

Cross-cultural differences in the epidemiology of unexplained fatigue syndromes in primary care

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Background Unexplained fatigue has been extensively studied but most of the samples used were from Western countries.

Aims To present international data on the prevalence of unexplained fatigue and fatigue as a presenting complaint in primary care.

Method Secondary analysis of the World Health Organization study of psychological problems in general health care. A total of 5438 primary care attenders from 14 countries were assessed with the Composite International Diagnostic Interview.

Results The prevalence of unexplained fatigue of 1-month duration differed across centres, with a range between 2.26 (95% CI 1.17–4.33) and 15.05 (95% CI 10.85–20.49). Subjects from more-developed countries were more likely to report unexplained fatigue but less likely to present with fatigue to physicians compared with subjects from less developed countries.

Conclusions In less-developed countries fatigue might be an indicator of unmet psychiatric need, but in more-developed countries it is probably a symbol of psychosocial distress.

Declaration of interest None.

Various studies have shown that unexplained fatigue syndromes are common conditions in both the community (Walker *et al*, 1993; Steele *et al*, 1998; Skapinakis *et al*, 2000) and primary care (Bates *et al*, 1993; McDonald *et al*, 1993; Hickie *et al*, 1996; Wessely *et al*, 1997). Fatigue is also common as a presenting complaint to primary care physicians (Cathebras *et al*, 1992; Fuhrer & Wessely, 1995). The majority of the studies, however, were carried out in well-developed countries. Data from less-developed countries are relatively sparse. The present paper aims to report the cross-cultural differences in the prevalence of fatigue syndromes, using data from the World Health Organization (WHO) international study of psychological problems in general health care carried out in 14 countries (Sartorius *et al*, 1993). We also examine the hypothesis that individuals from well-developed countries will be more likely to report fatigue compared with subjects from less-developed countries.

METHODS

General description of the data-set

The WHO collaborative study of psychological problems in general health care was an international prospective study carried out in 15 centres from 14 countries that examined the prevalence, 1-year outcome and public health implications of common mental disorders in primary care (Sartorius *et al*, 1993). Details on the methods of the study are given elsewhere (Von Korff & Üstün, 1995). Briefly, the study used a two-phase design in which 26 969 primary care attenders aged between 18 and 64 years were approached in each participating centre and asked to complete the 12-item general health questionnaire (GHQ-12; Goldberg & Williams, 1988). A total of 25 916 subjects agreed to participate (96% response rate, range across centres from 91% to 100%). Patients were

selected for the second phase assessment using a stratified random sampling procedure according to site-specific GHQ-12 thresholds (100% of the subjects scoring above the 80th percentile, 35% of those scoring between the 60th and 80th percentile and 10% of those scoring below the 60th percentile). The second phase assessment included the Composite International Diagnostic Interview (CIDI; Wittchen *et al*, 1991) modified for use in primary care and involved 5438 out of 8698 eligible subjects (62% response rate, range from 43% to 99%). Data collection took place between May 1991 and April 1992.

In a previous paper we reported the overall prevalence of unexplained fatigue syndromes and their association with psychiatric disorders (Skapinakis *et al*, 2003), whereas in this paper we focus on the differences between centres.

Measures

The CIDI is a fully structured interview developed for use in cross-cultural psychiatric epidemiology studies (Wittchen *et al*, 1991). The modified version used in the present study includes only the sections that assess mental symptoms common in primary care, notably the sections on somatisation, anxiety, depression and hypochondriasis, as well as a new section on neurasthenia. The primary care version rates both current (1-month) and life-time symptomatology. Non-English-speaking participating centres translated and back-translated the interview. Training and procedures for assuring reliability are described elsewhere (Von Korff & Üstün, 1995). The interviewer-observer reliability coefficient for the primary care version of CIDI was found to be 0.92 overall, ranging between 0.81 and 1.00 for individual sections.

