Frequency of attendance in general practice and symptoms before development of chronic fatigue syndrome: a case-control study

W T Hamilton, G H Hall and A P Round

SUMMARY

Background: *Chronic fatigue syndrome (CFS) research has concentrated on infective, immunological, and psychological causes. Illness behaviour has received less attention, with most research studying CFS patients after diagnosis. Our previous study on the records of an insurance company showed a highly significant increase in illness reporting before development of CFS.*

Aim: *To investigate the number and type of general practitioner (GP) consultations by patients with CFS for 15 years before they develop their condition.*

Design of study: *Case-control study in 11 general practices in Devon.*

Setting: *Forty-nine patients with CFS (satisfying the Centers for Disease Control criteria), 49 age, sex, and general practice matched controls, and 37 patients with multiple sclerosis (MS) were identified from the general practices' computerised databases.*

Method: *The number of general practice consultations and symptoms recorded in three five-year periods (quinquennia) were counted before development of the patients' condition.*

Results: *The median number of consultations was significantly higher for CFS patients than that of matched controls in each of the quinquennia: ratios for first quinquennium = 1.88,* P = *0.01; second quinquennium = 1.70,* P = *0.005; last quinquennium = 2.25,* P<*0.001. More CFS patients than controls attended for 13 of the 18 symptoms studied. Significant increases were found for upper respiratory tract infection (*P<*0.001), lethargy (*P<*0.001), and vertigo (*P = *0.02). Similar results were found for CFS patients when compared with MS.*

Conclusions: *CFS patients consulted their GP more frequently in the 15 years before development of their condition, for a wide variety of complaints. Several possibilities may explain these findings. The results support the hypothesis that behavioural factors have a role in the aetiology of CFS.*

Keywords: *fatigue; consultation rates; behavioural factors.*

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Introduction

RESEARCH on chronic fatigue syndrome (CFS)[1-3] has focused on infective, immunological, genetic,[4] and psychological causes. Illness behaviour has received less attention. Most research on illness behaviour has studied CFS patients after diagnosis,[5-7] which may introduce recall bias. Our previous study[8] investigated information recorded routinely, showing a highly significant increase in illness reporting before development of CFS. These records came from an insurance company so those studied may have been unrepresentative of the general population. We therefore investigated CFS patients in primary care by examining their general practitioners' (GPs') records for consultations prior to the development of CFS. Our hypothesis was that if the illness behaviour of CFS patients were abnormal then this would be reflected in a different pattern of GP usage before the onset of CFS.

Method

This was a case control study, based in 14 general practices in Devon, United Kingdom. All group practices in two towns were invited to enter. Three declined, two because their disease register was not computerised. The local research ethics committee approved the study.

The computerised disease registers of the practices were searched using the following terms: chronic fatigue syndrome, myalgic encephalomyelitis, postviral fatigue syndrome, postviral debility, and post-infectious encephalomyelitis. The practices had four different computer systems, so not all terms were searchable in each practice. Identified cases were compared with the Centers for Disease Control (CDC) 1994 criteria by using information extracted from their GP's records. The CDC criteria require four or more out of eight symptoms to have persisted or recurred for six or more months. A symptom noted within one year of diagnosis was accepted as a proxy for these. Thus, we established three categories of patient from those recorded as having CFS. First, those filling the CDC criteria in full, which are the focus of this study; second, those who did not have enough recorded symptoms to meet the criteria but otherwise would have (we counted only consultation numbers for this group); and finally, those failing the CDC criteria on other grounds, which were not studied further.

Two control groups were studied. The first was age, sex, and general practice matched controls, selected by using each practice's computerised age–sex register to identify the patient of the same sex nearest in age to the case

HOW THIS FITS IN

What do we know?
Most research on chronic fatigue syndrome (CFS) has concentrated on infective, immunological or psychological theories. Results have been inconclusive, and no widely accepted explanation has emerged.

What does this paper add?
Those who subsequently develop CFS have been consulting with their GPs significantly more than controls long before their condition is diagnosed. These consultations are for a wide variety of conditions. The results support the theory that behavioural factors are important in the aetiology of CFS.

patient. They were excluded if they had a condition that would have disqualified them from a diagnosis of CFS under the CDC criteria. Only cases and controls with 10 or more years of records prior to diagnosis were entered.

