Psychological Medicine, 1997, **27**, 343–353. Copyright © 1997 Cambridge University Press

A population-based incidence study of chronic fatigue

S. M. LAWRIE,[1] D. N. MANDERS, J. R. GEDDES AND A. J. PELOSI

From the Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital, Edinburgh

ABSTRACT

Background. Most research on syndromes of chronic fatigue has been conducted in clinical settings and is therefore subject to selection biases. We report a population-based incidence study of chronic fatigue (CF) and chronic fatigue syndrome (CFS).

Methods. Questionnaires assessing fatigue and emotional morbidity were sent to 695 adult men and women who had replied to a postal questionnaire survey 1 year earlier. Possible CFS cases, subjects with probable psychiatric disorder and normal controls were interviewed.

Results. Baseline fatigue score, the level of emotional morbidity and a physical attribution for fatigue were risk factors for developing CF. However, after adjusting for confounding, pre-morbid fatigue score was the only significant predictor. A minority of CF subjects, all female, had consulted their general practitioner; higher levels of both fatigue and emotional morbidity were associated with consultation. Possible CFS cases reported similar rates of current and past psychiatric disorder to psychiatric controls, but after controlling for fatigue or a diagnosis of neurasthenia the current rates were more similar to those of normal controls. Two new cases of CFS were confirmed.

Conclusions. Both fatigue and emotional morbidity are integral components of chronic fatigue syndromes. The demographic and psychiatric associations of CFS in clinical studies are at least partly determined by selection biases. Given that triggering and perpetuating factors may differ in CFS, studies that examine the similarities and differences between chronic fatigue syndromes and psychiatric disorder should consider both the stage of the illness and the research setting.

INTRODUCTION

In recent years, there has been considerable interest in syndromes of chronic fatigue, which are characterized by severe and persistent fatigue that is exacerbated by exertion and associated with psychiatric morbidity (Fukuda *et al*. 1994). Early studies suggested that such syndromes were the sequelae of an infectious illness, were found most commonly in females, the middle-aged, upper social classes and healthcare workers, and that a poor outcome was almost universal (Behan & Behan, 1988). The development of diagnostic criteria for chronic fatigue syndrome (CFS) allowed reliable epidemiological research to be conducted (Sharpe *et al*. 1991). Although two studies have found no evidence that CFS is caused by enteroviruses (Miller *et al*. 1991) or common viral infections (Wessely *et al*. 1995), another two have shown that both psychosocial factors and Epstein–Barr virus (Bruce-Jones *et al*. 1994) or a variety of viral infections (Cope *et al*. 1994) may be important in the development of chronic fatigue syndromes. Clinical research has repeatedly demonstrated that as many as two-thirds of CFS sufferers satisfy criteria for psychiatric disorders and this figure is substantially higher than that found in chronic medical conditions (see David, 1991 for review). Outcome studies have challenged suggestions of a uniformly bleak

[1] Address for correspondence: Dr Stephen M. Lawrie, Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital, Edinburgh EH10 5HF.

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

prognosis and indicated that psychiatric and psychological rather than physical measures predict long-term disability (Sharpe *et al.* 1992; Lawrie & Pelosi, 1994; Wilson *et al.* 1994).

These studies have been conducted in clinical settings and are liable to a number of biases, including selection bias. Presentation to general practitioners and onward referral to hospital specialists is 'filtered' by such factors as symptom severity, psychosocial stressors, socioeconomic status and the patients' attitudes to illness (Goldberg & Huxley, 1992). These considerations may be particularly pertinent in chronic fatigue because of commonly described difficulties in the doctor–patient relationship in 'Myalgic Encephalomyelitis (ME)' (ME Action Campaign, 1993; Scott *et al.* 1995). Indeed, there is already some evidence that the demographic and psychiatric associations of chronic fatigue syndromes are different in community samples (Lloyd *et al.* 1990; Buchwald *et al.* 1995; Lawrie & Pelosi, 1995) from those reported in clinical populations (David, 1991; McDonald *et al.* 1993; Euba *et al.* 1996).

We, therefore, conducted a 1 year follow-up of respondents to a previous prevalence survey in a general population setting (Lawrie & Pelosi, 1995), with the following aims: (i) to identify risk factors for the development of chronic fatigue; (ii) to examine the associations of general practice consultation for chronic fatigue; (iii) to establish any psychiatric or psychological differences between possible CFS cases, subjects with psychiatric morbidity and normal controls at interview; and (iv) to provide an estimate of the incidence of CFS.

METHOD

Survey subjects and questionnaire

A one in ten random sample of people aged 18 and over registered at Penicuik Health Centre, which covers about 75% of the local population, were sent (prevalence survey) questionnaires in August and September 1991 (Lawrie & Pelosi, 1995). The 695 (71%) respondents were surveyed again, 1 year later, for the current study (incidence survey). The fatigue questionnaire (David *et al.* 1990), contained nine questions on mental and physical aspects of fatigue over the previous 2 weeks – if a symptom was present, subjects indicated if the severity was the same, worse, or much worse than usual. A tenth question enquired about the frequency of tiredness. If subjects felt tired, they were asked to state the duration, their views on cause and whether they had consulted a doctor. Attributions for fatigue were categorized as physical (e.g. medical illness), psychological (e.g. psychiatric disorder), social (e.g. family problems), physiological (e.g. old age, lack of sleep) or occupational (e.g. long hours, workplace stress), with multiple attributions being allowed. A 12-item General Health Questionnaire (GHQ) was included as a measure of psychiatric morbidity (Goldberg & Williams, 1988). Information on demographics, physical and psychiatric histories, and current medication was also requested.