Measurement of fatigue: substantial unexplained fatigue

Fatigue was assessed using the neurasthenia section of the primary care version of the CIDI. Three screening questions were put to all subjects: Q1 'In the past month have you felt tired all the time?'; Q2 'Do you get easily tired while performing everyday tasks?'; and Q3 'Does even minimal physical effort cause exhaustion?' Then the interviewer asked a specific sequence of questions to determine the clinical importance and possible cause of the symptom. Fatigue was considered 'medically explained' if a doctor had given the

patient a definite diagnosis or if there had been any abnormalities reported on examination or further investigation. Subjects with medically unexplained fatigue were also asked a fourth question that assessed the severity of fatigue: Q4 'Is it difficult to recover from these periods of fatigue or exhaustion when you rest?'

Subjects with medically unexplained fatigue (at least one positive answer to questions Q1–Q3) who answered positively to question Q4 were classified as cases of substantial unexplained fatigue. In comparison with the ICD–10 definition of neurasthenia (World Health Organization, 1998), our definition of unexplained fatigue differs in that: it does not include the multiple somatic symptoms criterion (Criterion B in ICD–10); it refers to 1-month duration instead of 3 (Criterion D in ICD–10); and, it does not exclude other comorbid psychiatric disorders (Criterion E in ICD–10). Therefore, it is a much broader definition compared with ICD–10 neurasthenia.

Fatigue as the main reason for consultation

The above definition of fatigue is independent of whether the subjects complained of fatigue to their primary care physician. For comparison, we also report the prevalence of fatigue as a presenting complaint. Subjects were asked to report the three main reasons for their consultation, choosing from a list of symptoms. Those who reported weakness or lethargy (the only items in the list related to fatigue) as one of their main reasons for consultation were considered as having fatigue as a presenting complaint.

Measurement of morbidity

Psychiatric morbidity was assessed with the CIDI. Diagnostic algorithms were developed to give diagnoses according to the ICD–10 criteria. For the purposes of the present study, subjects were classified as cases of psychiatric morbidity if they had any of the following current ICD–10 disorders: depressive disorders (including dysthymia); generalised anxiety disorder; agoraphobia; panic disorder; somatisation disorder; and hypochondriasis.

Chronic physical morbidity was assessed by asking patients whether they were suffering from a list of common chronic medical conditions. Patients were classified as cases of chronic physical morbidity if

they were suffering from at least one chronic physical disorder.

Classification of primary care centres

Centres were entered into the analysis as dummy variables. However, for the economic development hypothesis, centres were classified into three categories according to the gross national income (GNI) per head in 2000 as follows: high-income countries, with more than US\$10 000 GNI per head (Athens, Berlin, Groningen, Mainz, Manchester, Nagasaki, Paris, Seattle, Verona); middle-income countries, with less than US\$10 000 but more than US\$1000 (Ankara, Rio de Janeiro, Santiago); and low-income countries, with less than US\$1000 (Bangalore, Ibadan, Shanghai). Data for the GNI per head were derived from the World Bank databases available on the internet (World Bank, 2000).

Analysis

All data analyses were conducted using Stata version 6.0 (Stata Corporation, 1999). The weighted prevalence with 95% confidence intervals of fatigue syndromes was estimated using the SVYPROP command. This command allows for sampling weights and is suitable for the analysis of the two-phase design of the study (Dunn *et al*, 1999). The association of GNI per head with fatigue was analysed by means of a series of logistic regression models (separately for each fatigue syndrome) using the SVYLOGIT command in Stata. We used fatigue case status (Yes–No) as the dependent variable, and the classification of centres according to GNI as the independent variable, adjusting for socio-demographic variables, psychiatric morbidity and physical morbidity. Odds ratios (with 95% CIs) of fatigue were calculated for each category of the GNI variable. Psychiatric and physical morbidity were entered into the models as binary variables. In all the analyses we used sampling weights.

RESULTS

Description of the sample

The sample at the baseline assessment ($n=5438$) was predominantly female (62%), 58% of the participants were older than 35 years, 62.1% were married, 57.4% had basic education and 58.7% were employed. As expected, socio-demographic

characteristics differed significantly between centres, reflecting the diverse cultures that are represented in this data-set.

Prevalence of fatigue syndromes

Table 1 shows the prevalence of substantial unexplained fatigue and fatigue as a presenting complaint across centres.

