

The prognosis of different fatigue diagnostic labels: a longitudinal survey

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Hamilton WT, Gallagher AM, Thomas JM and White PD. The prognosis of different fatigue diagnostic labels: a longitudinal survey. *Family Practice* 2005; **22**: 383–388.

Background. Several different diagnostic labels exist for the fatigue syndromes, including chronic fatigue syndrome (CFS), myalgic encephalomyelitis (ME) and postviral fatigue syndrome (PVFS). An allied condition is fibromyalgia. No study has examined prognostic differences across these different labels.

Objective. To compare the prognoses of patients labelled with different fatigue syndromes in primary care.

Methods. We performed a longitudinal survey, using electronic records from the General Practice Research Database. All 18 122 patients diagnosed by their GP with a fatigue syndrome from 1988–2001 with a minimum of one year of records after diagnosis were collated into four groups: CFS, ME, PVFS and fibromyalgia. CFS and ME were combined for the main analysis as no code for CFS was available until 1995. The length of illness was calculated as the interval between the diagnosis and the last recorded fatigue symptom, expressed as days per year, to account for differing lengths of record after diagnosis.

Results. Patients with CFS/ME combined had a worse prognosis (median length of illness 80 days per year; interquartile range 0–242) than fibromyalgia (51; 0–244) or PVFS 0 (0–108), a significant difference, $P < 0.001$. In a subgroup analysis, ME had a worse prognosis (median length of illness in days per year 106; interquartile range 0–259) than CFS (33; 0–170), $P < 0.001$, in spite of a better course before diagnosis. Secondary outcome measures were consistent with these results.

Conclusion. There were important differences in outcome between the various fatigue labels, with ME having the worst prognosis and PVFS the best. This could be an adverse effect of the label ME itself. Alternatively, patients who are destined to have a worse prognosis may preferentially attract the ME label. Our data support the first interpretation.

Keywords. Chronic fatigue syndrome, primary health care, prognosis.

Introduction

Chronic fatigue syndrome (CFS) is a relatively new name for a condition that has probably always existed. Other names are used, such as postviral fatigue syndrome

(PVFS) or myalgic encephalomyelitis (ME). Whether these different labels represent separate conditions or the same disorder is hotly debated. Each label is unsatisfactory in some way: for example, fatigue is not the only component of CFS, making this label unattractive to some. Equally, myalgic encephalomyelitis implies a pathological abnormality that has not been demonstrated, and postviral fatigue gives emphasis to what may have been only a triggering event. Fibromyalgia is characterised by widespread pain and muscle tenderness, but also has prominent fatigue and is closely related to CFS.^{1–3} These different labels may have arisen in part from medical specialism, in that particular labels are favoured by certain specialists.¹

Giving a condition a name helps to guide treatment and to advise on prognosis. It may also influence outcome.^{4–6} There have been few prognostic studies of

Received 25 June 2004; Accepted 30 December 2004.

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CFS and none has compared prognoses across the different fatigue syndrome labels.^{7–12} One report of the duration of prolonged fatigue in primary care patients found equal durations of illness between patients who satisfied the international criteria for CFS, and those who did not.^{13,14} Other reports on the duration of illness have focused on features such as illness beliefs, but not examined the effect of the illness label itself.¹⁵ Therefore, we designed a study to investigate the prognosis of fatigue syndromes with different labels.

Methods

This was a cohort study based on pre-existing medical records. All patients with a diagnostic label of a fatigue syndrome were identified from the UK General Practice Research Database (GPRD) for the years 1988–2001 inclusive. In GPRD practices all patient consultations are recorded on computers using one of two coding systems, Oxmis or Read.¹⁶ These systems allow recording of both symptoms and diagnoses. When the GPRD began, all systems used Oxmis. Although the Read system was developed in the early 1990s, its adoption by practices was usually linked to upgrades to the practice's software, and so there was very little use of Read codes before 1995. Since then Read coding has progressively increased and Oxmis decreased. The data are subjected to regular quality checks. Many studies have used the GPRD as their data source.

Identification of fatigue syndromes and symptoms

A list of fatigue syndromes was compiled from the library of Oxmis and Read codes (Table 1). We categorised the

TABLE 1 Codes from OXMIS and Read systems used to identify cases

Description	Oxmis (O) or Read (R)	Group	Number
Postinfluenza asthenia	O	PVFS	21
Postinfluenza debility	O	PVFS	687
Post viral debility	OR	PVFS	2421
Post viral (asthenic) syndrome	OR	PVFS	6224
Post viral fatigue syndrome	OR	PVFS	6530
Myalgic encephalomyelitis	OR	ME	1200
Chronic fatigue syndrome	R	CFS	159
Fibromyalgia	OR	Fibromyalgia	880
Total			18122

