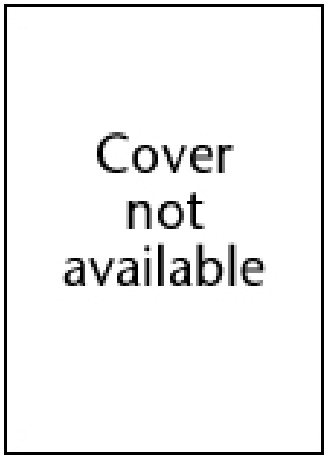

Primary Care & Community Psychiatry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t786314678

The prevalence and associations of unexplained chronic fatigue in Brazilian primary care

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Online Publication Date: 01 January 2007
To cite this Article: Cho, Hyong Jin and Wessely, Simon (2007) 'The prevalence and associations of unexplained chronic fatigue in Brazilian primary care', Primary Care & Community Psychiatry, 12:2, 81 - 87
To link to this article: DOI: 10.1080/17468840701680413
URL: http://dx.doi.org/10.1080/17468840701680413

PRIMARY CARE AND COMMUNITY PSYCHIATRY
VOL. 12, NO. 2, 2007, 81–87

ORIGINAL ARTICLE

The prevalence and associations of unexplained chronic fatigue in Brazilian primary care

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Abstract

Background: Unexplained chronic fatigue (UCF) and chronic fatigue syndrome (CFS) have been reported to be associated with female gender, older age, lower socioeconomic status and psychiatric disorders by previous studies, mostly conducted in Western developed countries. To date, there have been very few studies of UCF/CFS in Brazil.

Aim: We examined the prevalence and associations of UCF in Brazilian primary care. The main question was whether the profile of risk factors for UCF in Brazil is similar to that reported in Western developed countries.

Methods: A cross-sectional survey was conducted at two general practices in São Paulo. 304 consecutive attenders, aged 18–45 years, completed questionnaires on fatigue, psychological distress and socio-demographic characteristics. Those with substantial fatigue lasting 6 months or more were interviewed to ascertain the presence of CFS and psychiatric disorders. Patients suffering from substantial fatigue for 6 months or more with no medical explanation and no psychiatric exclusion diagnoses for CFS were classified as cases of UCF.

Results: The prevalence of UCF and CFS was respectively 10.9% and 1.3%. Psychological distress was significantly correlated with fatigue. Older age, female gender and higher education level were independent risk factors for UCF.

Conclusion: The prevalence of UCF and CFS in Brazilian primary care was comparable to that reported by the previous studies in Western affluent countries. However, while age and gender followed the previously observed pattern of association, an opposite pattern was found regarding education. Possible reasons for this unusual finding were discussed.

***Keywords*: Chronic fatigue syndrome – Primary care – Cross-sectional studies – Socioeconomic factors – Developing countries**

Received: 29 May 2007; *Accepted*: 13 September 2007

Introduction

Chronic fatigue syndrome (CFS) is characterised by severe physical and mental fatigue and fatigability, which cannot be explained by any other medical condition and have persisted for at least 6 months[1]. This main symptom is usually accompanied by disability and other symptoms such as muscle pain, joint pain, sleep disturbance, poor concentration, mood disturbance and headache. Chronic fatigue is defined as self-reported persistent or relapsing fatigue lasting 6 or more consecutive months[2]. Unexplained chronic fatigue (UCF) refers to the medically unexplained subtype of chronic fatigue and is the term of choice throughout this paper. A case of UCF which fails to meet criteria for CFS defines idiopathic chronic fatigue (ICF) and hence UCF encompasses ICF and CFS (Figure 1)[2,3].

