Prognosis of Chronic Fatigue in a Community-Based Sample

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Objective: This study examined predictors of fatigue severity and predictors of continued chronic fatigue status at wave 2 follow-up within a random, community-based sample of individuals previously evaluated in a wave 1 prevalence study of chronic fatigue and chronic fatigue syndrome that originally took place between 1995 and 1997. **Methods:** Wave 1 data were from a larger community-based prevalence study of chronic fatigue syndrome. In the present study, a second wave of data were collected by randomly selecting a sample of participants from the wave 1 sample of 18,675 adults and readministering a telephone screening questionnaire designed to assess symptoms of chronic fatigue syndrome. **Results:** Findings revealed that wave 1 fatigue severity was a predictor of fatigue severity at wave 2 in the overall sample of individuals with and without chronic fatigue. In the smaller sample of individuals with chronic fatigue, wave 1 fatigue severity, worsening of fatigue with physical exertion, and feeling worse for 24 hours or more after exercise significantly predicted continued chronic fatigue status (vs. improvement) at wave 2 follow-up. **Conclusions:** These findings underscore the prognostic validity of postexertional malaise in predicting long-term chronic fatigue and also highlight the importance of using population-based, representative random samples when attempting to identify long-term predictors of chronic fatigue at follow-up. **Key words:** epidemiology, chronic fatigue, chronic fatigue syndrome, prognosis, follow-up.

CF = chronic fatigue; CFS = chronic fatigue syndrome; GHQ = General Health Questionnaire; ROC = receiver operating characteristic.

INTRODUCTION

Fatigue is common, occurring in about 20% to 25% of the general population (1, 2). However, only about 5% report chronic fatigue (CF), which is defined as fatigue lasting 6 or more months (3–5). An even smaller percentage (0.4%) (6) are ultimately diagnosed with chronic fatigue syndrome (CFS), defined by 6 or more months of unexplained fatigue and at least four of eight recurrent, accompanying symptoms (7). In recent years, knowledge about the course and long-term prognosis of CF and CFS has been increasing. Follow-up studies of medical facility populations generally suggest that older age, longer duration of illness, attribution of illness to physical causes, coping styles, and psychiatric comorbidity are important predictors of long-term outcome in these populations (8). Most follow-up studies have relied on physician referrals from medical facilities (8) and have most likely underrepresented underserved minorities and individuals of low socioeconomic status.

The issue of sampling methodology is important in studies of this nature for a variety of reasons. Reviews of epidemiological studies have highlighted differences in prevalence rates, illness characteristics, and sociodemographic characteristics of individuals with chronic fatigue that, in large part, seem linked to the sociodemographic composition and healthcare utilization patterns of the populations sampled (9, 10). Recent findings from epidemiological studies of a randomly selected, urban, community-based population have evidenced higher rates of CF and CFS in minorities and people of lower socioeconomic status (6, 11). Given these findings, it is also possible that the same groups may demonstrate higher levels of illness severity and chronicity at follow-up.

To date, only one follow-up study of CF has used a community-based sample (12). Lawrie and Pelosi (13) found an initial prevalence of 560 per 100,000 among a random postal survey sample of 1039 patients registered at a British health center. Lawrie et al. (12) resurveyed respondents 1 year later and interviewed them again at an 18- to 22-month follow-up. Premorbid fatigue score was the only significant predictor for developing CF (psychiatric morbidity and physical attribution for fatigue were not risk factors).

Other follow-up studies of individuals with CF and CFS have relied on medical facility samples and have focused mainly on evaluating psychological and psychosocial predictors of outcome. In a primary care sample, Hickie et al. (14) examined fatigue severity and psychological distress scores at baseline and at a 12-month follow-up. Findings indicated that CF is a persistent diagnosis over time. Longitudinal patterns of comorbidity with psychological distress did not suggest a causal relationship or common vulnerability factor. Similarly, Van Der Linden et al. (15) examined the relationship between fatigue and psychiatric disorder at three time points. Results supported the existence of a pure, independent fatigue state over time that did not predict subsequent psychiatric disorder. In contrast, Wilson et al. (16) found that psychological

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Received for publication November 28, 2000; revision received June 11, 2001.

0033-3174/02/6402-0319

factors were important determinants of functional impairment among patients with CFS at 3-year follow-up. Participants who coped with distress by somatization and discounted the possible modulating role of psychosocial factors were more likely to have an unfavorable outcome. Kroenke et al. (2) found that a minority (28%) of individuals with CFS improved at 1-year follow-up. Older patients and individuals with higher scores on a measure of functional impairment had a poorer prognosis at follow-up.

Russo et al. (17) found that patients whose psychiatric disorders and physical examination signs were still present at follow-up were more likely to have persistent fatigue and work disability. Similarly, Clark et al. (18) found that the factors that predicted persistent illness in CF patients included having more than eight medically unexplained physical symptoms, a lifetime history of dysthymia, a duration of CF greater than 1½ years, less than 16 years of formal education, and age over 38 years. Bombardier and Buchwald (19) compared functional outcomes in patients with CF and CFS and found that individuals who met the Holmes et al. (20) definition of CFS had poorer prognosis than individuals who did not meet CFS criteria. Similar to Clark et al. (18), Sharpe et al. (21) found that the coexistence of dysthymia predicted poorer outcome across groups.