The second control group was of patients with multiple sclerosis (MS). Cases diagnosed after 1980 were selected to minimise any possible cohort effect. Only MS cases with abnormal evoked potentials, magnetic resonance or computerised tomography scanning, or oligoclonal bands in their cerebrospinal fluid, or with abnormal neurological signs and a consultant neurologist's diagnosis of MS were entered. For both CFS and MS cases, the date of diagnosis for the study was the first mention of CFS or MS as a possibility.

All records of GP consultations were assembled for the 15 years prior to diagnosis of illness or entry into the study as a control. The notes were checked for temporary resident, maternity, and contraception consultations, which may be stored on separate cards. Two practices used only computerised notekeeping from 1996 and 1990 respectively, so the relevant section of the computer record was printed for three patients after these dates. General practice notes are not usually signed, so it is impossible to know if any of the consultations, such as immunisations, were with non-medical members of the practice. The current postcode was recorded for each patient.

Each page in the records was photocopied, had the name removed, and given a randomly generated code number. Sets of photocopies containing sheets from cases and controls randomly sequenced were examined by one of the authors (GHH), who was blinded to case/control status. For each sheet, the number of consultations was counted in three time blocks: years -14 to -10 (quinquennium A), years -9 to -5 (quinquennium B) and years -4 to diagnosis (quinquennium C). Consultation numbers were also recorded for patients who did not have enough documented symptoms to fulfil the CDC criteria but who were recorded on the practice computers as having CFS.

Consultations were coded into one or more of 33 symptom groups derived from our previous work,[8] plus a category for illegible entries. Intra-observer variation was examined by repeat blind testing of a random sample of pages. There was overlap between some categories, which were therefore combined: chest infection and upper respiratory tract infection into upper respiratory tract infection (URTI); and low back pain, rheumatism, and orthopaedic disorders into joint disorders. A further 13 categories had 10 or fewer mentions in total. Thus, 18 groups were used for the analyses.

The number of consultations for each quinquennium for CFS, matched controls, and MS showed a skewed distribution. We therefore used medians and non-parametric tests for analysis. The significance of the difference in medians was tested by the Wilcoxon signed rank test for CFS versus matched control, and the Mann–Whitney test for CFS versus MS. The effect of including the patients who did not fulfil the CDC criteria by not having enough recorded symptoms was also examined.

To assess any effect of social class, conditional logistic regression was performed for CFS versus matched control in each quinquennium with the two variables entered: consultation numbers and Jarman score allocated according to enumeration district (as a proxy for socioeconomic status). Unconditional logistic regression was performed for CFS versus MS with the same variables, plus age and sex.

The number of individuals consulting for each of the 18 symptom groups was compared by combining quinquennia A and B. Quinquennium C results were not included because of the risk of bias by prodromal symptoms of CFS or MS. The mean number of symptom groups documented at each consultation was calculated. For CFS versus matched control, odds ratios (ORs) and 95% confidence intervals (CIs) for matched pairs were calculated for each symptom group, with McNemar's test used for significance. For CFS versus MS, ORs and CIs were calculated. For gynaecological disorders, contraception, pregnancy, and cervical smears, only women whose age at entry to the study was over 17, 20, 20, and 24 years respectively were analysed, as consultations for these items would not be expected five or more years before attaining these ages. The data were analysed using STATA.

Results

Entries into the study are summarised in Figure 1. Seventy patients did not fulfil the CDC criteria for the following reasons: 14 had fewer than four symptom categories recorded, 44 had a condition lasting under six months, and 12 had disqualifying diseases — severe asthma (2), chronic psychosis (2), substance abuse, anorexia, anaemia, hypothyroidism, multiple sclerosis, cardiomyopathy, ankylosing spondylitis, and rheumatoid arthritis.

Six matched controls were rejected. Two had missing notes, one had no record of any consultations in the 15 years, and three had illnesses that would have disqualified them from entry as a case — chronic psychosis, renal transplantation, and hypothyroidism. In each case, the next patient on the age–sex register replaced these six. Demographic details of the qualifying cases are shown in Table 1.