The prevalence of UCF/CFS varies widely according to the case definition, method and setting adopted in each study. The prevalence of UCF ranges from 4.2% to 23% in community[4–7]

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ISSN 1746–8841
doi:10.1080/17468840701680413

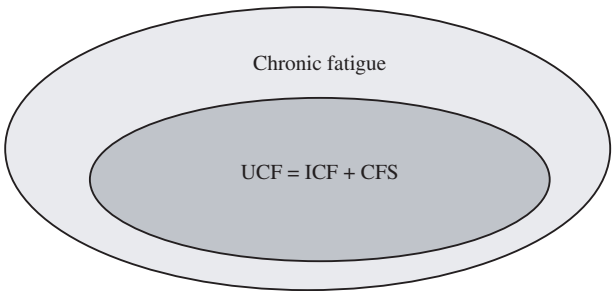

Figure 1. Chronic fatigue, unexplained chronic fatigue (UCF), idiopathic chronic fatigue (ICF) and chronic fatigue syndrome (CFS)

and from 8.4% to 41.2% in primary care[8–12]. Regardless of study setting, the prevalence of CFS ranges from 0.08 to 3.6%[4,7,9,13–16]. However, considering those studies using similar case definitions and methods, the variation is much less: 0.2–1.4% for CFS[4,7,9,15] using the Centers for Disease Control (CDC) 1994 criteria[2] and 8.7–18.3% for UCF[5-7,9,11,17] using the revised Clinical Interview Schedule[11] (CIS-R) or the Chalder Fatigue Questionnaire[18] (CFQ) [note that the CFQ was validated against the CIS-R].

Concerning the epidemiological associations of UCF, female gender has been an important vulnerability factor in most studies not only in healthcare services[19,20], which are usually attended by more women than men, but also in population-based research[6], which is not influenced by gender biases in help-seeking behaviour. Being female was associated with high likelihood of UCF even after adjusting for underlying psychological disorder[9]. Older age was also associated with UCF[5,11,14]. Despite the impression that higher socioeconomic status (SES) was associated with UCF created by studies from the specialist settings, most primary care and population-based studies have consistently shown an association with lower SES[12,21]. Another consistent and strong association reported is with presence of psychiatric disorders although the direction of causality is still a subject of debate[5,22–24]. Although a lot fewer studies have investigated the epidemiological associations of CFS, the overall pattern appears to repeat that of UCF regarding gender, age and SES [4,15] and also regarding psychiatric disorders[25].

To date, there have been very few studies of UCF/CFS in Brazil[17,26,27]. We have previously published a validation study of the CFQ in Brazilian primary care[28]. We now report on the prevalence and the epidemiological associations of UCF, a subsyndromal counterpart to CFS, using the data derived from the same study. The main question was whether the profile of risk factors for UCF in Brazil is similar to that reported in Western developed countries.

Methods

Subjects

The study comprised 304 consecutive attenders, aged 18-45 years, at two general practices – one public clinic and one private clinic – in southwest São Paulo. The age range was deliberately restricted in an attempt to reduce the likelihood of misdiagnosing medically explained fatigue as unexplained because medical disorders that cause fatigue such as anaemia, diabetes mellitus and hypothyroidism are much more prevalent in older age groups[29]. In order to comprise different social classes in proportion to the national census data in São Paulo[30], 30% of the sample was recruited from a private clinic. Ethical approval was obtained from the ethical committees of Municipal Department of Health of São Paulo and University of São Paulo Medical School.

Procedure

After signing an informed consent, the participants completed the CFQ, the 12-item General Health Questionnaire (GHQ-12)[31] and questions on sociodemographic characteristics – age, gender, skin colour, marital status, country of birth, state of birth, years of education, employment status, occupation, household income, number of household members, number of rooms in house, household appliances and number of medical consultations in last 6 months. Self-reported skin colour is the variable of race/ethnicity officially used in the Brazilian Census and considered to best reflect the Brazilian reality despite its limitations[32]. Household crowdedness – calculated as the number of household members divided by the number of rooms in a house – and number of household appliances are proxy measures of SES frequently used in developing countries[33,34]. The questionnaires were read out to the illiterate and functionally illiterate participants. Fatigue status including severity and duration was assessed with the CFQ, which classifies a score of four or more as substantial fatigue using bimodal scoring system[18,28]. The questionnaire also contains an open-ended question on causal attribution of fatigue (*Why do you think you are feeling tired? Please try to give one reason.*). Those patients with a score of four or more *and* a reported duration of 6 months or greater went through an interview with a psychiatrist (H.J.C.) and their medical records were systematically reviewed. The interview was conducted for the diagnosis of CFS and psychiatric disorders. Additional questions regarding the awareness of CFS, sick leave due to CFS and membership of a self-help organisation were also asked. For the diagnosis of CFS, it was

