependency;
- with concurrent physical problems that (in the doctor's judgement) could have caused fatigue symptoms;
- who were currently seeing a psychiatrist, counsellor, community psychiatric nurse, or physiotherapist, or
- who were unable to read English.

Box 1. Eligibility criteria.

research coordinator (LD) at the patient's surgery. At this appointment, informed consent was obtained, CFS status was established, information was collected from GPs' notes, and the patient completed questionnaires.

Diagnosis and definitions

At the beginning of each patient's appointment, following the attainment of informed consent, the research coordinator assessed each recruited patient for CFS status using a checklist modelled on the 1994 Centers for Disease Control case definition for CFS shown in Box 2.⁹ Those not meeting CFS criteria were classified as having chronic fatigue.

Self-report questionnaires

Most information was obtained from the patients via validated self-report questionnaires that were completed by each patient at their doctor's surgery in the presence of the researcher. Patients reported their age, the duration of their fatigue, whether they were a member of a self-help group, their employment status, and whether they had been referred to a psychiatrist in the past. An 11-item fatigue questionnaire determined fatigue severity,¹⁰ with those

Statistical analysis

Consultation frequency was extrapolated from the eight-month data to report a 12-month period. Comparisons between the group with CFS and the group with chronic fatigue were made using independent *t*-tests for continuous data that were normally distributed, Mann–Whitney tests for non-parametric or non-normally distributed continuous data, and χ^2 for categorical data. Risk ratios were calculated to describe unemployment, past psychiatric referral, and current psychotropic medication. Analysis was undertaken using SPSS and STATA software packages.

Results

General practitioners identified 178 patients; of these 141 consented to participate, were eligible, and completed assessments. Practices did not necessarily recruit patients for the 29-month duration of the study; the median duration of recruitment was 13 months (interquartile range [IQR] = 5.8 to 25.3). Seventy per cent ($n = 99$) were female, and the mean age of the group was 39.8 years (SD = 11.3). Self-reported median fatigue duration was 32 months (IQR = 13 to 61), and mean fatigue score on the 33-point scale was 24.9 (SD = 5.1). The median number of consultations in the eight months prior to recruitment was 5.0 (IQR = 4.0 to 8.0), estimated as 7.5 (IQR = 6.0 to 12.0) consultations over 12 months. Ninety-seven patients (69%) had chronic fatigue, and 44 (31%) had CFS according to CDC criteria.

Table 1 shows the demographic, fatigue, functioning, and mood characteristics of patients by CFS status. Although patients with CFS had significantly more fatigue symptoms and were more functionally impaired, median duration of fatigue was not significantly different from the group with chronic fatigue. The group with CFS were significantly more likely to be members of a self-help organisation, and consulted their GPs significantly more frequently, than the group with chronic fatigue (Table 1). They were also nearly twice as likely to be unemployed (risk ratio [RR] = 1.8; 95% confidence interval [CI] = 1.1 to 3.0).

Significantly higher average depression and anxiety scores were recorded in the group with CFS, who were significantly more likely to be depressed but not anxious. They

were twice as likely to be taking psychotropic medication (RR = 2.0; 95% CI = 1.2 to 3.2) and nearly twice as likely to report having had a psychiatric referral in the past (RR = 1.9; 95% CI = 1.1 to 3.2), than the group with chronic fatigue.

Using the attributions questionnaire, similar proportions in each group attributed their fatigue to mainly or only physical causes (CFS = 50%; chronic fatigue = 45%), with the remainder in each group attributing their fatigue to psychological or mixed physical and psychological causes (Table 2). The IPQ showed attributions in more detail. Using the items from the 'cause' dimension, patients in both groups endorsed a higher proportion of the psychological causal items than physical causal items. The CFS group endorsed 9% more psychological causes than physical causes, and the chronic fatigue group endorsed 18% more psychological causes than physical causes. The 9% difference between the two groups was not a significant one (95% CI = -3% to 22%; $P < 0.16$).