Consultation numbers for each quinquennium are shown in Figure 2. The difference in median consultation numbers between CFS and matched controls was significant for all three quinquennia: A = 7.5 (P = 0.007); B = 6 (P = 0.004); C = 14 (P<0.001). The difference in median consultation

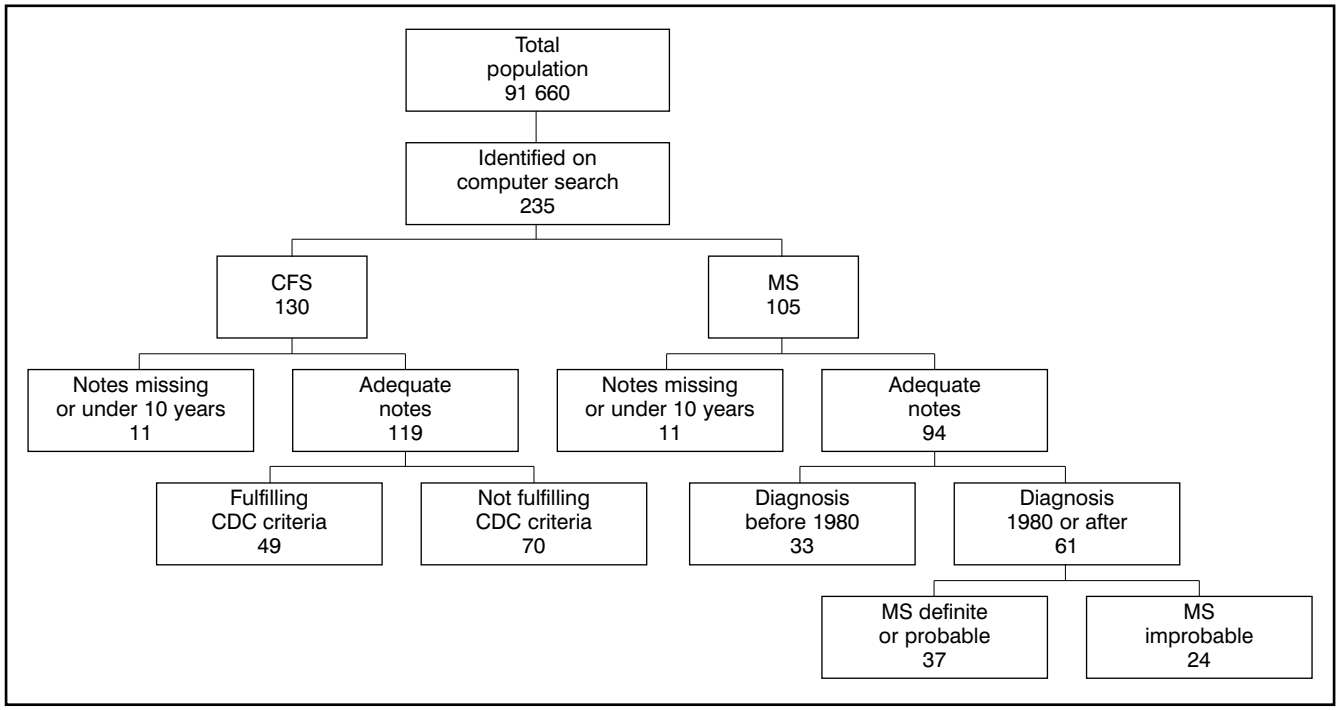

Figure 1. Identification of CFS and MS cases.

Table 1. Details of CFS and MS cases and matched controls.

Characteristic	CFS (*n* = 49)	Matched control (*n* = 49)	MS (*n* = 37)
Mean age at diagnosis (standard deviation)	34.8 (13.3)	34.8 (13.3)	37.2 (10.9)
Percentage male	22.4	22.4	37.8
Mean current Jarman score (confidence interval)	-2.2 (-7.2 to +2.8)	-0.1 (-5.1 to +4.9)	2.4 (-9.0 to +4.2)
Median date of onset (interquartile range)	May 1994 (August 1991–March 1995)	Defined as date of onset of matched case	April 1989 (November 1984–June 1994)

numbers between CFS and MS was significant for quinquennia A and C but not quinquennium B: A = 10 (P = 0.001); B = 3 (P = 0.08); C = 12 (P = 0.01). Analysis including the 14 patients who did not fulfil the CDC criteria only because they had not enough recorded symptoms made no difference to the medians in any quinquennia. Mean annual consultations were: CFS = 4.1, 4.2, 6.3; matched control = 2.7, 2.5, 3.1; MS = 2.2, 3.4, 4.1. The details of the logistic regression analyses are shown in Table 2. Multivariable results were similar to univariable results (data not shown).