assessed whether the patients met the CDC-1994 criteria[2] and/or the Oxford criteria[35]. The diagnosis of psychiatric disorders was made using the Primary Care Evaluation of Mental Disorders (PRIME-MD)[36]. Those with no medical explanation and no psychiatric exclusion diagnoses for CFS were classified as cases of UCF. The GHQ-12[31] – previously validated in Brazilian primary care [37] – was used to assess psychological distress over the past few weeks. Those who scored four or more by the bimodal scoring system were classified as cases of common mental disorder (CMD).

Analysis

Stata Version 9.1[38] was employed for all the statistical analyses and the significance level was set at $P \leq 0.05$. The prevalence of UCF and CFS was calculated with 95% confidence intervals (CIs). Logistic regression was used to quantify the effect of the exposure variables (clinic type, age, gender, self-reported skin colour, marital status, education, employment status, occupation, income per capita, household crowdedness and number of household appliances) on the main outcome variable, UCF. Univariate and multivariate analyses were conducted. All variables for which the association reached significance at $P \leq 0.10$ in univariate analysis according to likelihood ratio tests were included and kept in the multivariate model, using backward fitting. Possible interactions were also checked. Additionally, after obtaining the final multivariate model, the effect of the independent risk factors was adjusted for CMD as measured by GHQ-12. For the purpose of comparison, the effect of the same exposure variables on the secondary outcome variable, CMD, was also measured. Finally, Pearson product-moment correlations of the following pairs were estimated: 1) fatigue (CFQ score) versus psychological distress (GHQ-12 score) and 2) fatigue versus service use (reported number of medical consultations in last 6 months).

Results

The study sample ($n = 304$) was relatively young (mean age 31.0 years, standard deviation [SD] 8.1) given the age restriction of the recruitment strategy, and there were much more women (80.6%) than men. While 59.5% of the sample was married or cohabiting, 30.9% were single and 9.5% were separated, divorced or widowed. The mean education time was 9.7 years (SD 4.5). The mean CFQ and GHQ-12 scores using Likert system were respectively 11.5 (SD 6.5, range 0–33) and 12.5 (SD 7.8, range 0–35).

Table 1. Prevalence of unexplained chronic fatigue (UCF) and chronic fatigue syndrome (CFS) among 304 consecutive primary care attenders

Criteria	No. of subjects	Prevalence% (95% CI)
UCF	33	10.9 (7.6–14.9)
UCF without psychiatric comorbidity	10	3.3 (1.6–6.0)
CFS by CDC-1994 criteria	4	1.3 (0.4–3.3)
CFS by Oxford criteria	3	1.0 (0.2–2.9)

Table 2. Severity of fatigue and psychological distress of 116 participants with substantial fatigue* according to causal attribution of fatigue

Attribution	N (%)	Fatigue† (95% CI)	Psychological distress‡ (95% CI)
Normalising	68 (58.6)	17.1 (16.2–18.1)	17.2 (15.6–18.8)
Psychological	13 (11.2)	22.2 (18.5–25.9)	22.3 (18.3–26.3)
Physical	28 (24.2)	17.4 (15.2–19.6)	17.7 (14.1–21.2)
Other	7 (6.0)	15.0 (11.5–18.5)	15.9 (7.6–24.2)
Total	116 (100.0)	17.7 (16.7–18.6)	17.8 (16.4–19.2)

*CFQ $\geq$ 4 using bimodal scoring system.
†Mean score of the CFQ using Likert scoring system.
‡Mean score of the GHQ-12 using Likert scoring system.