In both systems, the same group of words may be arranged differently and given a different code. For instance, post viral fatigue syndrome, postviral fatigue syndrome and PVFS have different codes. All the variations were identified, and are available from the authors, but for brevity are not shown above.

syndrome codes into four groups: CFS, ME, PVFS, and fibromyalgia. The first occurrence of a syndrome code was identified and called the date of diagnosis. The full, anonymised records for all these patients were extracted. Patients with a subsequent diagnosis in a different group were classified by their first diagnosis. A list of 32 codes for fatigue symptoms was also compiled. It was largely comprised of the terms tiredness, fatigue, lethargy and their synonyms. This list is available from the authors. All fatigue diagnoses or symptoms recorded after the initial diagnosis were identified. Only patients whose records extended for at least one year after diagnosis were studied, to reduce biases caused by temporary residents (who register temporarily with a doctor when away from home) and to produce a period for study free from potential bias by the different length of records across the different labels.

Outcome measures

The duration of the illness was defined as the time interval between the date of initial diagnosis and the final occurrence of a fatigue symptom or diagnosis. There were differences in the duration of medical records after diagnosis among the groups, so the primary outcome measure was the duration of illness as a proportion of the total record duration.

Secondary measures of outcome included proportions of each group with a subsequent fatigue code in the records, the median number of fatigue records and consultations (for any reason) each year after diagnosis. In order to examine whether different diagnostic labels were influenced by illness characteristics before diagnosis, we also measured the number of fatigue records in the year before diagnosis for all those patients who had at least one year of pre-diagnosis data.

Additionally, to remove potential bias from the differing lengths of records after diagnosis, we reanalysed the data for the period from seven to 12 months after diagnosis. As entry to the study required a minimum of one year in the records, the different lengths of record after this will not have affected these analyses. This analysis measured the number of consultations, and the proportion of patients with at least one fatigue code recorded during this six-month period.

Statistical analysis

Firstly, CFS was combined with ME to create CFS/ME, because of the widely held consensus that the two terms are interchangeable (although we also examined whether this is true).¹⁷ Furthermore, over half of the total dataset was from Oxmis coded data, which has no code for CFS. CFS/ME was compared with both PVFS and fibromyalgia using the whole dataset. The Read-only dataset was used for the CFS versus ME comparison.

None of the measured outcomes was normally distributed. Satisfactory transformations could not be found, so non-parametric methods were used for the

analyses. The Kruskal-Wallis test was used to compare the three groups CFS/ME, fibromyalgia and PVFS in the whole dataset. Where there were only two comparison groups, these were compared using the Mann-Whitney test. Comparisons of proportions were performed by chi-squared tests. Analyses were performed with Stata, version 8.¹⁸

Results

We identified 18 122 patients with a fatigue syndrome and at least one year of records after diagnosis. Details of the age and sex distributions for each group are shown in Table 2. Of the CFS group 27 (17%) had a

subsequent diagnosis in a *different* group (11 ME, 2 fibromyalgia, 14 PVFS); of the ME group 226 (19%) had a subsequent diagnosis in a *different* group (61 CFS, 22 fibromyalgia, 143 PVFS); of the fibromyalgia group 74 (8%) had a subsequent diagnosis in a *different* group (12 CFS, 19 ME, 43 PVFS) and of the PVFS group 668 (4%) had a subsequent diagnosis in a *different* group (158 CFS, 391 ME, 119 fibromyalgia).

Table 3 shows the main outcome measures and the overall significance test results. Pair-wise comparisons showed the following differences. For CFS/ME versus PVFS all the outcome measures were significantly different ($P < 0.001$). For CFS/ME versus fibromyalgia, all differences in outcome measures, except length of illness ($P = 0.07$) and number of subsequent fatigue

TABLE 2 Details of patients with the fatigue syndromes and the coding system they appeared under

Group	Total	Number female (%)	Median age (IQR)	Number in Oxmis (%)	Number in Read (%)	Median (IQR) length of records after diagnosis, days
CFS	159	97 (61)	36 (26–47)	0 (0)	159 (2.0)	768 (575–1127)
ME	1200	853 (71)	40 (30–48)	679 (6.6)	521 (6.6)	1768 (1042–2678)
Fibromyalgia	880	685 (78)	47 (38–56)	202 (2.0)	678 (8.6)	971 (634–1441)
PVFS	15883	10428 (66)	39 (27–53)	9355 (91.4)	6528 (82.8)	1823 (1035–2777)
Total	18122	12063 (66)	40 (28–53)	10236	7886	1757 (987–2720)

The difference in length of records across the four diagnoses is significant ($P = 0.001$: Kruskal-Wallis test).