Identification of new chronic fatigue cases

Responses to the fatigue questions were scored 0/1/2/3 and summed to give a total fatigue score (range 0–27). A total fatigue score of 9 or more identifies those who consider fatigue to be a major problem (David *et al.* 1990). Subjects above the cut-off, with fatigue of at least 6 months duration, were classified as suffering from chronic fatigue. Those who had met criteria for chronic fatigue in the prevalence survey were excluded, as were those who described any physical or major psychiatric illnesses that could result in fatigue – according to the criteria of Sharpe *et al.* (1991). Health centre casenotes were cross-checked to ensure that illness self-reporting was reliable.

Incident CFS cases

If new chronic fatigue cases described fatigue that had been present most or all of the time ('possible CFS'), their primary care medical records were examined. Those with physical and major psychiatric causes of fatigue excluded by their general practitioner at a consultation within the previous 6 months satisfied British criteria for CFS (Sharpe *et al.* 1991).

Interview assessment

Due to resource constraints, a detailed interview assessment package was only given to 'possible CFS cases' (those with chronic fatigue present at least half the time and without any self-reported physical or major mental illness). All possible CFS cases, from both surveys, were contacted by letter in January 1994 and invited

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

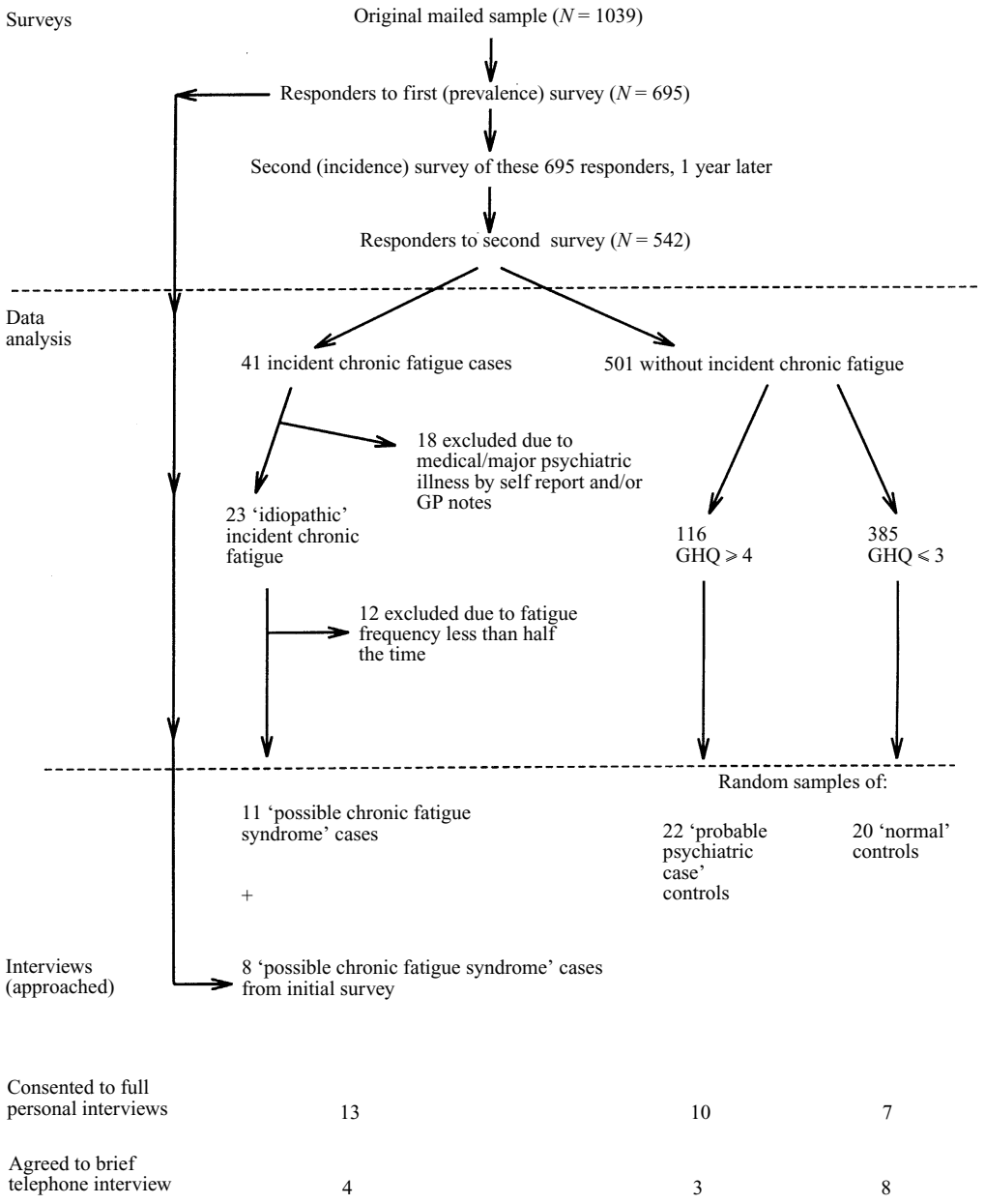


FIG. 1. The selection and number of subjects at each stage of the study.

to interview. A random sample of 'probable psychiatric case' controls, selected from subjects scoring above a 3/4 cut-off on the GHQ (0/0/1/1 scoring method), and a random sample of 'normal' controls, from participants with scores of three or less on the GHQ, were also asked to participate.