There were significant differences between groups in illness perceptions (Table 2): the group with CFS thought their fatigue would last longer (time-line), that it had had more serious consequences on their lives, and they identified more additional symptoms as part of their fatigue, than the group with chronic fatigue. Both groups perceived a similar level of control over their fatigue (cure/control).

All of the 12 possible symptoms, except for weight loss, were identified as being experienced as part of their fatigue by more than 60% of patients in both the group with CFS and the group with chronic fatigue. Both groups were highly symptomatic, identifying a large number of symptoms as part of their illness (CFS = 10.4/12; chronic fatigue = 8.7/12) (Table 2). Five symptoms were significantly more likely to be reported by those with CFS (dizziness, headaches, pain, sore joints, and breathlessness); all but the last being symptoms used in the criteria for diagnosing CFS.⁹

Discussion

Through the assessment of patients presenting to their GP with chronic fatigue, this study has elucidated the proportion of patients who present with chronic fatigue that meet criteria for CFS. Furthermore, it describes the social,

Table 1. Demographic, fatigue, functioning, and mood characteristics of patients by CFS status

Characteristic	CFS ($n = 44$)	Chronic fatigue ($n = 97$)	Test statistic
Age in years, mean (SD)	40.5 (10.4)	39.5 (11.8)	$P = 0.629$
Female sex, n (%)	33 (75.0)	66 (68.0)	$P = 0.434$
Consultations in past 12 months, ^a median (IQR)	11.3 (7.5–15.4)	7.5 (4.5–10.5)	$P = 0.001$
Unemployed, n (%)	12 (27.3)	12 (12.4)	$P = 0.029$
Member of self-help organisation, n (%)	9 (20.5)	0 (0)	$P = 0.001$
Self-reported fatigue duration in months, median (IQR)	32 (10–61)	32 (15–61)	$P = 0.645$
Fatigue (Likert scoring; scale = 0–33), mean (SD)	27.9 (4.4)	23.6 (4.9)	$P < 0.001$
Functional impairment (scale = 0–32), mean (SD)	24.9 (5.9)	17.7 (7.3)	$P < 0.001$
Depression score (HAD; scale = 0–21), mean (SD)	9.8 (3.8)	7.5 (3.1)	$P < 0.001$
Cases of depression, n (%)	21 (47.7)	17 (17.5)	$P < 0.001$
Anxiety score (HAD; scale = 0–21), mean (SD)	11.6 (4.9)	9.7 (4.1)	$P = 0.02$
Cases of anxiety, n (%)	26 (59.1)	42 (43.3)	$P = 0.082$
Current psychotropic medication prescription, n (%)	17 (39)	17 (18)	$P = 0.007$
Past psychiatric referral, n (%)	27 (61)	37 (37)	$P = 0.01$

^aEstimated from eight-months' data.

Table 2. Attributions and illness perceptions scores

	CFS (n = 44)	Chronic fatigue (n = 97)	Test statistic
Attributions, ^a n (%)			
Physical causes only	22 (50)	43 (45)	P = 0.566
Psychological/mixed	22 (50)	53 (55)	
Illness perceptions questionnaire			
Timeline (0–5), mean (SD)	3.3 (0.8)	3.0 (0.7)	P = 0.03
Consequences (0–5), mean (SD)	3.9 (0.6)	3.4 (0.6)	P < 0.001
Cure/control (0–5), mean (SD)	3.5 (0.6)	3.6 (0.5)	P = 0.115
Symptom identity (12), mean (SD)	10.4 (1.4)	8.7 (2.3)	P < 0.001
Causal statements endorsed (% psychological – % physical), mean (SD)	8.5 (31.8)	17.8 (37.7)	P = 0.159

^aOne patient did not answer this question.

psychological, and physical similarities and differences between CFS patients and the group of patients presenting with non-CFS chronic fatigue, and suggests how these have implications for clinical practice and future research.

Main findings

In this study over two-thirds of patients with chronic fatigue in primary care did not meet criteria for CFS. But in those that did, the impact of their fatigue was more psychologically, socially, and economically severe. It was not just the CFS diagnosing criteria in which the CFS patients demonstrated more severe illness; the CFS patients were also more depressed and anxious, identified a greater symptom severity, were more likely to have had past psychiatric referral and to be taking psychotropic medication, consulted significantly more frequently, and were more likely to be unemployed. Aside from fatigue duration, CFS and non-CFS patients were similar only in their perceptions of control over their fatigue and in the proportions attributing their fatigue to physical causes.