Of 116 patients who had a score above the cut-off for substantial fatigue (CFQ$\geq$4), 35 reported duration of 6 months or more. However, two of them had a medical cause to explain their fatigue. Hence, the prevalence of UCF was estimated to be 10.9% (Table 1). 23 out of 33 UCF patients had at least one psychiatric disorder according to the PRIME-MD, hence the prevalence of UCF without any comorbid psychiatric disorder was 3.3%. Four patients (1.3%) met the CDC-1994 criteria[2] for CFS and three patients (1.0%) met the Oxford criteria[35]. Of 116 fatigued patients, 59% had normalising attributions (e.g. physical activities, fostering children, stress and overworking), 24% attributed their fatigue to physical causes and 11% to emotional problems (Table 2). Those with psychological attributions had substantially higher fatigue and psychological distress score than those with normalising or physical attributions. Table 3 compares the proportion of those making physical attributions in the current study with previous primary care studies from Western affluent countries (see Discussion). For the 33 patients with UCF, 61%, 21% and 18% respectively presented normalising, psychological and physical attributions; only 3 had ever heard of or read about CFS and none had ever had a sick leave due to CFS or been a member of a self-help organisation.

Table 3. Proportion of patients making physical attributions of fatigue compared with previous primary care studies

Study (reference)	Proportion	Country	Inclusion criteria
Current study 2007	24%	Brazil	Currently fatigued according to a fatigue questionnaire
David et al 1990[19]	49%*	UK	Currently fatigued according to a fatigue questionnaire
Kirk et al 1990[41]	52%	USA	Complaining of fatigue as a main or important problem, lasting 1 month or more
Ridsdale et al 1999[42]	67%*	UK	Complaining of fatigue as a main or important problem, lasting 2 weeks or more
Ridsdale et al 2001[43]	51%*	UK	Complaining of fatigue as a main or important problem, lasting 3 months or more
Darbishire et al 2003[44]	46%*	UK	Complaining of fatigue as a main or important problem, lasting 6 months or more
Andrea et al 2003[45]	42%	Netherlands	Fatigue related visit to the general practitioner

* These proportions were recalculated based on the reported data in order to produce more comparable figures across the studies.

In the univariate analysis, higher education level, non-manual occupation, older age, attending a private clinic, female gender, higher number of household appliances and lower household crowdedness were significantly or marginally significantly associated with UCF (arranged here in descending order of association strength according to likelihood ratio tests; Table 4). Before starting the multivariate analysis, possible colinearity between the socioeconomic variables – all the aforementioned variables except age and gender – was checked and the correlation coefficients were not high enough to consider any colinearity. Hence, the initial model included all the seven variables above according to the backward fitting. The final multivariate model included age, gender and education (Table 5). Interactions between education and age and between education and gender were not important. The oldest age group was about four times more likely to suffer from UCF than the youngest age group (odds ratio [OR] 4.10, 95% CI 1.41–11.91) whilst women were approximately five times more likely to suffer (OR 5.17, 95% CI 1.17–22.89). Interestingly, the higher the education level, the higher was the risk of UCF. The patients with higher (i.e. post-secondary) education were about five times more likely to suffer from UCF (OR 4.97, 95%CI 1.82–13.61) than those with primary education, which was opposite to the pattern usually observed in previous studies[39]. When adjusted for CMD, female gender was no longer significantly associated with UCF (OR 3.62, 95% CI 0.80–16.40), but the ORs for higher education and highest age group were unaffected (respectively 4.92, 95% CI 1.74–13.92 and 4.12, 95% CI 1.37–12.32).

Finally, both following pairs of variables were significantly correlated: 1) fatigue versus psychological distress ($r = 0.66$, 95% CI 0.60–0.72, $P < 0.0001$) and 2) fatigue versus service use ($r = 0.26$, 95% CI 0.15–0.36, $P < 0.0001$).

Discussion

UCF is common in Brazilian primary care. The current study used a similar design to previous British primary care studies and the prevalence (10.9%) was similar to their estimates (11.3% in Wessely et al[9] and 11.2% in McDonald et al[8]). When comorbid psychiatric disorders were excluded, the prevalence fell to 3.3% (compared to 4.1% in Wessely et al[9]). As expected, CFS was less common: 1.3% according to the CDC-1994 criteria and 1.0% according to the Oxford criteria, which were again comparable to the British estimates, respectively 2.6% and 2.2% in the study of Wessely and colleagues[9]. The prevalence of both UCF and CFS was also within the range described in the Introduction.