The revised Clinical Interview Schedule (CIS-R), a standardized psychiatric interview developed for use in primary care (Lewis *et al.* 1992), was used to elicit symptoms and quantify them in terms of severity and frequency. Total scores above an 11/12 cut-off indicate a level of psychiatric morbidity that a general practitioner

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

would be concerned about. The CIS-R score can be adjusted for fatigue, by not including the score on this item (0–4) in the total score and lowering the cut-off to 10/11 (CIS-f). Supplementary questions were asked to screen for alcohol problems and the level of alcohol consumption. The Social Stresses and Supports Instrument (SSSI) was used to assess the current perception of six life areas (occupation, finance, housing, family, social and intimate relationships), each being scored −1/0/1 for negative, neutral or satisfying influences respectively (Jenkins *et al*. 1981). The fatigue and GHQ-12 questionnaires were re-administered, patients completed the Beck Depression Inventory (BDI) to give a measure of subjective depressive symptomatology (Beck *et al*. 1965), and the examiner completed the 17-item Hamilton Rating Scale for Depression (HAMD) as an objective measure (Hamilton, 1960). Finally, a semi-structured interview, devised for this study, enquired about past medical illnesses, satisfaction with their medical management, and any personal or family (first-degree relatives) history of psychiatric illness in the way that these questions are usually asked in a routine psychiatric assessment. Two of the authors (S.M.L. & D.N.M.) conducted the interviews and used all available information to reach consensus ICD-10 clinical diagnoses (WHO, 1992).

The interviews were conducted between February and June 1994, 18 to 22 months after the second survey. Subjects who had not replied to invitation by June 1994, or had indicated that they did not want to be interviewed, were contacted by telephone to ascertain their reason for refusal and, if permitted, to conduct a brief semi-structured interview over the phone. This consisted of asking subjects the duration of any fatigue or depression, their attribution for it and any personal or family psychiatric history. A brief screen for psychiatric symptoms was also conducted, to make current or past psychiatric diagnoses. The number of subjects in each part of the investigation is shown in Fig. 1.

Statistical analysis

One-way analysis of variance (ANOVA) was the main method of statistical comparison between groups on responses to the incidence survey questionnaire. A total GHQ-12 score was calculated using both 0/0/1/1 and 0/1/2/3 scoring methods (Goldberg & Williams, 1988). The Pearson correlation coefficient was determined between total fatigue and total GHQ-0/1/2/3 scores. The analyses of psychiatric (GHQ) associations used the 0/0/1/1 scoring method, as a cut-off of 3/4 identifies 'probable psychiatric cases' (Goldberg & Williams, 1988; Pawlikowska *et al*. 1994; Lawrie & Pelosi, 1995). ANOVA and chi-square tests were performed to examine the associations of medical consultation for chronic fatigue, and to compare the interview results in the three subject groups. All significance testing was two-tailed. Poisson distribution tables were consulted to give 95% confidence intervals (95% CI) for the incidence (and prevalence) of CFS.

To identify the risk factors for the subsequent development of chronic fatigue, several variables, from responses to the prevalence survey, were examined. The variables included in these analyses were: baseline age, sex, social class, total fatigue score, duration of fatigue, total GHQ-0/1/2/3 score and the various attributions for fatigue. Age, total fatigue scores and GHQ-0/1/2/3 scores were treated as continuous measures. Univariate logistic regression was performed to estimate the effect of the variables of interest, and multiple logistic regressions, using EGRET (SERC, 1991), to adjust for confounding. These analyses were repeated, including those chronic fatigue cases and controls suffering from physical or psychiatric illnesses, with illness as an additional variable.

RESULTS

Questionnaire responders and results

Of the 695 subjects, 542 returned the questionnaire – 252 (78%) men and 290 (78%) women. The mean age was 49·6 (95% CI 47·6–51·5) in men and 48·6 (46·6–50·6) in women. Responders in lower social classes (IIIM–V) were under-represented as compared to all health centre patients (Lawrie & Pelosi, 1995). Responders showed a tendency ($P = 0{\cdot}08$) to be older than non-responders, but other demographics were no different and the mean total fatigue scores in the prevalence survey were almost identical in subsequent responders and non-responders. The demographics of

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

Table 1. *Demographics and mean total fatigue scores in questionnaire responders*

	Men			Women		
	N	Mean fatigue score	95% CI	*N*	Mean fatigue score	95% CI
Age group*						
19–29	36	3·8	2·6–4·9	41	6·4	4·7–8·2
30–39	31	7·1	4·4–9·7	58	7·0	5·2–8·8
40–49	60	5·9	4·5–7·4	60	7·7	6·1–9·3
50–59	54	6·0	4·6–7·3	43	6·4	4·7–8·1
60–69	37	7·5	5·6–9·4	44	6·8	5·0–8·6
70–93	33	7·4	5·5–9·4	43	9·0	7·0–10·9
Marital status*						
Married	187	6·3	5·5–7·1	183	6·7	5·8–7·6
Widowed	14	9·3	5·3–13·3	39	7·6	5·9–9·3
Single	37	4·6	3·0–6·1	45	7·6	5·7–9·6
Divorced	7	7·7	1·6–13·8	15	9·6	6·4–12·8
Separated	3	7·3	0·0–23·9	7	10·4	3·1–17·7
Occupational classification*						
Social Class I	23	6·5	4·0–9·1	8	6·8	0·4–13·1
Social Class II	38	5·5	3·8–7·2	18	7·1	4·5–9·7
Social Class IIIN	94	5·6	4·5–6·7	79	6·3	5·1–7·6
Social Class IIIM	21	4·1	2·4–5·8	14	10·1	6·4–13·8
Social Class IV	6	9·8	4·1–15·6	37	7·3	5·0–9·6
Social Class V	—	—	—	—	—	—
Housewives	—	—	—	76	7·1	5·8–8·5
Retired	57	8·1	6·7–9·6	45	7·8	5·8–9·7
Unemployed	10	5·5	0·7–10·3	4	12·2	0·0–24·5
Students	2	2·0	0·0–27·4	6	5·2	0·0–12·2
Student nurses	—	—	—	2	11·5	0·0–81·4
Total	252	6·2	5·5–6·9	290	7·3	6·6–8·0

* The numbers in each demographic category do not total 252 men and 290 women as there were some missing values in each.