Others have highlighted the role of illness attributions in their evaluation of prognostic indicators of CF and CFS at follow-up. Sharpe et al. (21) found that longer illness duration, belief in a viral cause of the illness, limiting exercise, changing or leaving employment, belonging to a self-help organization, and current emotional disorder predicted greater functional impairment. Similarly, Vercoulen et al. (22) found that improvement in CFS was related to a sense of control over symptoms and to not attributing the illness to physical causes.

Despite growing knowledge about long-term predictors of outcome in this area, many follow-up studies are not prospective in that they either rely on retrospective self-report at a single point in time or longitudinal data are analyzed in a cross-sectional manner without taking into account the influence of baseline findings. Moreover, many CF follow-up studies use medical care samples and do not use random community samples of socioeconomically and ethnically diverse populations.

Between September 1995 and May 1997, a wave 1 study was conducted to estimate the prevalence of CFS using a randomly selected, representative community-based sample (6). Findings from that study indicated that CFS occurs in approximately 0.42% of the population (6). CFS was most prevalent among women, minority groups, and persons with lower educational and occupational status (6). The first objective of the present investigation was to identify sociodemographic and fatigue-related predictors of fatigue severity (23) among individuals in this sample at a 2-year follow-up (6, 11). It was hypothesized that wave 1 fatigue severity and fatigue status at wave 1 (CF group vs. healthy control group) would significantly predict fatigue severity at wave 2. The second objective of this study was to identify sociodemographic and fatigue-related predictors of continued CF status at 2-year follow-up (wave 2) among the CF group. It was hypothesized that wave 1 fatigue severity, functional disability, and other fatigue-related somatic symptoms at wave 1 (6) would predict continued CF outcome at wave 2.

METHODS

Participants

In the Spring of 1999 we attempted to reinterview a subsample of 223 participants randomly selected from the sample of 18,675 participants originally screened for CFS symptomatology in a CFS prevalence study (6, 11). In the original study (wave 1), we called 28,673 residential/working telephone numbers and were able to complete the interview for 18,675 adults aged 18 years or older (65.1% completion rate). Of that group, 780 answered "yes" to a question on the original wave 1 screening questionnaire assessing whether they had been experiencing severe fatigue, extreme tiredness, or exhaustion for a period of 6 months or longer and were thus designated as the CF group. The remaining 17,888 individuals, who answered "no" to the same question, were designated as no-CF control subjects (7 individuals were not included because fatigue-related data were missing). The wave 2 sample of 223 participants was stratified such that 67 participants were randomly selected from the group of 780 with CF at wave 1 (CF group) and 156 participants were randomly selected from the remaining 17,888 control subjects (control group). We sampled and interviewed as many individuals as our funding and staff could support, and we oversampled from the control group because we predicted lower retention rates for this sample because of less interest in the subject matter of fatigue.

Procedures

Using a retrospective cohort design, the present study involved a second wave of follow-up data collection (wave 2). The data were derived from a larger community-based prevalence study of CF and CFS (wave 1) (6, 11). This larger wave 1 study was carried out in three stages. In the present wave 2 study, only data from stage 1 of the wave 1 study were used. That stage entailed a cross-sectional screening telephone survey of a random sample of adults residing in Chicago. To assess changes in fatigue and identify predictors of fatigue severity and continued CF at follow-up, a wave 2 follow-up telephone screening questionnaire was administered to a stratified sample of 67 participants with 6 or more months of CF and 156 control subjects randomly selected from the original sample of stage 1 participants in the wave 1 study. Variables extracted from the stage 1 screening questionnaire administered in the wave 1 study were examined for their ability to predict fatigue severity and continued

CF status as assessed by the wave 2 follow-up screening questionnaire.

Four telephone interviewers with past survey research experience (three of whom worked as telephone interviewers in the original wave 1 prevalence study) were recruited, trained, and supervised in telephone survey interviewing. Telephone interviewing procedures and training protocol similar to those used in the wave 1 study were incorporated into the wave 2 follow-up study (see Ref. 11 for more details on these procedures). When necessary, we used any available tracking information collected during the wave 1 study to increase the likelihood of recontacting participants (eg, leaving the phone number of the project director with a friend or relative, using an alternative telephone number for the participant, using a home address, a work telephone number, and/or using the name and telephone number of a person who would know how to get in touch with them if they moved). Once contacted, respondents were reminded that they participated in the wave 1 study and were informed that the present study involved a 15-minute follow-up questionnaire administered by telephone to assess changes in fatigue and health status since the wave 1 study.