Prevalence of substantial unexplained fatigue differed fifteen-fold across primary care centres ($P<0.001$). Centres with high prevalence of substantial unexplained fatigue ($>10\%$) were Manchester, Santiago, Berlin, Groningen, Paris and Mainz, and centres with low prevalence ($<4\%$) were Bangalore, Shanghai, Seattle, Verona and Ibadan.

Fatigue as a presenting complaint (either weakness or lethargy) was reported by 6.27% of the subjects (95% CI 5.47–7.18) with wide variation across centres. Centres with high prevalence of fatigue as a presenting complaint ($>10\%$) were Bangalore, Ibadan, Nagasaki, Ankara and Paris, whereas centres with low prevalence ($<2\%$) were Manchester, Seattle, Mainz and Verona.

In the whole data-set, very few subjects with substantial unexplained fatigue presented with fatigue (11%; 95% CI 8.21–14.57).

Association with level of economic development

In the logistic regression analysis, unexplained fatigue was associated positively with GNI per head after adjustment for all other socio-demographic variables, psychiatric morbidity and chronic physical morbidity. High-income countries had an odds ratio of 2.62 (95% CI 1.67–4.11) compared with low-income countries (Table 2).

In contrast, fatigue as a presenting complaint was associated negatively with GNI per head, and subjects from higher-income countries had an odds ratio of 0.38 (95% CI 0.25–0.58) compared with subjects from lower income countries.

DISCUSSION

In this multi-national study in primary care, we found that unexplained fatigue was present in all cultures but the prevalence varied widely. Subjects from higher-income countries were more likely to report fatigue in response to direct questions compared

Table 1 Prevalence of substantial unexplained fatigue and fatigue as a presenting complaint in international primary care (n=5438)

Centre ¹ (Response rate) ²	Unweighted number of cases/Total number interviewed Weighted prevalence % (95% CI)	
	Substantial unexplained fatigue ³	Fatigue as a presenting complaint ⁴
Manchester (71%)	115/428 15.05 (10.85–20.49)	2/428 0.19 (0–0.76)
Santiago (46%)	61/274 12.86 (8.41–19.18)	3/274 2.17 (0.47–9.52)
Berlin (43%)	70/400 12.53 (8.77–17.6)	19/400 3.13 (1.81–5.36)
Groningen (69%)	78/340 11.75 (8.48–16.05)	26/340 6.90 (3.71–12.50)
Paris (62%)	69/405 10.89 (7.74–15.11)	59/405 10.35 (7.35–14.38)
Mainz (37%)	56/400 9.91 (7.27–13.38)	4/400 1.01 (0.31–3.22)
Nagasaki (74%)	37/336 8.05 (5.08–12.54)	62/336 10.87 (7.74–15.06)
Athens (43%)	22/196 8.00 (4.29–14.45)	4/196 3.79 (1.14–11.85)
Ankara (97%)	47/400 7.99 (5.11–12.28)	46/400 10.64 (6.94–15.97)
Rio de Janeiro (46%)	50/393 6.71 (4.30–10.33)	14/393 3.83 (1.69–8.45)
Bangalore (83%)	30/398 3.83 (2.46–5.91)	95/398 17.12 (13.18–21.94)
Shanghai (99%)	44/576 3.63 (2.34–5.59)	47/576 5.98 (3.83–9.20)
Seattle (61%)	26/373 3.37 (1.90–5.90)	3/373 0.25 (0–0.78)
Verona (55%)	18/250 2.34 (1.41–3.86)	7/250 1.84 (0.54–6.06)
Ibadan (88%)	11/269 2.26 (1.17–4.33)	47/269 16.09 (11.03–22.88)
All centres (63%)	734/5438 7.99 (7.13–8.85)	438/5438 6.27 (5.47–7.18)
	$\chi^2=6.64, d.f.=14, P < 0.001$	$\chi^2=10.51, d.f.=14, P < 0.001$

1. Centres arranged in rank order of substantial unexplained fatigue.
 2. Response rate at the second phase of the study.
 3. Elicited by diagnostic interview. See methods for definition.
 4. Subjects presented to the primary care physician with weakness or lethargy.

with subjects from lower-income countries. In contrast, subjects in higher-income countries were less likely to complain to their doctors of fatigue than those in poorer countries.

