Psychiatric Comorbidity in Persons With Chronic Fatigue Syndrome Identified From the Georgia Population

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Objective: To compare the prevalence of psychiatric disorders in persons with chronic fatigue syndrome (CFS) identified from the general population and a chronically ill group of people presenting with subsyndromic CFS-like illness ("insufficient symptoms or fatigue" (ISF)). Previous studies in CFS patients from primary and tertiary care clinics have found high rates of psychiatric disturbance, but this may reflect referral bias rather than true patterns of comorbidity with CFS. **Methods:** We used random digit dialing to identify unwell individuals. A detailed telephone interview identified those with CFS-like illness. These individuals participated in a 1-day clinical evaluation to confirm CFS or ISF status. We identified 113 cases of CFS and 264 persons with ISF. To identify current and lifetime psychiatric disorders, participants completed the Structured Clinical Interview for DSM-IV. **Results:** Sixty-four persons (57%) with CFS had at least one current psychiatric diagnosis, in contrast to 118 persons (45%) with ISF. One hundred one persons (89%) with CFS had at least one lifetime psychiatric diagnosis compared with 208 persons (79%) with ISF. Of note, only 11 persons (9.8%) with CFS and 25 persons (9.5%) with ISF reported having seen a mental healthcare specialist during the past 6 months. **Conclusions:** Our findings indicate that current and lifetime psychiatric disorders commonly accompany CFS in the general population. Most CFS cases with comorbid psychiatric conditions had not sought appropriate help during the past 6 months. These results demonstrate an urgent need to address psychiatric disorders in the clinical care of CFS cases.
Key words: chronic fatigue syndrome, psychiatric disorders, population-based study.

CFS = chronic fatigue syndrome; **CI** = confidence interval; **DSM** = Diagnostic and Statistical Manual for Mental Disorders; **ISF** = insufficient symptoms or fatigue; **OR** = odds ratio.

INTRODUCTION

Chronic fatigue syndrome (CFS) is an important public health problem with unique diagnostic and management challenges. Studies using population-based random samples estimated CFS prevalence as ranging from 0.24% to 2.54% (1). However, despite the prevalence of CFS several decades of scientific investigation have failed to identify physical signs or laboratory abnormalities diagnostic for the disorder. As a result, insight into the pathophysiology of CFS has proven elusive and treatment options remain limited (2).

Early reports indicated high comorbidity between states of chronic fatigue and a variety of psychiatric conditions, ranging from major depression to anxiety and substance disorders (3–6). Whereas these studies focused mainly on patients with chronic fatigue (defined by having fatigue persisting beyond 6 months), other studies found similar results in patients formally diagnosed with CFS (7–11). More recent studies have corroborated these earlier findings in both chronic fatigue and CFS (12–17). The frequent occurrence of psychiatric conditions in patients suffering from chronic fatigue or CFS might lead to the conclusion that CFS represented a psychiatric condition. However, it has been debated whether psychiatric conditions are a consequence or cause, or whether there is merely a coincidental overlap of symptoms between CFS and specific psychiatric conditions (18). In this context it needs to be considered that CFS and psychiatric conditions, such as major depression, share characteristic symptoms, such as fatigue, problems with concentration and sleep (19). This issue is particularly important when considering the fact that not all patients with chronic fatigue or CFS exhibit psychiatric symptoms.

It is possible that psychiatric comorbidity reflects the severity of CFS and attendant impairment. Previous studies have not examined the impact of illness severity or impairment on psychiatric comorbidity in CFS. Comparing CFS and subsyndromic CFS-like illness potentially elucidates the impact of illness severity and impairment on psychiatric comorbidity.