Fatigue and psychological distress were closely correlated as observed in numerous previous studies[6,40]. Fatigue was also significantly correlated with health service use. Medically unexplained fatigue has been consistently associated with increased health service use[5,9,20,24] and Brazilian primary care was no exception regarding this relationship. This finding, in conjunction with the relatively high prevalence of UCF, emphasises the importance of the topic in the Brazilian healthcare system.

Concerning causal attributions of fatigue, a direct comparison with previous studies is difficult due to the difference in study design, but overall, the proportion of physical attribution observed in the current study was substantially lower than in previous primary care studies conducted in Western affluent countries (Table 3)[19,41–45]. The most important methodological difference between the studies presented in Table 3 is the inclusion criteria to estimate the proportions of those making physical attributions, and this should be taken into account. The current study also showed that patients making psychological attributions were significantly

Table 4. Associations between unexplained chronic fatigue and characteristics of 304 consecutive primary care attenders according to univarite logistic regressions

Variable	Category	Cases N (%)	Total N	OR	95% CI	*P*-value*
Clinic type	Public	17 (8.0)	212	1		0.02
	Private	16 (17.4)	92	2.41	1.16–5.02	
Age	18 to 25	5 (5.3)	95	1		0.02
(years)	26 to 35	10 (9.4)	107	1.86	0.61–5.64	
	36 to 45	18 (17.7)	102	3.86	1.37–10.85	
Gender	Male	2 (3.4)	59	1		0.02
	Female	31 (12.7)	245	4.13	0.96–17.77	
Self-reported	White	18 (11.7)	154	1		0.87
skin colour	Yellow	1 (12.5)	8	1.08	0.13–9.29	
	Brown	10 (11.1)	90	0.94	0.42–2.15	
	Black	4 (7.7)	52	0.63	0.20–1.95	
Marital status	Married + Cohabit	19 (10.5)	181	1		0.54
	Single	9 (9.6)	94	0.90	0.39–2.08	
	Sep + Div + Wid	5 (17.2)	29	1.78	0.61–5.20	
Education	Primary	7 (6.0)	116	1		0.007
	Secondary	12 (9.7)	124	1.67	0.63–4.40	
	Higher	14 (21.9)	64	4.36	1.66–11.47	
Employment	Student + HM	5 (7.7)	65	1		0.56
Status	Employed	22 (12.8)	172	1.76	0.64–4.86	
	Unemployed	5 (8.2)	61	1.07	0.29–3.90	
	Leave + Retired	1 (16.7)	6	2.40	0.23–24.74	
Occupation	Non-manual	17 (19.3)	88	1		0.007
	Manual	12 (6.4)	187	0.29	0.13–0.63	
	Never worked	4 (13.8)	29	0.67	0.21–2.18	
Income	Up to 150	7 (6.2)	113	1		0.11
per capita (R$)	Up to 330	11 (12.8)	86	2.22	0.82–5.99	
	More than 330	15 (14.3)	105	2.52	0.99–6.46	
Crowdedness	<0.8	16 (15.4)	104	1		0.10
(person/room)	<1.3	11 (10.8)	102	0.66	0.29–1.51	
	≥1.3	6 (6.1)	98	0.36	0.13–0.96	
No. of	4 to 8	10 (9.6)	104	1		0.03
household	9 to 11	8 (6.6)	121	0.67	0.25–1.75	
Appliances	12 to 16	15 (19.0)	79	2.20	0.93–5.21	

Sep = Separated, Div = Divorced, Wid = Widowed, HM = Homemaker, R$ = Real (Brazilian currency)
**P*-value from likelihood ratio test

Table 5. Associations between unexplained chronic fatigue and characteristics of 304 consecutive primary care attenders according to multivariate logistic regressions

Variable	Category	Adjusted OR*	95% CI	*P*-value†
Age (years)	18 to 25	1		0.02
	26 to 35	2.54	0.80–8.01	
	36 to 45	4.10	1.41–11.91	
Gender	Male	1		0.008
	Female	5.17	1.17–22.89	
Education	Primary	1		0.005
	Secondary	2.03	0.74–5.50	
	Higher	4.97	1.82–13.61	