Measures

The wave 2 Follow-Up CFS Screening Questionnaire, highly similar to the wave 1 CFS Screening Questionnaire, has been found to have high discriminant validity and excellent test-retest and interrater reliability (24). In a study using receiver operating characteristic (ROC) analysis (24), the instrument was able to discriminate precisely between CFS and healthy control populations (area under the curve = 1). The wave 2 follow-up version of this questionnaire was used in the present study to assess characteristics of fatigue at follow-up. The main difference between the wave 1 (original) and wave 2 (follow-up) questionnaires involved the addition of the General Health Questionnaire (GHQ) (25) to the wave 2 questionnaire. Like the wave 1 questionnaire, the wave 2 measure consisted of two parts. Part 1 was administered to all participants and reassessed participants' sociodemographic characteristics, fatigue severity (23), and interference of fatigue with usual daily activities. Basic demographic data included age, ethnicity, socioeconomic status, work status, marital status, parental status (including number of children), and gender. The revised scoring rules for Hollingshead's (26) scale, developed and validated by Wasser (27), were used to determine socioeconomic status. Part 2 was administered to participants reporting 6 or more months of chronic fatigue. It reassessed for the presence of the eight minor symptoms of CFS (7) and also measured characteristics associated with fatigue, such as fatigue duration, frequency of fatigue, attributions about the cause of fatigue, and fatigue-related functional impairment.

The Fatigue Scale (22), also administered in the original wave 1 study (6,11), was also contained within part 1 of the wave 2 follow-up questionnaire. This scale was originally used in a hospital-based case control study (28) and in a study designed to measure response to treatment (29). David et al. (30) found a continuous distribution of fatigue scores on this scale in a sample in Great Britain, and this scale was endorsed by Barofsky and Legro (31) in their review of measures of fatigue. The Fatigue Scale produces a total score, a score reflecting mental fatigue, and a score reflecting physical fatigue. The Fatigue Scale was further refined by Chalder et al. (23). Despite its brevity, the scale was found to be reliable and valid, and it had good face validity and reasonable discriminant validity (area under the ROC curve = 0.85) (23). The 11-item scale was scored according to the continuous scoring procedure, with codes ranging from 0 to 3 and total scores ranging from 0 to 33 (with higher scores signifying greater fatigue). The Fatigue Scale is commonly used in community-based studies of fatigue, CF, and CFS (4, 32).

The GHQ was designed for use in general population surveys, in primary medical care settings, and among general medical outpatients to detect diagnosable psychiatric disorders (25). Shortened versions have been used to measure psychological and somatic distress and to screen for psychiatric "caseness" in community-based and clinic studies of CF and CFS (4, 32, 33). More than 50 validation studies conducted on various versions of the GHQ have shown moderate to high levels of internal consistency and moderate correlations with psychiatric diagnoses (34). Buchwald et al. (33) concluded that the GHQ provides an inexpensive and quick screening for psychiatric disorder in patients with CF and CFS. In the present study, the 12-item version of the GHQ was used. Each GHQ item contains a four-option continuum with codes ranging from 0 to 3; higher scores signify greater likelihood of psychiatric disorder. This scale was scored by summing the codes for each item for a total score (with higher scores signifying greater emotional distress). This continuous scoring procedure is endorsed by Goldberg and Williams (35) as a means of understanding GHQ findings according to a dimensional model for psychological ill health.

Statistical Analyses

Because of limitations imposed by small sample size, this study used a two-stage approach to data analysis in which a series of univariate comparisons were conducted to identify specific variables that would serve as predictors of fatigue at follow-up in regression models. For all univariate analyses, categorical data were analyzed using chi-square tests, and continuous data were analyzed using independent-samples *t* tests.

In the first set of analyses, CF and healthy control groups identified in wave 1 were compared in terms of sociodemographic and fatigue-related characteristics. Variables demonstrating significant differences between the CF and control groups were then entered as predictors of wave 2 fatigue severity in a series of hierarchical multiple regression analyses using the overall sample. Wave 1 fatigue severity was always entered as the first variable so that other predictors could be tested for their independent contributions to the model.

In the second set of analyses, the wave 1 CF group was divided into two groups according to wave 2 fatigue status. Those who indicated that they had been experiencing CF for the past 6 or more months were designated as the "fatigued" group ($N = 26$), and those indicating that they were no longer experiencing CF were designated as the "improved" group ($N = 25$). Using univariate analyses, fatigued and improved groups were then compared in terms of wave 1 fatigue-related characteristics and emotional distress. Variables demonstrating significant differences were then entered as predictors of improved vs. fatigued outcome at wave 2 in a series of hierarchical logistic regression analyses. Wave 1 fatigue severity was always entered as the first variable so that other predictors could be tested for their independent contributions to the model.

Variables used in the analyses were selected and scored as follows. Wave 1 and wave 2 fatigue severity scores were obtained by summing all of the items in the Chalder et al. (23) fatigue severity scale in the wave 1 screening questionnaire and in the wave 2 follow-up questionnaire, respectively. Other characteristics related to fatigue, as well as the eight minor CFS symptoms (7), were analyzed from both the wave 1 and wave 2 CFS screening questionnaires. Although sociodemographic characteristics were assessed at both time points, wave 1 sociodemographic data were used in all analyses involving sociodemographic data. Preliminary analyses in-

dicated no significant differences between wave 1 and wave 2 sociodemographic data.