Only two of the aforementioned studies examined participants with chronic fatigue (15) or CFS (17) recruited from the community. All other studies investigated psychiatric comorbidity of CFS in participants from primary or tertiary clinical settings. Of note, previous research has shown that only around 15% of all potential CFS cases in the general population receive a formal diagnosis of CFS and therefore might not be captured in the aforementioned research using clinical samples (20,21). Consequently, the available findings are biased inasmuch as they reflect comorbidity rates in a small subgroup of treatment-seeking CFS cases.

We therefore sought to a) describe the prevalence of Axis I psychiatric disorders in cases with CFS identified from the general population; b) compare the prevalence to a group of persons identified from the same population with subsyndromic CFS-like illness (we call this group "insufficient symptoms or fatigue" (ISF)); and c) describe psychiatric/psychological treatment seeking in cases with CFS and persons with ISF.

METHODS

This study adhered to US Department of Health and Human Services human experimentation guidelines and received Institutional Review Board approval from the Centers for Disease Control and Prevention (CDC) and collaborating institutions. All participants gave their informed consent.

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Study Design

Study participants were identified during a survey of unwellness in metropolitan, urban, and rural populations of Georgia, conducted between September 2004 and July 2005 (22). The study used random digit dialing to screen 2562 metropolitan households, 3496 urban households, and 4779 households in rural areas. Of 8862 adults selected for detailed telephone interviews, 1874 refused to participate, 134 were ineligible, 1272 were out of scope (including physical/mental impairment, unable to contact, language barriers, and deceased); 5630 persons aged 18 to 59 years completed the detailed phone interview, representing a 75% response rate. Based on responses to the detailed telephone interview, subjects were asked to attend a 1-day clinical evaluation for which they received $250 as compensation. A total of 469 volunteers who fit the criteria for CFS (CFS-like) were eligible for clinical evaluation based on a detailed telephone interview, and 292 persons (67%) completed clinical assessment. A total 481 of the eligible well were invited to participate, based on having matched the CFS-like subjects by age (±3 years), sex, race/ethnicity, and geographic stratum, and 223 persons (46%) completed clinical assessment. A total of 505 with chronic unwellness (at least one of the four most common CFS defining symptoms—fatigue, cognitive impairment, unrefreshing sleep, muscle or joint pain—for ≥6 months) who did not meet the full criteria for CFS based on the telephone interview were randomly selected to participate and 268 persons (53%) completed the clinical assessment. Of 292 persons with CFS-like illness, potential exclusionary conditions could not be determined in one person due to incomplete laboratory results. A total of 141 persons with CFS-like illness had exclusionary conditions for CFS, and 66 persons with CFS-like illness did not meet the CFS case definition criteria. Further, 84 persons with CFS-like illness, 26 who were "Chronically unwell not CFS-like," and 3 "Well" subjects were finally classified as having CFS. A total of 66 persons finally classified as having ISF came from the CFS-like group, 126 came from "Chronically unwell not CFS-like," and 72 came from the initial "Well" group (1). Subjects not completing the clinical assessment were nonresponders. The main reasons for nonresponses to clinic assessment were "No time/clinic day too long/has to work" (29%), "No reason/not interested" (24%), "Personal problems/situation/illness" (16%). There was no significant difference between nonresponders and subjects completing the clinical assessment with respect to age, sex, and race (data not shown).

Clinical Assessment

CFS is a diagnosis of exclusion and cannot be reached by fulfilling the CDC criteria alone. Therefore, a thorough medical and psychiatric history and assessment are required before the diagnosis can be formally established. During the clinical evaluation, we identified medical and psychiatric exclusionary and comorbid conditions and classified participants as CFS or ISF or Well. A review committee comprised of CDC and Emory University physicians and psychologists reviewed medical history, clinical, laboratory, and psychiatric evaluations to determine the presence of medical and psychiatric conditions.

Psychiatric Conditions

Several psychiatric conditions are considered exclusionary for CFS and ISF including lifetime diagnoses of bipolar disorder, schizophrenia of any subtype, delusional disorders of any subtype, dementias of any subtype, organic brain disorders, major depressive disorder with psychotic or melancholic features, alcohol or substance abuse within 2 years before onset of the fatiguing illness, and anorexia nervosa or bulimia within 5 years before onset of the fatiguing illness (23). Consequently, no rates for any of these conditions will be reported in this paper.