TABLE 3 Comparison of CFS/ME with fibromyalgia and PVFS

Outcome measure	CFS/ME ($n = 1359$)	Fibromyalgia ($n = 880$)	PVFS ($n = 15883$)	Significance
Median (IQR) length of illness in days per year followed	80 (0–242)	51 (0–244)	0 (0–108)	$P = 0.001$
Number (%) with a subsequent fatigue symptom or diagnosis	913 (67.2)	530 (60.2)	6672 (42.0)	$P < 0.001$
Median (IQR) number of subsequent fatigue symptoms or diagnoses per year	0.29 (0–0.78)	0.31 (0–0.89)	0.00 (0–0.29)	$P = 0.001$
Median (IQR) number of primary care consultations per year after diagnosis	6.9 (3.8–11.0)	9.9 (5.7–15.7)	6.0 (3.3–9.9)	$P = 0.001$
Number (%) with a fatigue symptom or diagnosis in months 7–12 after diagnosis	330 (24.3)	677 (23.1)	1610 (10.1)	$P < 0.001$
Median (IQR) number of primary care consultations in months 7–12 after diagnosis	4 (2–8)	5 (3–10)	3 (1–6)	$P < 0.001$
Number (%) with a fatigue symptom in the year <i>before</i> diagnosis ^a	275 (34.9)	67 (8.7)	2258 (19.4)	$P < 0.001$

IQR = interquartile range.

Statistical testing: Chi-squared for measures expressed as a percentage; Kruskal-Wallis for measures expressed as medians.

^a For this measure, only patients with a minimum of one year's records before diagnosis were studied (CFS/ME $n = 788$, fibromyalgia $n = 774$, PVFS $n = 11639$).

TABLE 4 Comparison of CFS and ME using only Read data

Outcome measure	CFS (<i>n</i> = 159)	ME (<i>n</i> = 521)	Significance
Median (IQR) length of illness in days per year followed	33 (0–170)	106 (0–259)	<i>P</i> < 0.001
Number (%) with a subsequent fatigue symptom or diagnosis	92 (57.9)	370 (71.0)	<i>P</i> = 0.002
Median (IQR) number of subsequent fatigue symptoms or diagnoses per year	0.35 (0–0.88)	0.28 (0–0.62)	<i>P</i> = 0.74
Median (IQR) number of primary care consultation per year after diagnosis	5.7 (3.0–10.4)	7.0 (4.1–10.5)	<i>P</i> = 0.02
Number (%) with a fatigue symptom or diagnosis in months 7–12 after diagnosis	35 (22.0)	125 (24.0)	<i>P</i> = 0.61
Median (IQR) number of primary care consultation in months 7–12 after diagnosis	3 (1–7)	4 (2–7)	<i>P</i> = 0.02
Number (%) with a fatigue symptom or diagnosis in the year <i>before</i> diagnosis ^a	54 (42.2)	104 (33.7)	<i>P</i> = 0.09

IQR = interquartile range.

Statistical testing: Chi-squared for measures expressed as a percentage; Mann–Whitney for measures expressed as medians.

^a For this measure, only patients with a minimum of one year's records before diagnosis were studied (CFS *n* = 128, ME *n* = 309).

symptoms or diagnoses per year (*P* = 0.76), were highly significant (*P* < 0.001). Patients with CFS/ME had had significantly more fatigue codes in the year before diagnosis than both PVFS and fibromyalgia.

Table 4 shows the comparison of CFS with ME. For three of the four measures of continuing ill health, ME was significantly worse than CFS. Patients with ME had fewer fatigue codes in the year before diagnosis than CFS, but this was of marginal significance (*P* = 0.09).

Discussion

Summary of main findings

Patients with the different fatigue syndrome labels had different prognoses. PVFS was the label with the best prognosis, followed by fibromyalgia, and then CFS. ME had the worst prognosis of the four. This was the generally the case however we measured outcome. The differences among the labels were both statistically and clinically significant.

Strengths and limitations of study

The first question is whether our results could have arisen because of biases in the methods. Clearly, taking the interval between the initial diagnosis code and the final fatigue symptom code as a proxy for the duration of illness is an oversimplification. Patients may have continuing symptoms which they no longer report to their doctor. Fatigue symptoms are very prevalent in the community, but are much less frequently reported to a doctor.¹⁹ Approximately 1.4–2.5% of patients have a fatigue symptom recorded in their primary care notes

each year.^{20,21} However, there is no reason to expect that the different labels should have induced different patterns of primary care use, or reporting of fatigue. The other potential bias with our using the final symptom code to represent the end of the illness is that patients with longer records would have more opportunity to report a symptom (which may be unrelated to their initial illness). Our use of the length of illness adjusted for the duration of records partially overcame this, with no change in the findings. The results for 7–12 months after diagnosis were free from this possible bias, and are similar to the main findings, so the effect of this bias, if any, was minor.