RESULTS

Sixty-seven participants with CF and 156 control subjects without CF were randomly selected from a preexisting sample of 18,675 individuals who completed an initial CFS telephone screening questionnaire in the wave 1 study (6, 11). Of the 156 randomly selected control subjects, 78 (50.0%) individuals were contacted and administered the wave 2 follow-up telephone screening questionnaire. Of the 67 randomly selected CF individuals, 51 (76.1%) were contacted and administered the follow-up survey. Chi-square analyses comparing individuals who completed the wave 2 questionnaire (participants) and those who did not (nonparticipants) were conducted to determine comparability of samples with respect to sociodemographic characteristics of marital status, gender, ethnic identification, occupation, education, and familial status. An independent-samples t test was used to compare participants and nonparticipants in terms of wave 1 baseline fatigue severity (23). No significant differences between participants and nonparticipants were found.

Comparisons of Chronic Fatigue and Control Groups

Comparisons of wave 1 sociodemographic and fatigue-related characteristics according to wave 1 CF and healthy control groups are presented in the following section. With respect to fatigue severity, individuals in the CF group (mean = 18.49, SD = 5.50) demonstrated significantly higher fatigue severity than individuals in the control group (mean = 13.35, SD = 3.47) ($t(127) = -6.52$, $p < .01$). Chi-square analyses of sociodemographic characteristics revealed significant differences between groups in terms of marital status ($\chi^2(4) = 10.66$, $p < .05$). A higher percentage of CF participants were divorced compared with control subjects (22.0% vs. 5.1%), and a higher percentage of control subjects were married (48.7%) as compared with CF participants (32.0%). In relation to disability status, a greater proportion of individuals in the CF group (22.0%) were receiving disability income as compared with control subjects (1.3%) ($\chi^2(1) = 15.87$, $p < .01$). Individuals in the CF group were significantly older (mean = 44.98, SD = 12.55) than those in the control group (mean = 39.36, SD = 12.45) ($t(127) = -2.50$, $p < .05$). No other significant sociodemographic differences were found. A significantly higher proportion of individuals in the CF group also reported that fatigue caused moderate (43.1%) or severe (25.5%) interference with usual daily activities as compared with control subjects (10.3% and 2.6%, respectively) ($\chi^2(3) = 46.86$, $p < .01$).

Predictors of Wave 2 Fatigue Severity

After these univariate analyses, hierarchical multiple regression analyses were performed to determine predictors of fatigue severity at wave 2 for the overall sample. Because there were a number of variables for which significant differences between the CF and control groups occurred, a series of separate hierarchical multiple regression analyses were conducted to incorporate each of the significant wave 1 variables according to the following procedures. All independent variables considered were forced into the equation in a predetermined order, and each was examined separately for what it added to the equation at its own point of entry. An α level of 0.05 was used for all regression analyses. The wave 1 fatigue severity score (23) was always entered first, and each significant variable from wave 1 was entered separately into each of the regression equations. When each of these four variables (age, marital status, disability status, and impact of fatigue on usual daily activities) were entered individually into the regression equation, wave 1 fatigue severity was consistently the only significant predictor of wave 2 fatigue severity (all $F(2)$ values > 33.37, all p values $< .05$).

Predictors of Continued Fatigue Status at Wave 2

Next, we sought to identify potential predictors of continued CF status at Wave 2 follow-up within our sample of 51 individuals with CF. Those who indicated they had been experiencing CF for the past 6 or more months on the wave 2 follow-up questionnaire were designated as the "fatigued" group ($N = 26$), and those indicating they were no longer experiencing CF were designated as the "improved" group ($N = 25$). Table 1 presents comparisons of the fatigued and improved groups according to wave 1 sociodemographic characteristics. Chi-square analyses were used to test significant group differences for categorical variables, and a t test was used to test the continuous variables of age and number of children. One significant difference emerged with respect to work status ($\chi^2(4) = 13.61$, $p < .01$). A greater proportion of individuals in the fatigued group were either on disability or working part time, and a greater proportion of individuals in the improved group were either unemployed, retired, or working full time.

To identify additional potential predictors of continued CF status at wave 2, we conducted a series of

TABLE 1. Wave 1 Sociodemographic Characteristics for Fatigued and Improved Groups

	Fatigued (N = 26)	Improved (N = 25)	p
Age, mean (SD), y	44.31 (10.28)	45.12 (14.67)	0.819
No. of children, mean (SD)	2.38 (1.90)	1.42 (1.69)	0.064
Race, %			0.172
African American	34.6	20.8	
Caucasian	42.3	66.7	
Latino	11.5	12.5	
Other	11.5	0.0	
Gender, %			0.401
Female	73.1	80.0	
Male	26.9	20.0	
Marital status, %			0.526
Married	30.8	29.2	
Separated	0.0	8.3	
Divorced	23.1	25.0	
Widowed	3.8	0.0	
Never Married	42.3	37.5	
Parent, %	73.1	58.3	0.212
Education, %			0.831
Less than high school	3.8	12.0	
Some high school	11.5	16.0	
High school degree or equivalent	38.5	28.0	
Partial college	26.9	20.0	
Standard college degree	11.5	16.0	
Graduate or professional degree	7.7	8.0	
Occupation			0.465
Farm laborer	8.0	8.7	
Unskilled worker	28.0	17.4	
Machine operator	12.0	8.7	
Skilled manual worker	8.0	0.0	
Clerical or sales worker	4.0	26.1	
Technician	16.0	17.4	
Manager	16.0	13.0	
Administrator	8.0	8.7	
Higher executive	0.0	0.0	
Work status, %			0.009
Receiving disability income	34.6	8.7	
Unemployed	15.4	30.4	
Working part time	23.1	0.0	
Working full time	23.1	47.8	
Retired	3.8	13.0	