The mean number (confidence interval) of symptoms recorded per consultation in quinquennia A and B combined were 1.10 (1.07–1.14) for CFS, 1.09 (1.05–1.12) for matched controls, and 1.10 (1.07–1.13) for MS. Table 3 shows the ORs of patients from the CFS group compared with those from the control groups of consulting for the various symptom groups during the decade 14 to five years before diagnosis. In 13 out of 18 symptom groups the ORs exceed 1.0 for both sets of comparisons. Where the ORs are less than 1.0, female reproductive conditions predominate. The largest differences are seen for the complaints relating to URTI and lethargy. There were only three consultations for glandular fever throughout the study.

Discussion

The significant excess of GP consultations for 15 years prior to the onset of CFS is a striking finding. Patients who subsequently develop CFS consult their GP almost twice as often as controls, up to 15 years before they are diagnosed as having CFS.

One possibility is that the case selection has either caused or exaggerated the findings. The prevalence in this study is 0.05% — low when compared with questionnaire surveys of primary care populations,[9-12] which report a prevalence of 0.1–1.1%. Such surveys can uncover cases previously unrecognised,[11-13] with only one in ten of those fulfilling CFS criteria actually considering themselves to have CFS.[14] One study asking GPs to identify CFS cases from their practices showed a prevalence of 0.1%.[15]

Chronic fatigue syndrome cases were found from computer searches that identified patients with fatigue syndromes, 40% of whom fulfilled the CDC criteria. One CDC requirement is for four symptom categories to be present for six months; this may be applied retrospectively by monitoring spontaneous reporting of symptoms.[16] We accepted a mention of each category in the notes as sufficient, which

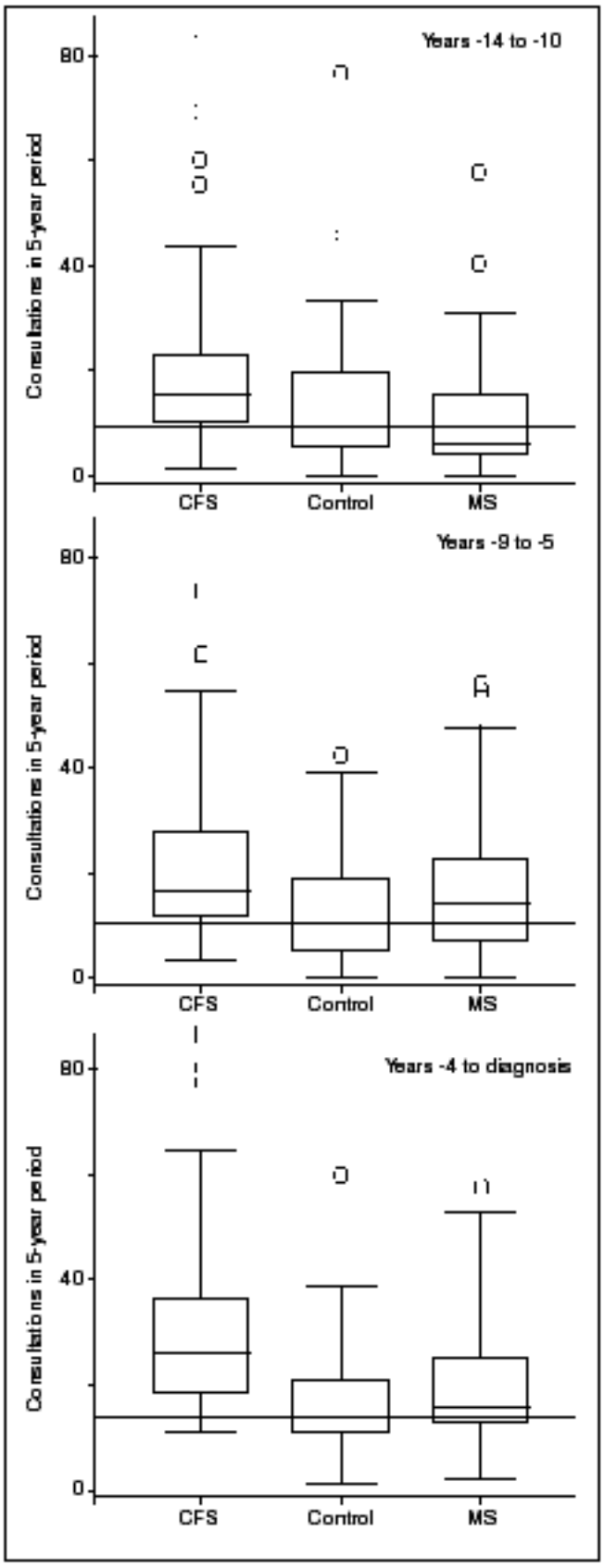

Figure 2. Box-whisker plot of number of consultations for CFS, controls and MS. The horizontal line is the median for controls in each graph.