Label selection

There are several aspects to the choice of a particular label by the GP. Firstly, before Read coding, doctors were unable to use the label of CFS: we cannot know what label they used at that time. Secondly, the patient may have had a particular preference for one of the labels: indeed they may have self-diagnosed their condition before consulting their GP.² Equally, the doctor may have had a preference which might have been influenced by their knowledge of the patient's recent history, although we found no significant difference in premorbid fatigue reporting between CFS and ME. The proportion of patients in this study whose label changed was fairly low (4% to 19%), suggesting that once given a particular label, patients and their doctors stick with it. Some doctors dispute the utility of any of the fatigue syndrome labels, while others have personal preferences for one or other of the labels.²² Finally, there are secular changes—or to put it more

simply, fashions—for particular labels.^{23–26} We cannot know how much any of these factors influenced the choice of label.

Interpretation of the findings

ME had the worst prognosis of the fatigue syndrome labels. The simple explanation that ME is a different illness which carries a poorer prognosis is hard to accept as this would imply that GPs are able to differentiate it from the other conditions. This may be true when comparing ME with PVFS, since ME is by definition a chronic illness, whereas PVFS need not be. But this would not explain the difference between ME and CFS, since both conditions are chronic.

More likely are two competing explanations. The first explanation is that the label itself confers a worse prognosis.²⁷ Giving a disease label can lead to increased illness behaviour, as has been seen with hypertension.²⁸ A study comparing matched fatigued patients found that those who attributed their fatigue to ME had a worse prognosis than patients who attributed their fatigue to psychological or social factors.²⁹ It is possible that the label ME with its suggestion of an untreatable pathological process may somehow render the patient less able to combat their symptoms and disability than other labels. The second explanation is that those who are destined to have a worse prognosis preferentially attract the label ME, perhaps by self-diagnosis. Previous studies have shown that belief in a physical cause for the illness is linked with a worse prognosis. More patients diagnosed with ME believe the illness has a physical cause than those not so labelled.³⁰ It is possible that patients with these beliefs reject the alternative labels in favour of ME, and the GP accepts this.

Significantly more patients with CFS/ME had fatigue symptoms recorded before diagnosis than those with PVFS or fibromyalgia (Table 3). As PVFS has a triggering illness implied in its name this is not surprising. It is likely that the diagnosis of CFS or ME is deferred until the condition has been present for some time: indeed some doctors may be reluctant to give the disease label until six months have passed, as this time period is given in the international research criteria for diagnosis.¹³ However, premorbid illness cannot explain the worse prognosis of ME when compared to CFS, as the premorbid reporting of fatigue was higher in the CFS group, albeit with marginal significance.

PVFS had the best prognosis, with over half of patients making no further complaint of fatigue. It is likely that the simple explanation is the correct one: that fatigue syndromes after a recognisable viral infection have a better prognosis.³¹ Most patients with a fatigue syndrome can identify a triggering event in the months before development of their condition.³² In a prospective primary care study of 'postviral' fatigue the worse prognosis occurred in those with less evidence of an initial viral infection.³³ Our results suggest that the condition may be more benign if the trigger is a definite viral infection.

Fibromyalgia is defined by muscular tenderness and widespread pain rather than fatigue.³ Considering we used fatigue symptoms to identify continuing ill health it is remarkable that the prognosis of fibromyalgia was so poor. Our results are further evidence that fibromyalgia can be included within the rubric of fatigue syndromes.¹ However, fibromyalgia appears different from the other labels in this study, by occurring in individuals on average seven years older, in a higher proportion of women, and in having an intermediate prognosis. The remarkably higher consultation rate after diagnosis with fibromyalgia cannot be explained by the age difference, as female consultation rates change relatively little between the ages of 16 and 74.³⁴

There is considerable debate in the patient and researcher communities about whether fatigue syndromes are essentially one illness with several synonyms, or whether there are distinct subgroups which should be studied separately. This is the first study to show an important difference among the groups. However, caution should be exercised before using this study to strengthen the case for there being distinct subgroups. This is because we cannot be sure which came first: the different prognosis or the different label, although finding no significant difference in recorded fatigue before the diagnosis of CFS and ME suggests the latter interpretation. This can only be answered by a study examining the process by which patients and doctors agree their specific fatigue syndrome labels. The worse prognosis of the label ME needs further investigation.

Acknowledgements

We would like to thank our patients and colleagues, including Michael Sharpe, Nicola Wiles and Pat Mathewson who commented on earlier drafts of the paper.

Declaration

Funding: this study was funded by the Department for Work and Pensions. The research was conducted independently from the funding source. WTH is funded through RCGP/BUPA and NHS Fellowships, and his practice is funded through the NHS R&D General Practice scheme.

Ethical approval: obtained from the Scientific and Ethical Advisory Group of the GPRD.

Conflicts of interest: none.

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