simple univariate analyses comparing the fatigued and improved groups with respect to the wave 1 Chalder fatigue severity score, the total continuous score of emotional distress measured by the GHQ (25), and a number of wave 1 questionnaire items measuring characteristics related to fatigue. These results are presented in Table 2. The fatigued group had a significantly higher overall fatigue severity score (22) at wave 1 than the improved group ($t(49) = -3.70$, $p < .01$). Fatigued participants were also found to report significantly higher levels of emotional distress on the GHQ as compared with improved participants ($t(49) = -2.05$, $p < .05$). A significantly higher proportion of the fatigued participants, as compared with the improved participants, indicated their fatigue was made worse by physical exertion ($\chi^2(1) = 7.51$, $p < .01$). A significantly higher proportion of the fatigued participants indicated that their fatigue was present for more than 50% of the time as compared with the improved participants ($\chi^2(1) = 9.69$, $p < .01$). Fatigued participants were also found to be significantly more functionally impaired than improved participants ($\chi^2(6) = 12.75$, $p < .05$).

In addition, we compared the fatigued and improved groups in terms of duration of fatigue in years, each of the eight minor symptoms of CFS (7), and the frequency of total CFS minor symptoms (7) as measured by the screening questionnaire. These results are presented in Table 3. Individuals in the fatigued group reported a significantly higher frequency of CFS symptoms ($t(49) = -2.59$, $p < .05$), felt significantly worse for 24 hours or more after exercising (postexertional malaise) ($\chi^2(1) = 8.67$, $p < .01$), reported significantly more joint pain ($\chi^2(1) = 5.99$, $p < .05$), and had significantly more unrefreshing sleep ($\chi^2(1) = 4.24$, $p < .05$) as compared with the improved group.

Within the CF group, a series of hierarchical logistic regression analyses were then conducted to determine whether the significant wave 1 variables identified in the initial analyses were predictors of fatigued (vs. improved) outcome at follow-up. The Chalder et al. (23) fatigue severity score at wave 1 was always entered as the first variable in the equation, and each variable demonstrating a significant relationship to improved vs. fatigued outcome were entered subsequently. After entry of wave 1 fatigue severity, only two other variables, both assessing postexertional malaise, significantly predicted fatigued outcome at follow-up. The first of these variables was the item "Is your fatigue made worse by physical exertion?"; the second was "Do you feel worse for 24 hours or more after exercising?".

After this series of individual logistic regression analyses, those variables that were significant predictors of fatigued outcome at wave 2 follow-up were entered into a single hierarchical logistic regression analysis. Thus, wave 1 fatigue severity was entered first, the item "Is your fatigue made worse by physical exertion?" was entered second, and the item "Do you feel worse for 24 hours or more after exercising" was entered last. Findings indicated that all three of these wave 1 variables significantly predicted fatigued outcome at wave 2 follow-up. The parameter estimates (b), odds ratios, 95% confidence intervals, and significance levels are presented in Table 4.

TABLE 2. Wave 1 Characteristics of Fatigue for Fatigued vs. Improved Groups

	Fatigued (N = 26)	Improved (N = 25)	p
Fatigue severity score (23), mean (SD)	21.04 (5.13)	15.96 (4.64)	0.001
GHQ Emotional Distress Index, mean (SD)	19.31 (7.31)	15.20 (6.98)	0.046
Frequency of fatigue or lack of energy, %			0.291
Not at all	0.0	4.3	
Less than once a week	0.0	4.3	
1–4 times a week	30.8	43.5	
More than 4 times per week	69.2	47.8	
Feel better for days at a time, %	38.5	58.3	0.131
Feel better for weeks or more at a time, %	12.0	25.0	0.211
Fatigue problem began in, %			0.512
Less than 24 hours	11.5	0.0	
1–2 days	3.8	8.7	
3–6 days	11.5	8.7	
1 week–1 month	15.4	17.4	
Longer than 1 month	34.6	26.1	
Childhood or adolescence	0.0	4.3	
Don't know	23.1	34.8	
Progress of fatigue, %			0.110
Getting worse over time	56.0	26.1	
Staying the same	36.0	60.9	
Getting better over time	8.0	13.0	
Experience high levels of fatigue after normal daily activities, %	80.0	60.9	0.111
Fatigue made worse by physical exertion, %	84.6	47.8	0.007
Fatigue made worse by mental exertion, %	61.5	34.8	0.056
Fatigue made worse by emotional distress, %	73.1	78.3	0.466
Fatigue begins after physical or mental exertion, %			0.836
Immediately	56.0	42.9	
1 h	16.0	23.8	
1–3 h	20.0	23.8	
>3 h	8.0	9.5	
Duration of fatigue after physical or mental exertion, %			0.527
1 h	12.0	10.0	
1–3 h	20.0	35.0	
>3 h	68.0	55.0	
Fatigue present for more than 50% of the time, %	100.0	68.2	0.002
Description of fatigue during the last month, %			0.047
Bedridden	0.0	4.5	
Can walk around the house	15.4	0.0	
Can do light housework	23.1	18.2	
Can only work part time	26.9	4.5	
Can work full time but no energy left	15.4	27.3	
Can work full time and some family responsibility	19.2	36.4	
Can do all work without any energy problems	0.0	9.1	
Medical doctor overseeing fatigue problem, %	57.7	52.2	0.460
Consulted a doctor about fatigue, %	73.1	69.6	0.517
Fatigue can be explained by ongoing strenuous physical activity, %	15.4	4.3	0.215
Chronic fatigue and all symptoms go away with extended rest, %			0.297
Yes, for a long period of time	4.0	13.0	
Yes, for a short period of time	52.0	60.9	
No, not at all	44.0	26.1	
Attribution regarding cause of fatigue problem, %			0.702
Definitely physical	30.8	21.7	
Mainly physical	15.4	8.7	
Equally physical and psychological	46.2	52.2	
Mainly psychological	3.8	13.0	
Definitely psychological	3.8	4.3	