To identify exclusionary and comorbid psychiatric conditions, licensed and specifically trained psychiatric interviewers administered the research version of the Structured Clinical Interview for DSM-IV (SCID), which uses the definitions and criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (24). The SCID is a semistructured interview administered by a trained clinician. Using a decision tree approach, the SCID guides the clinician in testing diagnostic hypotheses as the interview is conducted. The output of the SCID is a record of the presence or absence of each of the disorders being considered, for current episode (past month) and for lifetime occurrence. Our analysis is based on the following major axis I diagnostic classes: mood episodes and disorders, psychotic symptoms, substance use disorders, anxiety disorders, eating disorders, and adjustment disorder.

Medical Conditions

To screen for medical conditions considered exclusionary for CFS, participants completed past medical history questionnaires. A standardized physical examination was performed. Blood and urine specimens were obtained for laboratory screening tests to identify possible underlying or contributing medical conditions as stipulated by the case definition. In addition, subjects brought all their current prescription and over-the-counter medications and supplements to the clinic; the medical staff inspected them and recorded the data.

Classification of Subjects

Case Definitions

CFS is defined by a) clinically unexplained (i.e., by other primary diagnoses that might explain fatigue) persistent or relapsing fatigue of at least 6 months' duration that is not the result of ongoing exertion, is not substantially alleviated by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities; and b) concurrent occurrence of at least four of eight accompanying symptoms (unusual postexertional malaise, unrefreshing sleep, significant impairment in memory/concentration, headache, muscle pain, joint pain, sore throat, and tender lymph nodes) (25). As recommended by the International CFS Study Group (23), participants were classified as CFS or ISF (i.e., unwell but not meeting criteria for CFS), or Well based on standardized reproducible criteria that measure specifics of the 1994 case definition (25). Specifically, we used the Short-Form Health Survey (SF-36) (26) to measure functional impairment,

TABLE 1. Measurement of the CDC 1994 Case Definition

Domain:	Impairment	Fatigue	Accompanying Symptoms
	"Substantial reduction in occupational, educational, social, or recreational activities"	"Severe fatigue"	"Substantial accompanying symptoms"
	Scores <25th percentile of published US population on the physical function (≤70), or role physical (≤50), or social function (≤75), or role emotional (≤66.7) subscales of the SF-36	≥Medians of the MFI general fatigue (≥13) or reduced activity (≥10) scales	≥4 symptoms and scoring ≥25 on the CDC SI Case Definition Subscale

CDC = Centers for Disease and Prevention; SF-36 = Short-Form Health Survey; MFI = Multidimensional Fatigue Inventory; CDC SI = CDC Symptom Inventory.

TABLE 2. Demographic Features of Cases With CFS and ISF

	CFS (n = 113)	ISF (n = 264)	Statistics (df)	p
Mean age (95% CI)	44.3 (42.4–46.2)	43.1 (41.9–44.4)	t (375) = 1.02	.31
Age, n (%)			χ^2 (3) = 1.67	.64
18–29	10 (8.8)	35 (13.3)		
30–39	23 (20.4)	48 (18.2)		
40–49	41 (36.3)	97 (36.7)		
50–59	39 (34.5)	84 (31.8)		
Sex, n (%)			χ^2 (1) = 1.27	.26
Male	21 (18.6)	63 (23.9)		
Female	92 (81.4)	201 (76.1)		
Race, n (%)			χ^2 (1) = 0.0	.99
White	84 (74.3)	196 (74.2)		
Non-White	29 (25.7)	68 (25.8)		

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue; CI = Confidence Interval.

the Multidimensional Fatigue Inventory (27) to assess fatigue status, and the CDC Symptom Inventory (28) to evaluate occurrence, frequency, and severity of the eight CFS defining symptoms (Table 1). Subjects who met all three criteria when they entered the clinical study were classified as CFS (n = 113); those who met some but not all three criteria were considered as ISF (having insufficient symptoms or fatigue) (n = 264); those who met none of the criteria were classified as Well (n = 124).