Limitations and strengths

These results should be interpreted in the context of the following limitations. First,

this is a study carried out in primary care and therefore the results cannot be generalised to the general population. Second, response rates for the second phase baseline assessment were below 50% for five centres. Therefore, a systematic bias in either direction cannot be ruled out, even though participation was not related significantly to age, gender or screening GHQ-12 score. Third, although CIDI has been developed

for use in cross-cultural epidemiological research, this does not prove its cultural validity. Fourth, medical causes of fatigue were excluded in a crude way by asking patients if a doctor had given them a definite diagnosis for their symptom or if there had been any abnormalities reported on examination or further investigation.

Despite these limitations our study had the advantage of investigating fatigue in a large multicultural sample using the same methodology. We are not aware of any other studies that used such a culturally diverse sample. The present research was therefore able to study fatigue independently of the confounding effect of the sociocultural context.

Prevalence of fatigue syndromes across centres

The prevalence of substantial unexplained fatigue differed significantly across centres, with an average prevalence of 7.99% (95% CI 7.13–8.85) in primary care but with a range between 2.26 and 15.05 in different countries.

The prevalence estimates reported from studies carried out in Western countries are generally consistent with the estimates provided here for similar countries. For example, Buchwald *et al* (1987) found a prevalence of unexplained chronic fatigue of 21% in an American primary care centre. In Australia, 24% of the primary care attenders reported substantial unexplained fatigue (Hickie *et al*, 1996), whereas in Canada 14% reported this (Cathebras *et al*, 1992). In UK primary care the prevalence of unexplained fatigue has been found to be approximately 10% (David *et al*, 1990; Wessely *et al*, 1997). By contrast, studies from the more-developed countries that used more culturally heterogeneous samples reported lower prevalence rates compared with the rates mentioned previously, for example 2% in a multi-racial sample in San Francisco (Steele *et al*, 1998) and 6.4% in a study of Chinese-Americans in Los Angeles (Zheng *et al*, 1997). In the present study we also observed lower rates of fatigue in Asian countries.

Differences in the prevalence

In order to explain the reported differences in the prevalence of unexplained fatigue we examined whether economic factors at the aggregate level influence rates of fatigue. The classification of centres according to

Table 2 Association of gross national income (GNI) per head and substantial unexplained fatigue or fatigue as a presenting complaint in international primary care

GNI per head ²	Unweighted number of cases/Total number interviewed Odds ratios (95% CI) ¹	
	Substantial unexplained fatigue ³	Fatigue as presenting complaint ⁴
Low income	85/1243 1.00 (reference)	189/1243 1.00 (reference)
Middle income	158/1067 1.67 (1.04–2.66)	63/1067 0.39 (0.23–0.68)
High income	491/3128 2.62 (1.67–4.11)	186/3128 0.38 (0.25–0.58)

1. Odds ratios adjusted for all socio-demographic variables, psychiatric morbidity and chronic physical morbidity.

2. Primary care centres were classified according to GNI per head. See methods for included centres.

3. Elicited by diagnostic interview. See methods for definition.

4. Subjects presented to the primary care physician with weakness or lethargy.

the GNI per head for the country of location showed that subjects coming from middle- or high-income countries were more likely to report substantial unexplained fatigue compared with subjects from low-income countries. Therefore, there is an indication that economic development might influence the reporting of unexplained fatigue. It is worth noting that this pattern was not found when similar analyses were carried out for other unexplained somatic symptoms such as pain, headache, dizziness, excessive flatulence and palpitations (data on file). These symptoms, unlike fatigue, tended to be less prevalent in higher-income countries. Therefore, this finding cannot be attributed to a general tendency for unexplained functional symptoms to be reported more commonly in well-developed countries.