Table 2. *Risk factors (odds ratios and 95% confidence intervals) for the development of chronic fatigue* (N = 23) *at 1 year*

	Univariate analyses	Multivariate analyses
Fatigue levels	1·14 (1·06–1·22)*	1·11 (1·02–1·21)*
GHQ scores	1·11 (1·04–1·18)†	1·04 (0·96–1·14)†
Physical attribution for fatigue	2·65 (0·96–7·27)	1·35 (0·44–4·14)

* Per point increment on a scale of 0–27.
† Per point increment on a scale of 0–36.

respondents and mean total fatigue scores in each category are shown in Table 1. The mean total fatigue score was 6·2 (5·5–6·9) in men and 7·3 (6·6–8·0) in women ($F_{1,532} = 4{\cdot}4$, $P = 0{\cdot}04$). The mean total GHQ-0/0/1/1 scores were not significantly higher in women (2·2, 1·8–2·5) than men (1·8, 1·5–2·2) ($P = 0{\cdot}2$). Total fatigue and total GHQ scores were significantly correlated in men ($r = 0{\cdot}56$, $P < 0{\cdot}001$) and women ($r = 0{\cdot}61$, $P < 0{\cdot}001$). A total of 56 (32%) women reported having consulted their doctor with fatigue, as compared to 25 (16%) men ($\chi^2 = 12{\cdot}0$, $P = 0{\cdot}0005$); statistically significant higher fatigue and GHQ scores were associated with consultation.

Incident chronic fatigue

Of the 96 chronic fatigue cases identified in the prevalence survey, 80 returned the second questionnaire and were excluded from subsequent analyses. An incidental finding of interest is that 49 of these subjects no longer satisfied chronic fatigue criteria. Forty-one new chronic fatigue cases were identified, but 13 had physical illnesses and five had major psychiatric disorders (e.g. schizophrenia) by self-report or examination of medical records. Twenty-three (5%) incident cases of unexplained chronic fatigue were therefore confirmed (12 male, 11 female), with a mean age of 49·6 (95% CI 42·1–57·1, range 22–89). The social class distribution was even: classes I–IIIN ($N = 8$), IIIM–V (7), and others (8). Their mean total fatigue score was 12·8 (11·3–14·4, range 9–20) and was most commonly attributed to physiological ($N = 11$), psychological (6) or occupational (6) reasons. Eleven (48%) scored as probable psychiatric cases on the GHQ. Even though none of these subjects had met criteria for chronic fatigue 1 year earlier, they reported fatigue duration of 8–216 months and their baseline mean total fatigue scores had been 8·1 (6·0–10·3). These fatigue scores showed a tendency to be higher than baseline scores in those who did not develop chronic fatigue (6·0, 5·3–6·7, $P = 0{\cdot}08$).

The results of analyses examining risk factors for chronic fatigue are summarized in Table 2. Age, total fatigue scores and total GHQ-0/1/2/3 scores were approximately normally distributed and of linear effect. By univariate logistic regression, each point increment in baseline total fatigue score increased the odds ratio (OR) of developing new chronic fatigue by 1·14 (1·06–1·22, $P < 0{\cdot}001$). Each point increment of the total GHQ-0/1/2/3 score increased the OR by 1·11 (1·04–1·18, $P = 0{\cdot}003$). No other variables were statistically significant risk factors

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

for the development of chronic fatigue, although a physical attribution for fatigue showed a tendency to do so (OR = 2·65, 0·96–7·27, P = 0·06). In multivariate analyses, controlling for the effects of confounding between fatigue and psychological morbidity, total fatigue scores significantly predicted subsequent chronic fatigue (1·11, 1·02–1·21, $P = 0·015$), while GHQ scores did not (1·04, 0·96–1·14, $P = 0·3$). Similarly, after controlling for fatigue levels, physical attribution was no longer a significant risk factor (OR = 1·35, 0·44–4·14, $P = 0·6$). When those with physical or major psychiatric illnesses were included in the analyses, the results showed a similar pattern except that neither illness (OR = 0·94) nor physical attribution (OR = 1·27) were significant risk factors for chronic fatigue.

Only four new chronic fatigue cases, all female, indicated that they had consulted their general practitioner for fatigue. Comparing them with the six women who reported that they had not consulted, revealed that both higher mean total fatigue scores ($F_{1,8} = 10·7$, $P = 0·01$) and higher GHQ-0/0/1/1 scores ($F_{1,8} = 10·8$, $P = 0·01$) were associated with consultation. Three of the four females who consulted were probable psychiatric cases, as compared to one non-consulter (Fisher's exact two-tailed, $P = 0·2$). Including the subjects with self-reported illnesses gave the same pattern of results.