Although a well control group was ascertained in this study design, we were not able to compare the CFS and ISF groups with a well control group. This was because, by virtue of our screening process, participants for the current study were selected based on their responses to questions as to whether they had symptoms of fatigue, cognitive impairment, sleep problems, or pain symptoms. Because all of these symptoms predominate in psychiatric disorders, persons who responded negatively to these questions would have had negligible or no chance of having a psychiatric disorder. For the current study, we have therefore restricted analyses to subjects meeting the criteria for either CFS or ISF.

Statistical Analyses

Crude prevalence rates of psychiatric comorbidity were computed for both groups. Age-standardized prevalence rates of comorbidity were computed using the 2000 US Census population as the standard population (US Census 2000, US Department of Commerce, Economics and Statistics Administration. US Census Bureau. Issued July 2002). Ten-year age group proportions were derived from the standard population and multiplied by our crude prevalence estimates for each age-group to obtain products that were summed to produce age-standardized rates per 100. The 10-year age group proportions that were used are the following (in parentheses): ages 18 to 29 years (0.2848); ages 30 to 39 years (0.2646); ages 40 to 49 years (0.2604); ages 50 to 59 years (0.1901). All age-standardized rates are presented as percents. The χ^2 or Fisher's Exact Tests were used to compare the distribution of categorical variables between the CFS and ISF groups, including demographic variables, psychiatric diagnoses, and treatment-seeking variables. A t test was used to compare mean ages between the CFS and ISF groups. Odds ratios (ORs) for predicting the co-occurrence of psychiatric disorder with CFS were also estimated using logistic regression models. Multivariate logistic regression was performed to adjust ORs for age, sex, race (White/Black/all others), and geographic strata. For each estimate, 95% Confidence Intervals (CIs) were computed.

RESULTS

Demographic features were similar among participants with CFS and ISF (Table 2).

Affective disorders were highly prevalent in both groups (Table 3). The crude prevalence of current affective disorders was 31.8% for the CFS group and 12% for ISF group. A majority of the CFS group (80.2%) and ISF group (54%) had an affective disorder sometime in their lifetime. Among persons with CFS, the most common affective disorder at the time of clinic and at any time in their lifetime was major depressive disorder (22.1%, 65.5%, respectively). This was also true for the ISF group, with 4.9% determined to have a major depressive disorder at the time of clinic, and 45.2% having had a major depressive disorder at some time in their lifetime.

Current substance disorders are considered exclusionary for the diagnosis of CFS and are therefore not included in this report. The CFS and ISF groups had similar rates of lifetime substance disorders (33% versus 30.8%, respectively) (Table 4).

Anxiety disorders were also highly prevalent in both the CFS and ISF groups (Table 5). A current anxiety disorder was detected in 45.9% of the CFS group and 35.3% of the ISF group; 61.6% of the CFS group and 46.9% of the ISF group were determined to have had an anxiety disorder during their lifetime. Generalized anxiety disorder represented the most prevalent current anxiety disorder among the CFS group (21.4%), whereas posttraumatic stress was the most common anxiety disorder among the ISF group (11%). For lifetime rates, posttraumatic stress disorder was the most common anxiety disorder among both the CFS group (37.5%) and the ISF group (21.3%).

Eating disorders were diagnosed in 4.5% of the CFS group and 2.7% of the ISF group at the time of clinic, whereas 8.8% of persons with CFS and 4.5% of those with ISF had an eating disorder during their lifetime (Table 6). Binge eating was the most common eating disorder diagnosed among both groups at the time of clinic (CFS: 4.5%, ISF: 2.7%) and ever during the lifetime (CFS: 7.1%, ISF: 3.0%).