*Adjusted for age, gender and education.
†*P*-value from likelihood ratio test.

more fatigued and psychologically distressed than those with normalising or physical attributions. Whilst this replicates the findings of two recent studies[45,46], two more dated studies correlated physical attribution with higher fatigue severity[6,19]. It has been suggested that people with more severe fatigue are more likely to make a physical attribution for their fatigue[46]. Moreover, prospective studies of CFS have reported physical attribution to be a predictor of poor outcome[47]. However, at least concerning fatigue as a non-specific symptom in community and primary care population, it is possible that people who attribute their fatigue to psychological causes may be experiencing higher levels of distress and they communicate their distress reporting higher levels of both psychological symptoms and fatigue[46]. This hypothesis also seems to concur with the aforementioned high correlation between fatigue and psychological distress[6,40]. The low awareness of CFS and the absence of either sick leave due to CFS or self-help group membership among the UCF patients may reflect the fact that CFS is a little known condition in Brazil[27].

Older age, female gender and higher education level were shown to be independent risk factors

for UCF. The finding that older age and female gender are associated with UCF is not surprising, but more intriguing is the association between higher education level and UCF because in previous studies the opposite has been true[39].

With regard to the possible reasons for this unusual pattern of association, the methodological issues should be first considered. The sample size of the current study was relatively small and statistical power could be a problem, which, however, seems unlikely given the magnitude of the effect sizes. Another point against the possibility of this association being a mere chance or spurious finding is that the other socioeconomic variables also presented a similar pattern at least in the univariate analysis (attending a private clinic, non-manual occupation and lower crowdedness were significantly associated with UCF). Nevertheless, it is harder to exclude the possibility of bias. We did attempt to reduce selection bias by reproducing the distribution of social classes in São Paulo. 30.3% of the sample came from a private clinic, which would be unusual for a UK study but reflects the nature of health care in São Paulo, where approximately 30% of the population are covered by private or institutional health insurance services. However, the fact that the study participants were recruited from only two general practices in a non-random mode (i.e. recruitment of consecutive attenders) might still have led to a selection bias. Against this are the findings on CMD, which were in keeping with the literature (data available from the authors on request).

While a few community and primary care studies have reported a lack of association between education and UCF[5,7,48], we found one study from South Korea reporting a significant association between higher educational qualification and UCF[14]. The authors wrote: ''These results may be due to the different perception of fatigue, which is a subjective symptom, but further epidemiological research is needed in Korea.'' Given that the Korean as well as the Brazilian sociocultural environment is certainly different from Western affluent countries such as the UK and the US, perhaps different sociocultural settings could lead local people to experience and view fatigue, an essentially subjective symptom, in different manners. For example, in response to a same vignette describing everyday fatigue, European American women were more likely than their South Asian counterparts to medicalise fatigue symptoms and view them as a severe and long-term condition in need of treatment[49]. Furthermore, it is also possible that higher education level may be associated with a more westernised world view in such countries as Brazil and South Korea and consequently with more chronic and severe fatigue. However, the current study can only generate this hypothesis and further studies are required to replicate this finding in Brazil and investigate the possible reasons.

In conclusion, the prevalence of UCF/CFS and the associations of age, gender and psychological distress with UCF were comparable to those reported in the literature and in Western affluent countries. However, the causal attribution of fatigue and the association between education and UCF presented some distinctive features.

Conflict of interest: none

Acknowledgement

Dr Cho received a scholarship from the Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). Prof Paulo Rossi Menezes, Prof Célia Maria Sivalli Campos, Ms Milena Oshiro and Mr Arthur Rovida are thankfully acknowledged for their valuable contribution to the study. The authors are also grateful to the doctors, staff and patients of UBAS-Hospital Universitário da Universidade de São Paulo and UBS Jardim Boa Vista, specially to Ms Ana Lúcia Mendes Lopes, Ms Marina Hideko Anabuki and Dr Maria da Glória Pereira de Castro Casanova.

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