Interview results

The eight possible CFS cases from the first survey and 11 new possible CFS cases from the second survey were approached for interview. The randomly selected psychiatric ($N = 22$) and normal ($N = 20$) controls were also contacted. The response rate was low, but the general practitioners and ourselves were reluctant to make further attempts to include non-responders in the research. Thirteen CFS subjects, 10 psychiatric controls and seven normal controls consented to full interview – a response rate of 49 % – but a further 15 subjects agreed to a brief telephone interview, bringing the effective response rate to 74 %. The reasons given for non-response to full interview were: not seeing the study's relevance ($N = 6$), not having received the invitation (3), forgetting to reply (2) and being too busy to reply (2) or too depressed (1). One subject could not be contacted, another remained unwilling to participate for private reasons and the remainder were ex-directory. Non-responders to interview were more likely to be young, female and single, but their scores on the incidence survey fatigue and GHQ questionnaires were very close to those of responders.

Consensus psychiatric diagnoses from interview data were reached in nine (53 %) possible CFS cases, eight (61 %) psychiatric controls and two (13 %) normal controls. In addition, as the interview followed the questionnaire sweep by as much as 22 months, retrospective psychiatric diagnoses were made in a further four (24 %) possible CFS and one (8 %) psychiatric control subject. Thus, a total of 13 (77 %) possible CFS cases were given an ICD-10 psychiatric diagnosis – depressive illness ($N = 4$), neurasthenia (3), dysthymia (2), generalized anxiety disorder (2), somatization disorder (1) and non-organic sleep-wake cycle ('jet-lag') disorder (1) – as were nine (69 %) psychiatric controls (seven depression, one anxiety, one mixed) and two (13 %) normal controls (one depression, one mixed).

The information gained from subjects by either home or telephone interviews is shown in Table 3. Possible CFS subjects were over-represented in the middle-age, single and upper social class categories. Current psychiatric diagnoses were found in a significantly larger proportion of possible CFS cases than normal controls (Yates' corrected chi = 3·9, $P = 0·047$). Possible CFS cases also showed a tendency to a past psychiatric history as compared to normal controls (Fisher's exact two-tailed test, P = 0·09), but no difference in numbers with a family history of psychiatric illness ($P = 0·5$). No differences were found between possible CFS cases and psychiatric controls in the proportions with current, past or family psychiatric histories.

Full interview information is only available for the 30 cases who consented to home interview. No statistically significant differences were found in the rates of current psychiatric, CIS-R or CIS-f cases between possible CFS and normal or psychiatric controls, although the numbers of subjects are small. There were 6/13 CIS-R cases in possible CFS subjects, as compared with 6/10 of those with psychiatric morbidity and 1/7 normal controls, but only 3/13 possible CFS cases were above the CIS-f cut-off. All the psychopathology rating scale scores were higher in possible CFS cases than in

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

Table 3. *Telephone and home interview information in* 45 *responders*

	Possible CFS cases ($N = 17$)	Psychiatric controls ($N = 13$)	Normal controls ($N = 15$)
Interviewed: personal/telephone	13/4	10/3	7/8
Sex: male/female	9/8	7/6	8/7
Mean age (years)	44·4 (40·0–49·8)	50·1 (40·2–60·0)	49·0 (38·1–60·0)
Age group: 19–39/40–59/60–93	5/11/1	5/3/5	6/4/5
Marital status: married/single	10/7	11/2	11/4
Social class: I–IIIN/IIIM–V/other	12/4/1	5/5/3	5/7/3
Current psychiatric diagnosis	9 (53%)*	8 (61%)	2 (13%)*
Past psychiatric history	6 (35%)	5 (39%)	1 (7%)
Family psychiatric history	5 (31%)	3 (23%)	3 (20%)

* $P < 0{\cdot}05$, possible CFS *versus* normal controls.

Table 4. *Characteristics of chronic fatigue syndrome cases*

	Sex	Age	Social class	Fatigue score	Fatigue duration (months)	Attribution for fatigue	GHQ score	Medical records	Interview diagnosis
Incident									
Case 1	M	49	I	18	6	Stress, tension, inter-continental travel	9	Dupuytren's contracture, pruritus ani, past history of post-viral fatigue and Hepatitis A	Non-organic sleep–wake disorder ('jet lag')
Case 2	F	56	IIIN (retired)	11	18	Family stresses and deaths	4	Insomnia and chest pain	Generalized anxiety disorder
Prevalent									
Case 3	M	37	IIIN (self-employed)	19	33	Lyme disease (treatment unresponsive)	10	Anxiety, palpitations, insomnia, weakness, tremor, and 'ME'	Generalized anxiety disorder
Case 4	F	47	II (retired)	18	72	Myalgia	2	Painful weak legs, and 'ME'	Somatization disorder

normal controls, but the only difference to approach significance was in HAMD scores (8·5 and 4·3 respectively; $t = 1{\cdot}9$, $P = 0{\cdot}08$). Similarly, mean scores on the rating scales (except fatigue) were lower in possible CFS cases than in psychiatric controls, but the only tendency to significance was to lower CIS-f scores (6·9 and 13·1 respectively; $t = -1{\cdot}8$, $P = 0{\cdot}09$). The mean SSSI scores were very similar across all three patient groups. Possible CFS subjects were not statistically more likely to attribute their fatigue to physical (4/13) causes than psychiatric controls (1/10, Fisher's exact $P = 0{\cdot}3$), or to be open by critical of doctors (5/13 and 2/10 respectively, Fisher's exact $P = 0{\cdot}6$), but again the numbers responding are small.