TABLE 3. Average Number and Percentage of Reported Symptoms for Fatigued and Improved Groups

	Fatigued (N = 26)	Improved (N = 25)	p
Mean (SD) no. of symptoms	4.96 (1.73)	3.52 (2.22)	0.013
Mean (SD) duration of fatigue, y	3.11 (3.01)	2.89 (2.54)	0.782
Sore throat, %	42.3	40.0	0.547
Painful glands, %	34.6	28.0	0.418
Muscle aches or pain, %	80.8	68.0	0.235
Feel worse for ≥24 hours after exercising, %	69.2	28.0	0.004
New headaches, %	30.8	16.0	0.181
Joint pain, %	80.8	48.0	0.015
Not rested after a night of sleep, %	88.5	64.0	0.041
Concentration or memory problems interfere with work or study, %	69.2	60.0	0.346

TABLE 4. Summary of Logistic Regression Analysis for Variables Predicting Fatigue Status (N = 51)

Predictors	b	Odds Ratio	95% CI
Fatigue severity score	0.23*	1.26	1.05–1.50
Is your fatigue made worse by physical exertion?			
Yes	1.84*	6.31	1.17–34.05
No[a]			
Feel worse for ≥24 hours after exercising?			
Yes	1.63*	5.12	1.14–22.98
No[a]			
Constant	−6.17**		
Model: $\chi^2 = 23.74$, $df = 3$, $p < .01$.			

[a] Parameter used as reference category in logistic regression.
* Significance at $p \leq .05$.
** Significance at $p \leq .01$.

DISCUSSION

The present study examined predictors of fatigue severity and continued CF status at wave 2 follow-up within a random community-based sample of individuals previously evaluated in a prevalence study (6, 11). Fifty percent of control subjects and 76.1% of individuals with CF randomly selected for interview from the wave 1 study (6, 11) were contacted and administered a follow-up telephone screening questionnaire assessing changes in fatigue severity, fatigue-related symptomatology, and emotional distress. These completion rates are comparable with rates from other community-based follow-up studies (36–38). To identify wave 1 predictors of fatigue severity at wave 2 follow-up, a series of simple univariate analyses were conducted comparing individuals with and without CF. Findings revealed significant differences between the CF and control groups with respect to wave 1 fatigue severity (23), age, marital status, disability status, and effects of fatigue on usual daily activities.

However, when the effects of each of these variables over and above wave 1 fatigue severity were tested separately as potential predictors of fatigue severity at wave 2 follow-up, none emerged as significant predictors. Thus, wave 1 fatigue severity was the only variable that significantly predicted fatigue severity at wave 2 in the overall sample of individuals with CF and control subjects. In part, these results are consistent with findings from prior studies of mixed populations, which have identified markers of more severe illness, such as fatigue severity and more severe disability, as predictors of poorer outcome (8). However, in contrast to prior reports of increasing age and changing or leaving employment as predictors of poorer outcome (8, 19), age and unemployment status did not emerge as significant predictors of fatigue severity at the wave 2 follow-up in the present study.

A number of variables were associated with significant differences between individuals with CF who remained fatigued at follow-up (fatigued group) and those who no longer had CF (improved group). These included work status, wave 1 fatigue severity (23), worsening of fatigue with physical exertion, past-month functional capacity, GHQ index of emotional distress, the frequency of eight minor CFS symptoms (7), postexertional malaise for 24 hours or more, joint pain, and unrefreshing sleep. However, when the effects of these variables on wave 2 fatigue status were examined, not in isolation but in relation to wave 1 fatigue severity, results of logistic regression analysis indicated that wave 1 fatigue severity, worsening of fatigue with physical exertion, and postexertional malaise for 24 hours or more were the only significant predictors of continued CF status at the wave 2 follow-up. With the exception of wave 1 fatigue severity predicting continued CF status, these results contrast with those of prior studies, which highlight the relationships between age, illness duration, illness attributions, and fatigue at follow-up (8).