may have favoured the selection of higher consulting patients for entry to the study. However, adding the 14 potential cases who failed to fulfil the CDC criteria only because they had not enough recorded symptoms had no effect on the results. Furthermore, the counting of symptoms is the most controversial part of the CDC criteria.[16,17] The female preponderance in this study mirrors previous series, as does the age range. It is likely, therefore, that the CFS cases in this study represent the reality of CFS diagnosed in the community.

The controls are typical in terms of their consultation rate. The mean national rate was reported as 3.4 consultations per year in 1981–1982, and 3.5 consultations per year in 1991–1992.[18] By 1997, it had increased to 5.6 consultations per year.[19] The rate is lowest in age groups 5–15 years and 16–44 years, being 2.3 and 2.1 respectively in 1991–1992.[18] The rise in rates in all groups in this study reflects the ageing of the patients, plus recent national increases in consultation patterns. The close matching of the CFS and control groups eliminates a differential ageing effect. The MS group were older at diagnosis, which may explain some of the rise in their consultation numbers compared with controls.

Finally, factors other than age and sex may affect the consultation rate. Lower socioeconomic status is associated with increased consultations.[20] Our CFS cases and controls had similar current Jarman scores — a weak proxy for socioeconomic status at the time of onset of their condition — and the logistic regression did not show these to be a significant contribution to increased consultation numbers. Consultation rates are related to housing tenure and employment status; this was not measured in our study. Nonetheless, the matching of cases and controls eliminated the major determinants of consultation rates,[21] so it is unlikely that the differences between the consultation rates can be explained by the other factors.

The higher number of GP consultations in patients who years later develop CFS can be explained by an increased number of illnesses, by perceiving symptoms more readily as illness, by an increased tendency to consult with a similar number of illnesses, or by a mixture of these. CFS patients not only consulted their doctors more often than other patients but also for a wider range of symptoms; only two complaints were less frequent in the CFS group when compared with matched controls, and five when compared with MS. URTI and lethargy showed the highest relative increase. It is difficult to equate this wide spectrum of increased complaints with an infectious or immunological explanation. Furthermore, searches for immunological or infectious abnormalities in CFS remain inconclusive, despite extensive research.[2]

Another possibility is that CFS patients in our study already had their illness, albeit undiagnosed,[22] in quinquennia A or B, so accounting for the increased consultation rate. The date of diagnosis was taken as the first mention of CFS or its synonyms in the notes. One study of 64 CFS patients[23] showed that 58 recalled a definite onset in the months prior to diagnosis and only two reported several years of fatigue prior to diagnosis. Therefore, it is very unlikely that our results can be explained by this mechanism once the five years prior to diagnosis have been excluded. This contrasts

Table 2. Logistic regression: CFS versus controls and CFS versus MS.

		CFS versus controls		CFS versus MS	
		Odds ratio (95% CI)[a]	*P*-value	Odds ratio (95% CI)[a]	*P*-value
Quinquennium A	Consultation numbers	1.03 (1.00–1.06)	0.06	1.05 (1.01–1.09)	0.03
	Jarman score	0.99 (0.97–1.02)	0.51	1.00 (0.98–1.03)	0.75
	Age (years)	-	-	0.97 (0.94–1.01)	0.17
	Sex[b]	-	-	1.21 (0.43–3.40)	0.72
Quinquennium B	Consultation numbers	1.06 (1.01–1.10)	0.007	1.02 (0.99–1.05)	0.26
	Jarman score	0.99 (0.96–1.02)	0.76	1.00 (0.98–1.02)	0.95
	Age (years)	-	-	0.98 (0.95–1.01)	0.32
	Sex[b]	-	-	1.61 (0.59–4.37)	0.35
Quinquennium C	Consultation numbers	1.09 (1.04–1.15)	0.001	1.04 (1.00–1.07)	0.03
	Jarman score	0.99 (0.96–1.04)	0.77	1.00 (0.97–1.02)	0.83
	Age (years)	-	-	0.98 (0.94–1.01)	0.23
	Sex[b]	-	-	1.30 (0.46–3.63)	0.63

[a]Odds ratio for each extra consultation. [b]Odds ratio for being female.