Chronic fatigue syndrome cases

Only two subjects satisfying British criteria for CFS (Sharpe *et al*. 1991), were identified among the new chronic fatigue cases. The others were excluded for self-reported or casenote diagnoses of medical illnesses, not meeting the frequency criterion for fatigue, or having no record of a medical consultation excluding illness in the previous 6 months. A further two cases of CFS were found who had been ill at the time of the prevalence survey. The annual incidence of CFS was therefore 370/100000 (95% CI 40–1330) of the population and the prevalence 740/100000 (200–1890). The cases were equally divided between the sexes, of upper social class, but

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

none were healthworkers (see Table 4). The incident cases both scored highly on the GHQ and one had a psychiatric diagnosis at interview. Both prevalent, longstanding, cases had attracted labels of 'ME' from doctors and also had psychiatric diagnoses. Eighteen months later, both remained unwell whereas the two incident cases described having recovered within a year.

DISCUSSION

We have prospectively examined risk factors for the development of chronic fatigue, interviewed subjects with possible CFS and provided an estimate of the incidence of CFS in a population based study. Our choice of sampling frame is likely to have avoided the selection biases of studying patients attending primary care or hospital specialists. The main findings of our study are that a measure of fatigue significantly predicted the incidence of chronic fatigue, whereas emotional distress and attributional factors did not do so after controlling for confounding, and that possible CFS sufferers have relatively high levels of psychiatric morbidity that fall after allowing for fatigue. However, some limitations of the study must be borne in mind: the small numbers of subjects, the dependence on self-report, and the use of general practice records rather than a specific medical examination.

We report a cross-sectional correlation between fatigue and GHQ scores, as have previous studies (Pawlikowska *et al.* 1994; Lawrie & Pelosi, 1995). This could simply reflect similarities in the symptoms they measure, and might explain why GHQ score was not a risk factor for chronic fatigue after controlling for fatigue. However, the correlation value suggests that only about 30% of the variance in fatigue is explained by the GHQ, and latent trait analysis of GHQ scores suggests that there is a fatigue dimension at the borderline of psychiatric 'caseness' (Woods & Goldberg, 1991). Psychiatric morbidity is therefore associated with, but is not a necessary risk factor for, chronic fatigue. Similarly, fatigue in the general population is most commonly attributed to psychosocial factors at a particular point in time (Pawlikowska *et al.* 1994; Lawrie & Pelosi, 1995), as was chronic fatigue in this study, but they do not increase the risk of developing chronic fatigue 1 year later. The relatively high scores of fatigue at baseline, the long (albeit self-reported) duration of fatigue in some incident chronic fatigue cases, and the association between pre-morbid fatigue and the development of chronic fatigue all suggest that the severity and chronicity of fatigue fluctuate in the general population, with some individuals periodically satisfying syndromal criteria as a result of an interaction between constitutional disposition to fatigue and various stressors.

In other prospective studies of risk factors for chronic fatigue syndromes, in subjects attending doctors with infectious illnesses, the subsequent development of chronic fatigue has been related to pre-morbid levels of fatigue and psychiatric morbidity (Wessely *et al.* 1995), a belief in physical rather than psychological aetiology (Cope *et al.* 1994), social adversity (Bruce-Jones *et al.* 1994), and depressive personality (Imboden *et al.* 1961). In this study, we have replicated reports that baseline fatigue and emotional distress are independent risk factors (Cope *et al.* 1994; Wessely *et al.* 1995), and that the GHQ effect is non-significant in multivariate analysis (Cope *et al.* 1994). We interpret the loss of effects for psychological measures after adjusting for fatigue as evidence that these act partly as markers of severity. However, the failure of this study and another (Wessely *et al.* 1995) to confirm a significant predictive effect for attribution may reflect differences in the measures used or in methods of subject selection.

We did not study the role of infectious illnesses as risk factors for the onset of chronic fatigue, even though there is some evidence to link them to syndromes of chronic fatigue (Bruce-Jones *et al.* 1994; Cope *et al.* 1994), as this demands that subjects are selected as patients who are consulting doctors. A minority of the incident cases in this population based study reported a medical consultation for fatigue, and those that did were more likely to be female and have higher levels of both fatigue and psychiatric morbidity. Although these results are based on small numbers, they are in agreement with previous research (David *et al.* 1990; Cathebras *et al.* 1992; Ridsdale *et al.* 1993; Fuhrer & Wessely, 1995). Symptom severity and psychiatric disorder seem to increase the likelihood of medical consultation, resulting in a gradient

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

of fatigue and psychopathology from the community to primary care and on to hospital clinics.

Nonetheless, a strong relationship between chronic fatigue syndromes and psychiatric morbidity is a consistent finding, regardless of whether the study is conducted on population based subjects (Lloyd *et al.* 1990; Pawlikowska *et al.* 1994; Lawrie & Pelosi, 1995), general practice attenders (Cathebras *et al.* 1992; McDonald *et al.* 1993; Euba *et al.* 1996) or hospital clinic patients (David, 1991; Euba *et al.* 1996). As in this study, where about one-half of those with chronic fatigue and three-quarters of those with possible or confirmed CFS were probable psychiatric cases, the association increases the nearer cases come to satisfying CFS criteria (Lawrie, 1993; Pawlikowska *et al.* 1994; Lawrie & Pelosi, 1995). Such psychiatric morbidity cannot be simply interpreted as secondary because CFS subjects attending doctors have been shown to resemble psychiatric more closely than chronically medically ill or normal controls; not only in the prevalence of current psychiatric diagnoses, but also in terms of previous psychiatric illnesses (David, 1991). Although our results are based on small numbers, they suggest that these associations are also found in a general population setting. However, it should be noted that the prevalence of psychiatric diagnoses is reduced by a third if neurasthenia is excluded, and was halved when fatigue was controlled for with the CIS-f. CFS should not, therefore, be seen as simply a manifestation of psychiatric disorder, such as depression, as this ignores the difference between presenting complaints of fatigue as opposed to low mood, and also disregards some differences in the quality of affective disorder in CFS and classically depressed subjects (Powell *et al.* 1990).