In part, differences observed between this study and prior studies may stem from the use of different sampling methodologies between studies. Our sample was generated using randomized, population-based sampling methods, whereas a number of previous studies have used samples of convenience, such as tertiary care clinic samples. In contrast to clinic samples, which tend to be biased in terms of ethnic homogeneity, use of medical care, age (typically over 30), and tendency toward medical attribution for symptoms (18, 22), the random community population we sampled was more heterogeneous in terms of these variables and likely more representative of the general

population. In addition, although most other studies have used correlational analyses (19) or have reported basic proportional and percentage data (39), the present study analyzed multivariate relationships in predicting outcome at follow-up. In the present study, the contrast in the abundance of significant findings when simple univariate analyses were used as compared with fewer findings when regression analyses were used underscores the importance of considering multivariate relationships when generating conclusions about predictors of outcome in investigations of CF.

Findings for the significance of postexertional malaise in predicting continued fatigue status at follow-up can be interpreted as supporting the prognostic validity of this symptom in predicting long-term CF and should be considered in the future design of measures to assess characteristics of illnesses involving CF. In a recent study, Jason and Taylor (40) found that postexertional malaise was the single most important factor in discriminating CFS and medically explained CF from idiopathic CF. In addition, postexertional malaise also discriminated medically explained CF from psychiatrically explained CF (40). Thus, fatigue resulting from physical exertion not only seems to be a key discriminator of more severe fatigue-related illnesses, but also seems to be an important prognostic indicator of poorer outcome at follow-up.

This study had a number of limitations. One central limitation was the small sample size, which required us to conduct a series of univariate analyses to select variables for the predictive model, thereby limiting the extent to which multivariate statistics could be used. Another limitation that, in part, contributed to the small sample size was the lower follow-up completion rate of 50% for the control sample. Although most follow-up studies of CF are characterized by small sample size (8) and our 50% rate was higher than that found in other large-scale, community-based follow-up studies (36–38), it was lower than the rate we achieved for the CF sample (76.1%). It is possible that individuals in the control sample were less likely to participate because of lack of interest in the subject matter of fatigue. This was a preliminary investigation, and as such the initial follow-up sample targeted for interview was small. It would be important to test and replicate these findings in a future study involving the entire wave 1 sample of 18,675 individuals. In addition, measures of some variables found to be predictors of fatigue in previous studies, such as categorical measures of the presence vs. absence of psychiatric disorder, were not included in the present study.

In summary, results from the present investigation support the validity of fatigue severity (23) both as a predictor of fatigue severity at follow-up within a mixed sample of individuals with and without CF and also as a predictor of continued CF status among a sample of individuals with CF only. In contrast to findings from prior studies (8), findings from the present investigation also underscore the validity of postexertional malaise as a predictor of continued CF within a sample of individuals with CF. Differences in findings between the present study and previous studies not only highlight the importance of using random community-based sampling procedures when conducting epidemiological research, but also emphasize the utility of multivariate and logistic regression procedures in accurately testing and identifying predictors of outcome. (41–44)

Financial support for this study was provided by Grant AI36295 from the National Institute of Allergy and Infectious Disease, National Institutes of Health.

REFERENCES

1. Chen M. The epidemiology of self-perceived fatigue among adults. Prev Med 1986;15:74–81.
2. Kroenke K, Wood D, Mangelsdorff D, Meier N, Powell J. Chronic fatigue in primary care: prevalence, patient characteristics, and outcome. JAMA 1988;260:929–34.
3. Jason LA, Taylor R, Wagner L, Holden J, Ferrari JR, Plioplys AV, Plioplys S, Lipkin D, Papernik M. Estimating rates of chronic fatigue syndrome from a community based sample: a pilot study. Am J Commun Psychol 1995;23:557–68.
4. Pawlikowska T, Chalder T, Hirsch SR, Wallace P, Wright DJ, Wessely SC. A population based study of fatigue and psychological distress. BMJ 1994;308:763–6.
5. Price RK, North CS, Wessely S, Fraser VJ. Estimating the prevalence of chronic fatigue syndrome and associated symptoms in the community. Public Health Rep 1992;107:514–22.
6. Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor R, McCready W, Huang CF, Plioplys S. A community-based study of chronic fatigue syndrome. Arch Intern Med 1999; 159:2129–37.
7. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med 1994;121:953–9.
8. Joyce J, Hotopf M, Wessely S. The prognosis of chronic fatigue and chronic fatigue syndrome: a systematic review. Q J Med 1997;90:223–33.
9. Katon WJ, Walker EA. The relationship of chronic fatigue to psychiatric illness in community, primary care, and tertiary care samples. In: Bock GR, Whelan J, editors. Chronic fatigue syndrome. New York: John Wiley; 1993. p. 193–211.
10. Friedberg F, Jason LA. Understanding chronic fatigue syndrome: an empirical guide to assessment and treatment. Washington DC: American Psychological Association; 1998.
11. Jason LA, Jordan KM, Richman JA, Rademaker AW, Huang CF, McCready W, Shlaes J, King CP, Landis D, Torres S, Haney-Davis T, Frankenberry EL. A community-based study of prolonged fatigue and chronic fatigue. J Health Psychol 1999;4: 9–26.
12. Lawrie SM, Manders DN, Geddes JR, Pelosi AJ. A population-