Despite the observation that the CFS patients experienced a greater symptom severity than the non-CFS chronic fatigue patients, 11 out of the 12 additional symptoms were reported as being experienced as part of their fatigue by over 60% of patients with chronic fatigue. Furthermore, the non-CFS patients also reported important levels of fatigue severity, functional impairment, anxiety, and depression as part of their fatigue, with some taking psychotropic medications and some being unable to work.

Strengths and limitations

The strengths of this diagnostic study include its low refusal rate and its primary care location. These have the advantage of excluding the bias of secondary and tertiary care studies and making the results more generalisable to the population of patients with chronic fatigue. Furthermore, the identification of only patients with fatigue of more than six months' duration makes the two groups comparable and different only in regard to whether or not they conform to CFS criteria.

A limitation of this study is that for a diagnosis to be really important it is necessary to show a relationship between diagnosis and outcome with or without recommended therapeutic interventions,¹⁶ and this has yet to be undertaken.

Agreement with existing literature

That less than one-third of patients met criteria for CFS is consistent with evidence from a previous, similarly designed and located study, in which 32% of patients consulting with chronic fatigue met criteria for CFS,³ but is significantly lower than the reported 59% proportion who experience CFS presenting to specialists.¹⁷ Moreover, that patients with CFS were more severely affected than patients with non-CFS fatigue, although a new finding in primary care, was expected, based on the defining criteria for each,⁹ and the characteristics of patients with chronic fatigue and CFS reported previously. For example, a previous study of patients with CFS in specialist care reported similarly high levels of fatigue, functioning, depression, and the proportion with a history of psychological distress to levels reported in the CFS patients in this study,¹⁸ although unemployment levels were significantly lower in this study. Similarly, a previous study of patients with more than three months of fatigue in primary care reported similar levels of fatigue, functioning, depression, anxiety, psychotropic medication use, and the proportion of self-help group members, to the non-CFS patients in this study.³

Less expected, however, was the significant fatigue duration and additional symptoms experienced by the non-CFS patients, a demonstration of illness severity that is supported by economic analyses of the same patients in which McCrone *et al* (2003) report that the CFS and non-CFS patients had similarly high service use costs, mainly composed of informal care requirements.¹⁹ Furthermore, in specialist settings, between 65%¹³ and 79%¹⁸ of patients with CFS have physical illness attributions, whereas only half of the CFS patients in this study attributed their fatigue to physical causes. This is not only similar to the proportion of non-CFS patients in this study with physical illness attributions, but similar to the 53% proportion with physical illness attributions previously demonstrated in primary care patients presenting with fatigue of at least three months' duration.³

Implications for future research and clinical practice

That patients with CFS have a greater fatigue severity than patients with non-CFS chronic fatigue not only suggests that they may be more difficult to manage, but that they may require a greater amount of recommended therapy than patients with non-CFS chronic fatigue. This has implications

for future clinical practice as it implies that it may help for GPs to diagnose CFS before recommending management. However, that both groups of patients are as likely to report psychological attributions about the cause of their fatigue suggests a similar openness to recommended therapeutic interventions that are composed of both cognitive and behavioural principles, than may be the case when patients are referred and treated by specialists.

The potential implication for clinical practice of diagnosing CFS also has implications for future research, because to determine the usefulness of distinguishing between CFS and non-CFS in primary care requires knowledge of whether outcome with or without therapy in this setting can be predicted by characteristics such as CFS status or attributions. Randomised controlled trials of complex interventions for CFS and non-CFS chronic fatigue can provide this knowledge and may provide support for the recommendation that fatigue and CFS can be effectively managed in primary care.