One of the distinguishing features between syndromes of chronic fatigue and depressive illness is the attribution of fatigue to a physical rather than psychological cause. Our failure to replicate this in community subjects may be due to type II error, but it is also possible that these views are markers of symptom severity. Certainly, such attribution is more common in patients seen in hospital settings than in primary care (David *et al.* 1990; David, 1991; Cathebras *et al.* 1992; McDonald *et al.* 1993; Euba *et al.* 1996), and is still less common in the general population (Pawlikowska *et al.* 1994; Lawrie & Pelosi, 1995). Alternatively, a conviction that fatigue is physical in order could influence consulting a doctor and be reinforced by investigations and onward referral. Whatever the interpretation, these views are important as they are associated with a poor long-term outcome (Sharpe *et al.* 1992; Wilson *et al.* 1994). Although we did not measure outcome systematically, our finding that more than one half of the chronic fatigue cases had improved within 1 year, at least to the point where they no longer satisfied criteria for chronic fatigue, is in keeping with similar figures for primary care patients with fatigue (Cathebras *et al.* 1992) and chronic fatigue (Ridsdale *et al.* 1993) and suggests that prognosis may be better in such 'subsyndromes' than in full-blown CFS.

Factors determining medical consultation could also account for some of the apparent excess of females and those of upper social classes in clinical studies of CFS. These demographic associations are less strong in population based research (Lloyd *et al.* 1990; Buchwald *et al.* 1995; Fuhrer & Wessely, 1995; Lawrie & Pelosi, 1995). The CFS cases identified in this survey were equally divided between the sexes, as were chronic fatigue and possible CFS cases, although these findings are based on small numbers. The upper social class of sufferers could be attributable to response bias away from lower social classes in this study (Lawrie & Pelosi, 1995), or reflect doctors' diagnostic habits in clinical samples (Fuhrer & Wessely, 1995; Euba *et al.* 1996). The annual incidence of CFS, at 370/100000/year, has wide confidence intervals (40–1330) because of the very small number of cases detected. It may be a conservative estimate as we excluded subjects who had not seen their general practitioner in the previous 6 months, and also excluded those with any physical illness as we could not make a judgement about the adequacy of any medical treatment (Sharpe *et al.* 1991; Fukuda *et al.* 1994). Alternatively, our figure could be an overestimate as we had no specific measure of functional impairment. There are very few reliable studies with which our incidence figure can be compared, but it accords with that which can be extrapolated from another study (of 280/100000/year, Wessely *et al.* 1995). The prevalence of CFS in this study (0·74%) is in keeping with our previous estimate

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

of 0·56% (Lawrie & Pelosi, 1995) and with a figure of 0·4% from the USA (Bates *et al.* 1993). The lower rates in other prevalence studies could be attributable to requirements for physician notification and the use of more strict diagnostic criteria (Lloyd *et al.* 1990; Buchwald *et al.* 1995).

In conclusion, it can be seen that different factors are predominantly responsible for syndromes of chronic fatigue at different stages (Woods & Goldberg, 1991). Research findings suggest that they are characterized by both fatigue and psychiatric morbidity, triggered by psychosocial and physical stressors and maintained by biological and psychological factors. Future studies must, therefore, consider both the setting and the stage of illness in which patients are seen to avoid potentially misleading conclusions about the aetiology and outcome of the condition.

This study was supported by the Scottish Home and Health Department. We are grateful to the staff and patients of Penicuik Health Centre for their assistance. Mrs McColl, the practice manager, was especially helpful in accessing the health centre computerized list of registered patients and arranging the inspection of casenotes. Dr Begg and the other general practitioners ensured that our correspondence to the study subjects was encouraging without being pressurizing.

REFERENCES

Bates, D. W., Schmitt, W., Buchwald, D., Ware, N., Lee, J., Thoyer, E., Kornish, R. J. & Komaroff, A. L. (1993). Prevalence of fatigue and chronic fatigue in a primary care practice. *Archives of Internal Medicine* **153**, 2759–2765.

Beck, A. T., Ward, C. H., Medelson, M., Mock, J. & Erbaugh, J. (1965). Assessment of depression. *Archives of General Psychiatry* **4**, 561–571.

Behan, P. O. & Behan, W. M. H. (1988). The postviral fatigue syndrome. *CRC Critical Reviews in Neurobiology* **42**, 157–178.

Bruce-Jones, W. D. A., White, P. D., Thomas, J. M. & Clare, A. W. (1994). The effect of social adversity on the fatigue syndrome, psychiatric disorders and physical recovery, following glandular fever. *Psychological Medicine* **24**, 651–659.

Buchwald, D., Umali, P., Umali, J., Kith, P., Pearlman, T. & Komaroff, A. L. (1995). Chronic fatigue and the chronic fatigue syndrome: prevalence in a Pacific Northwest health care system. *Annals of Internal Medicine* **123**, 81–88.

Cathebras, P. J., Robbins, J. M., Kirmayer, L. J. & Hayton, B. C. (1992). Fatigue in primary care: prevalence, psychiatric comorbidity, illness behaviour and outcome. *Journal of General Internal Medicine* **7**, 276–286.

Cope, H., David, A., Pelosi, A. & Mann, A. (1994). Predictors of chronic 'postviral' fatigue. *Lancet* **344**, 864–868.

David, A., Pelosi, A., McDonald, E., Stephens, D., Ledger, D., Rathbone, R. & Mann, A. (1990). Tired, weak or in need of rest: fatigue among general practice attenders. *British Medical Journal* **301**, 1199–1202.