based incidence study of chronic fatigue. Psychol Med 1997;27: 343–53.
13. Lawrie SM, Pelosi AJ. Chronic fatigue syndrome in the community: relevance and associations. Br J Psychiatry 1995; 166:793–7.
14. Hickie I, Koschera A, Hadzi-Pavlovic D, Bennett B, Lloyd A. The temporal stability and co-morbidity of prolonged fatigue: a longitudinal study in primary care. Psychol Med 1999;29:855–61.
15. Van Der Linden G, Chalder T, Hickie I, Koschera A, Sham P, Wessely S. Fatigue and psychiatric disorder: different or the same? Psychol Med 1999;29:863–8.
16. Wilson A, Hickie I, Lloyd A, Hadzi-Pavlovic D, Boughton C, Dwyer J, Wakefield D. Longitudinal study of outcome of chronic fatigue syndrome. BMJ 1994;308:756–9.
17. Russo J, Katon W, Clark M, Kith P, Sintay M, Buchwald D. Longitudinal changes associated with improvement in chronic fatigue patients. J Psychosom Res 1998;45:67–76.
18. Clark MR, Katon W, Russo J, Kith P, Sintay M, Buchwald D. Chronic fatigue: risk factors for symptom persistence in a 21/2 year follow-up study. Am J Med 1995;98:187–202.
19. Bombardier CH, Buchwald D. Outcome and prognosis of patients with chronic fatigue vs. chronic fatigue syndrome. Arch Intern Med 1995;155:2105–10.
20. Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schonberger LB, Straus SS, Jones JF, Dubois RE, Cunningham-Rudles C, Pahwa S, Tosato G, Zegans LS, Purtilo DT, Brown W, Schooley RT, Brus I. Chronic fatigue syndrome: a working case definition. Ann Intern Med 1988;108:387–9.
21. Sharpe M, Hawton K, Seagroat V, Pasvol G. Follow-up of patients presenting with fatigue to an infectious diseases clinic. BMJ 1992;305:147–52.
22. Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G. Prognosis in chronic fatigue syndrome: a prospective study on the natural course. J Neurol Neurosurg Psychiatry 1996;60:489–94.
23. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP. Development of a fatigue scale. J Psychosom Med 1993;37(pt 2):147–53.
24. Jason LA, Ropacki MT, Santoro NB, Richman JA, Heatherly W, Taylor R, Ferrari JR, Plioplys AV, Plioplys S, Rademaker A, Golding J. A screening instrument for chronic fatigue syndrome: reliability and validity. J Chronic Fatigue Syndrome 1997;3: 39–59.
25. Goldberg D. The detection of psychiatric illness by questionnaire. London: Oxford University Press; 1972.
26. Hollingshead AB. Four factor index of social status. Available from: Department of Sociology, Yale University, New Haven CT; 1975.
27. Wasser TE. Statistical correction of Hollingshead's four factor index of social status. Psychol Health. In press 2002.
28. Wessely S, Powell R. Fatigue syndromes: a comparison of chronic 'postviral' fatigue with neuromuscular and affective disorders. J Neurol Neurosurg Psychiatry 1998;52:940–8.
29. Butler S, Chalder T, Ron M, Wessely S. Cognitive behaviour therapy in chronic fatigue syndrome. J Neurol Neurosurg Psychiatry 1991;54:153–8.
30. David AS, Pelosi A, McDonald E, Stephens D, Ledger D, Rathbone R, Mann A. Tired, weak, or in need of rest: fatigue among general practice attenders. BMJ 1990;301:1199–202.
31. Barofsky I, Legro MW. Definition and measurement of fatigue. Rev Infect Dis 1991;13:S94–7.
32. Loge JH, Ekeberg O, Kaasa S. Fatigue in the general population: normative data and associations. J Psychosom Res 1998;45: 53–65.
33. Buchwald D, Pearlman T, Kith P, Katon W, Schmaling K. Screening for psychiatric disorders in chronic fatigue and chronic fatigue syndrome. J Psychosom Res 1997;42:87–94.
34. Bowling A. Measuring health: a review of quality of life measurement scales. Philadelphia: Open University; 1991.
35. Goldberg D, Williams P. A users guide to the General Health Questionnaire. Windsor, Berkshire, UK; NFER-Nelson; 1988.
36. Kawakami N, Iwata N, Fujihara S, Kitamura T. Prevalence of chronic fatigue syndrome in a community population in Japan. Tohoku J Exp Med 1998;186:33–41.
37. Ferrara A, Barrett-Connor E, Shan J. Total LDL and HDL cholesterol decrease with age in older men and women. Circulation 1997;96:37–43.
38. Eaton WW, Anthony JC, Romanoski A, Tien A, Gallo J, Cai G, Neufeld K, Schlaepfer T, Laugharne J, Chen LS. Onset and recovery from panic disorder in the Baltimore epidemiologic catchment area follow-up. Brit J Psychiatry 1998;173:501–7.
39. Reyes M, Dobbins JG, Nisenbaum R, Subedar NS, Randall B, Reeves WC. Chronic fatigue syndrome progression and self-defined recovery: evidence from the CDC surveillance system. J Chronic Fatigue Syndrome 1999;5:17–27.
40. Jason LJ, Taylor RR Applying cluster analysis to define a typology of chronic fatigue syndrome in a medically-evaluated, random community sample. Manuscript submitted for publication 1999.