This is a difficult finding to interpret because economic development might be associated with many other (confounding) variables such as organisation of primary health care or local diagnostic preferences. To find out whether a similar pattern is observed for primary care patients, who presented to primary care physicians with complaints of weakness or lethargy ('presenting fatigue'), we carried out a similar analysis with the presenting complaint of fatigue as the dependent variable. This showed a very different picture; subjects from high- or middle-income countries were less likely to present with fatigue compared with those from low-income countries.

Past research in developed countries, in both the community and primary care, has

shown that subjects with fatigue usually attribute their symptoms to psychosocial causes. For example, in a community study in the UK almost half of the subjects attributed fatigue to psychosocial causes such as work, family and lifestyle (Pawlikowska *et al*, 1994) and similar findings have been reported in primary care (David *et al*, 1990). If psychosocial explanations are prevalent then it seems reasonable that fatigue will not be a presenting complaint in primary care in developed countries. In that case, fatigue is more of a social 'metaphor' rather than a legitimate or useful medical complaint (Lee & Wong, 1995). By contrast, in less-developed countries a somatic presentation might ensure an appropriate medical examination. This reminds us of the process of 'facultative somatisation' described by Goldberg & Bridges (1988) where patients present with somatic symptoms as a 'ticket of admission' to the primary care clinic. Simon *et al* (1999) have reported a similar finding in their study of the relation between somatic symptoms and depression. Analysing the same dataset used in the present study, they found that a somatic presentation of depression was more common at centres where patients lacked an ongoing relationship with a primary care physician. All the centres from low-income countries and most of the centres from middle-income countries were of this type.

Given the strong association of psychiatric disorders with fatigue (Skapinakis *et al*, 2000), we think that this finding might have important clinical implications. In less-developed countries, the complaint

of fatigue might be an indicator of hidden psychiatric morbidity. By contrast, in more-developed countries, although syndromes of fatigue are common, they should not be always considered as evidence of unmet need as they might represent a common expression of psychosocial distress.

ACKNOWLEDGEMENTS

The data reported in this article were collected as part of a World Health Organization's Psychological Problems in General Health Care project. Participating investigators include: O. Ozturk and M. Rezaki (Ankara, Turkey); C. Stefanis and V. Mavreas (Athens, Greece); S. M. Channabasavana and T. G. Sriram (Bangalore, India); H. Helmchen and M. Linden (Berlin, Germany); W. van der Brink and B. Tiemens (Groningen, The Netherlands); M. Olatawura and O. Gureye (Ibadan, Nigeria); O. Benkert and W. Maier (Mainz, Germany); R. Gater and S. Kisely (Manchester, UK); Y. Nakane and S. Michitsuji (Nagasaki, Japan); Y. Lecrubier and P. Boyer (Paris, France); J. Costa e Silva and L. Villano (Rio de Janeiro, Brazil); R. Florenzano and J. Acuna (Santiago, Chile); G. E. Simon and M. von Korff (Seattle, USA); Y. He-Quin and X. Shi Fu (Shanghai, China); and M. Tansella and C. Bellantuono (Verona, Italy). The study advisory group includes J. Costa e Silva, D. P. Goldberg, Y. Lecrubier, M. von Korff and H.-U. Wittchen. Coordinating staff at World Health Organization headquarters include N. Sartorius and T. B. Ustun. This paper was started while P.S. was studying for a PhD degree at the University of Wales College of Medicine. P.S. was funded throughout his studies by the Alexander S. Onassis Public Benefit Foundation.

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CLINICAL IMPLICATIONS

- Prevalence of unexplained fatigue in primary care differs widely across countries.
- Patients from well-developed countries are more likely to report fatigue in response to direct questions but are less likely to present with fatigue to physicians compared with patients from less-developed countries.
- Presenting fatigue in less-developed countries might be an important indicator of hidden psychiatric need.

LIMITATIONS

- The study was carried out in primary care and results cannot be generalised to the general population.
- Participation rates for the baseline assessment were relatively low for some centres.
- Medical causes of fatigue were excluded in a crude way by asking patients if a doctor had given them a definite diagnosis for their symptom or if there had been any abnormalities reported on examination or further investigation.

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(First received 30 April 2002, final revision 7 October 2002, accepted 21 October 2002)

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