Table 3. Comparison of number of patients attending for each symptom group in quinquennia A and B combined.

	CFS versus control		CFS versus MS	
Symptom	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
URTI	8.5 (2.0–76)	<0.001	3.3 (1.0–10)	0.04
Lethargy	7.0 (2.1–37)	<0.001	2.8 (1.4–6.9)	0.02
Vertigo	3.8 (1.2–16)	0.02	1.6 (0.6–4.2)	0.35
Non-specific abdominal pain	2.3 (0.93–6.0)	0.08	2.0 (0.8–4.8)	0.12
Dyspepsia	2.3 (0.63–10)	0.27	1.3 (0.5–3.7)	0.60
Other	2.3 (0.53–14)	0.34	0.88 (0.2–4.6)	0.88
Headache	2.0 (0.62–7.5)	0.30	1.1 (0.4–2.6)	0.88
Urinary	1.9 (0.75–5.1)	0.21	1.7 (0.7–3.9)	0.25
Illegible	1.7 (0.62–5.1)	0.36	1.5 (0.7–3.4)	0.33
Immunisations	1.6 (0.63–4.1)	0.40	2.7 (1.0–7.2)	0.05
Anxiety or depression	1.6 (0.56–4.8)	0.48	2.1 (0.9–5.0)	0.09
Joint disorders	1.2 (0.46–3.3)	0.82	0.53 (0.2–1.3)	0.15
Gynaecological[a]	1.2 (0.3–4.2)	1.0	0.60 (0.2–1.8)	0.38
Viral infection	1.0 (0.33–3.1)	1.0	1.1 (0.4–2.6)	0.87
Contraception[b]	1.0 (0.3–3.3)	1.0	1.1 (0.4–3.3)	0.82
Cervical smears[c]	1.0 (0.2–5.4)	1.0	0.48 (0.2–1.5)	0.22
Skin disorder	0.67 (0.24–1.8)	0.50	2.6 (1.1–6.4)	0.03
Pregnancy[b]	0.29 (0.03–1.5)	0.18	0.66 (0.2–2.0)	0.46

[a]For CFS/control $n = 35$, for MS $n = 23$. [b]For CFS/control $n = 32$, for MS $n = 22$. [c]For CFS/control $n = 30$, for MS $n = 19$.

with MS, where the initial symptom is frequently undiagnosed; optic neuritis can precede the diagnosis of MS by up to 18 years.[24] This may explain the rise in consultations in quinquennium B, as well as the effect of age discussed earlier.

Is it possible that the cases had one of the synonyms for what we now call CFS in the 15 years before they were finally given that diagnosis? Studies of fiction[25] and of the medical literature[26] make it clear such a syndrome has been around for centuries but attracting different labels. The advantage of our detailed examination of the records is that we would have identified such conditions had they been present.

Different behaviour and use of health professionals with common symptoms is one explanation for our findings. This would explain both the increased number of consultations, and the wide variety of complaints. Consultations with a doctor may not be for treatment; they may be for reassurance, prevention, certification or many other reasons. Our study was not designed to establish if one of these categories was more prevalent.

Our results, plus those of our previous study,[8] suggest the possibility that behavioural factors do have a role in the development of CFS. Illness behaviour lies on a continuum, with differing opinions on what is considered abnormal.[27] The Pilowski definition of abnormal illness behaviour, which uses the words 'inappropriate' and 'maladaptive',[28] is rightly seen as pejorative.[27] Studies of illness behaviour in CFS have consistently shown high disease conviction[5-7] and increased somatic concern compared with psychological concern,[6,7] though not higher than MS controls.[7] All the studies were retrospective and the findings could represent changes in illness behaviour as a result of the illness. In a prospective study of CFS after acute infections[29] the best predictors for development of CFS were previous fatigue and psychological distress. Additionally, cognitive behavioural therapy, which addresses beliefs about symptoms and illness, in particular those that can block recovery, is the only treatment shown to be helpful in a systematic review.[30] Our results add support to this. We consider that more

emphasis should be given to this area, both for funding treatment of CFS and for research on CFS.

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