David, A. S. (1991). Postviral fatigue syndrome and psychiatry. *British Medical Bulletin* **46**, 966–988.

Euba, R., Chalder, T., Deale, A. & Wessely, S. (1996). A comparison of the characteristics of chronic fatigue syndrome in primary and tertiary care. *British Journal of Psychiatry* **168**, 121–126.

Fuhrer, R. & Wessely, S. (1995). The epidemiology of fatigue and depression: a French primary-care study. *Psychological Medicine* **25**, 895–905.

Fukuda, K., Straus, S. E., Hickie, I., Sharpe, M. C., Dobbins, J. G. & Komaroff, A. (1994). The chronic fatigue syndrome: approach to its definition and study. *Annals of Internal Medicine* **121**, 953–959.

Goldberg, D. P. & Huxley, P. (1992). *Common Mental Disorders: A Biosocial Model*. Routledge: London.

Goldberg, D. P. & Williams, P. (1988). *A User's Guide to the General Health Questionnaire*. NFER-NELSON Publishing Company Ltd: Windsor, Berks.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry* **23**, 56–62.

Imboden, J. B., Canter, A. & Cluff, L. E. (1961). Convalescence from influenza: a study of the psychological and clinical determinants. *Archives of Internal Medicine* **108**, 115–121.

Jenkins, R., Mann, A. H. & Belsey, E. (1981). The background, design and use of a short interview to assess social stress and support in research and clinical settings. *Social Science and Medicine* **15E**, 195–203.

Lawrie, S. M. (1993). Chronic Fatigue in the Community and its Psychiatric Associations. M.Phil thesis, University of Edinburgh.

Lawrie, S. M. & Pelosi, A. J. (1994). Chronic fatigue syndrome: prevalence and outcome. *British Medical Journal* **308**, 732–733.

Lawrie, S. M. & Pelosi, A. J. (1995). Chronic fatigue syndrome in the community: prevalence and associations. *British Journal of Psychiatry* **166**, 793–797.

Lewis, G., Pelosi, A. J., Araya, R. & Dunn, G. (1992). Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychological Medicine* **22**, 465–486.

Lloyd, A. R., Hickie, I., Boughton, C. R., Spencer, O. & Wakefield, D. (1990). Prevalence of chronic fatigue syndrome in an Australian population. *Medical Journal of Australia* **153**, 522–528.

McDonald, E., David, A. S., Pelosi, A. J. & Mann, A. H. (1993). Chronic fatigue in primary care attenders. *Psychological Medicine* **23**, 987–998.

ME Action Campaign (1993). *Interaction: Number 12*. ME Action Campaign: London.

Miller, N. A., Carmichael, H. A., Calder, B. A., Behan, P. O., Bell, E. J., McCartney, R. A. & Hall, F. C. (1991). Antibody to coxsackie B virus in diagnosing postviral fatigue syndrome. *British Medical Journal* **302**, 140–143.

Pawlikowska, T., Chalder, T., Hirsch, S. R., Wallace, P., Wright, D. J. M. & Wessely, S. C. (1994). Population based study of fatigue and psychological distress. *British Medical Journal* **308**, 763–766.

Powell, R., Dolan, R. & Wessely, S. (1990). Attributions and self-esteem in depression and chronic fatigue syndromes. *Journal of Psychosomatic Research* **34**, 665–673.

Ridsdale, L., Evans, A., Jerrett, W., Mandalia, S., Osler, K. & Vora, H. (1993). Patients with fatigue in general practice. *British Medical Journal* **307**, 103–106.

Scott, S., Deary, I. & Pelosi, A. J. (1995). General practitioners' attitudes to patients with a self-diagnosis of myalgic encephalomyelitis. *British Medical Journal* **310**, 508.

Sharpe, M. C., Archard, L. C., Banatvala, J. E., Borysiewicz, L. K., Clare, A. W., David, A., Edwards, R. H., Hawton, K. E., Lambert, H. P., Lane, R. J., Mann, A., McDonald, L., Mowbray, J., Pearson, D., Pelosi, A., Peto, T., Preedy, V., Smith, A., Smith, D., Taylor, D., Tyrell, D., Wallace, P., Wessely, S. & White, P. D.

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press

(1991). A report – chronic fatigue syndrome: guidelines for research. *Journal of the Royal Society of Medicine* **84**, 118–121.
Sharpe, M., Hawton, K., Seagroatt, V. & Pasvol, G. (1992). Follow up of patients presenting with fatigue to an infectious diseases clinic. *British Medical Journal* **305**, 147–152.
Statistics and Epidemiological Research Corporation (1991). *EGRET: Epidemiological Graphs*, *Estimation and Testing*. SERC: Seattle, Washington.
Wessely, S., Chalder, T., Hirsch, S., Pawlikowska, T., Wallace, P. & Wright, D. J. M. (1995). Post-infectious fatigue: prospective cohort study in primary care. *Lancet* **345**, 1333–1338.
Wilson, A., Hickie, I., Lloyd, A., Wakefield, D., Broughton, C. & Dwyer, J. (1994). Longitudinal study of outcome of chronic fatigue syndrome. *British Medical Journal* **308**, 756–759.
Woods, T. O. & Goldberg, D. P. (1991). Psychiatric perspectives: an overview. *British Medical Bulletin* **47**, 908–918.
World Health Organization (1992). *The ICD-10 Classification of Mental and Behavioural Disorders*. WHO: Geneva.

https://doi.org/10.1017/S0033291796004357 Published online by Cambridge University Press