References

- Skapinakis P, Lewis G, Meltzer H. Clarifying the relationship between unexplained chronic fatigue and psychiatric morbidity: results from a community survey in Great Britain. *Am J Psychiatry* 2000; **157**: 1492-1498.
- Office of Population Censuses and Surveys. *Living in Britain: Results from the 1998 General Household Survey*. London: HMSO, 2000.
- Ridsdale L, Godfrey E, Chalder T, et al. Chronic fatigue in general practice: is counselling as good as cognitive behaviour therapy? A UK randomised trial. *Br J Gen Pract* 2001; **51**: 19-24.
- Mulrow CD, Ramirez G, Cornell JE, et al. *Defining and managing chronic fatigue syndrome*. Evidence Report/Technology Assessment No 42. Prepared by San Antonio Evidence-Based Practice Centre at the University of Texas Health Science Centre at San Antonio under contract No. 290-97-0012. [AHRQ Publication No. 02-E001.] Rockville MD: Agency for Healthcare Research and Quality, 2001.
- Fitzgibbon EJ, Murphy D, O'Shea K, Kelleher C. Chronic debilitating fatigue in Irish general practice: a survey of general practitioners' experience. *Br J Gen Pract* 1997; **47**: 618-622.
- Prins JB, Bleijenberg G, Rouweler EK, et al. Doctor-patient relationship in primary care of chronic fatigue syndrome: perspectives of the doctor and the patient. *J Chron Fat Synd* 2000; **7(4)**: 3-15.
- Baylis R, Borysiewicz, Boyd R, et al. *Chronic Fatigue Syndrome: Report of a Joint Working Group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners*. London: RCP, 1996.
- Department of Health. *Report of the Working Party on CFS/ME to the Chief Medical Officer for England and Wales*. London: Department of Health, 2002.
- Fukuda K, Straus SE, Hickie I, et al (International Chronic Fatigue Syndrome Study Group). The chronic fatigue syndrome: a comprehensive approach to its definition and study. *Ann Int Med* 1994; **121**: 953-959.
- Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. *J Psychosom Res* 1993; **37**: 147-153.
- Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; **67**: 361-370.
- Marks I. *Behavioural Psychotherapy: Maudsley Pocket Book of Clinical Management*. Bristol: Wright Publishing, 1986.
- Wessely S, Powell R. Fatigue syndromes: a comparison of chronic 'postviral' fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg Psychiatry* 1989; **52**: 940-948.
- Weinman J, Moss-Morris R, Horne R. The Illness Perception Questionnaire: a new method for assessing the cognitive representation of illness. *Psychol Health* 1996; **11**: 431-445.
- Moss-Morris R, Petrie K, Weinman J. Functioning in chronic fatigue syndrome: do illness perceptions play a regulatory role? *Br J Health Psychol* 1996; **1**: 15-25.
- Sackett D, Richardson W, Rosenberg W, Haynes R. *Evidence-based medicine: how to practice and teach EBM*. New York: Churchill Livingstone, 1997.
- Clark M, Katon W, Russo J, et al. Chronic fatigue: risk factors for symptom persistence in a 2 1/2-year follow-up study. *Am J Med* 1995; **98**: 187-195.
- Deale A, Chalder T, Marks I, Wessely S. Cognitive behaviour therapy for chronic fatigue syndrome: a randomised controlled trial. *Am J Psychiatry* 1997; **154**: 408-414.
- McCrone P, Darbishire L, Ridsdale L, Seed PT. The economic cost of chronic fatigue and chronic fatigue syndrome in UK primary care. *Psychol Med* 2003; **33**: 253-261.

Acknowledgements

This research was supported by the Linbury Trust. We thank the many people who provided constructive input to this study, particularly Drs P White, K Harvey, and M Hotopf, Professors R Jones and S Wessely, and our reviewers. Thanks also to patients who took part and the practices, particularly the lead GPs: Drs J Lee, M Whyte-Venables, M Ashworth, R Byng, C Cheal, G Earnshaw, D Abraham, A Surawy, AL Hastie, D Kay, KA Khan, H Cohen, MA Whitehead, C Challecombe, C McCarthy, J Boxer, P Bowskill, V Thapar, MA Palmer, I Bandara, K Gordge, H Knights, and A Stimmler.