Finally, adjustment disorder was diagnosed in 4 persons with CFS (3.5%) and 17 persons with ISF (6.5%). The two groups did not differ regarding this diagnosis (χ^2 (1) = 1.3; p = .33).

Age-standardized rates of comorbid conditions were computed for broad categories of disorders (affective, anxiety, eating, substance disorders, both current and lifetime) (based on census data from the US). As Table 7 indicates, age-

TABLE 3. Prevalence of Affective Disorders Among Cases With CFS and Persons With ISF

	CFS	ISF	Comparison
	n Affected/Total (%) (95% Exact Confidence Limits)	*n* Affected/Total (%) (95% Exact Confidence Limits)	
Affective disorders			
Current	34/107 (31.8%) (23.1%–41.5%)	31/258 (12.0%) (8.3%–16.0%)	χ^2 (1) = 20.2; $p < .001$
Lifetime	89/111 (80.2%) (72.8.9%–87.6%)	141/261 (54.0%) (47.8%–60.2%)	χ^2 (1) = 22.6; $p < .001$
Major depressive disorder			
Current	25/113 (22.1%) (14.9%–30.9%)	13/264 (4.9%) (2.7%–8.3%)	χ^2 (1) = 25.83; $p < .001$
Lifetime	74/113 (65.5%) (56.0%–74.2%)	118/261 (45.2%) (39.1%–51.5%)	χ^2 (1) = 13.0; $p < .001$
Dysthymia			
Current	7/108 (6.5%) (2.7%–12.9%)	8/260 (3.1%) (1.3%–6.0%)	χ^2 (1) = 2.3; $p = .13$
Depression NOS			
Current	4/113 (3.5%) (1.0%–8.8%)	10/261 (3.8%) (1.9%–6.9%)	$p = .58$
Lifetime	13/112 (11.6%) (6.3%–19.0%)	26/259 (10.0%) (6.7%–14.4%)	χ^2 (1) = 0.20; $p = .65$
Mood GMC			
Current	2/112 (1.8%) (0.2%–6.3%)	0/263 (0%) (N/A)	$p = .09$
Lifetime	4/112 (3.6%) (1.0%–8.9%)	0/264 (0%) (N/A)	$p < .05$
Mood substance			
Current	0/112 (0%) (N/A)	0/264 (0%) (N/A)	N/A
Lifetime	2/112 (1.8%) (0.2%–6.3%)	2/264 (0.8%) (0.1%–2.7%)	$p = .35$

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue; NOS = not otherwise specified; GMC = due to general medical condition. Fisher's Exact Test was used when cell sizes were <5.

TABLE 4. Prevalence of Substance Disorders Among Cases With CFS and Persons With ISF

	CFS	ISF	Comparison
	n Affected/Total (%) (95% Exact Confidence Limits)	*n* Affected/Total (%) (95% Exact Confidence Limits)	
Substance disorders			
Lifetime	37/112 (33.0%) (24.4%–42.6%)	81/263 (30.8%) (25.3%–36.8%)	χ^2 (1) = 0.18; $p = .67$
Alcohol abuse			
Lifetime	17/111 (15.3%) (9.2%–23.4%)	37/263 (14.1%) (10.1%–18.9%)	χ^2 (1) = 0.1; $p = .75$
Alcohol dependence			
Lifetime	15/111 (13.5%) (7.8%–21.3%)	40/263 (15.2%) (11.1%–20.1%)	χ^2 (1) = 0.18; $p = .67$
Nonalcohol abuse			
Lifetime	7/113 (6.2%) (2.5%–12.4%)	12/264 (4.5%) (2.4%–7.8%)	χ^2 (1) = 0.45; $p = .50$
Nonalcohol dependence			
Lifetime	7/113 (6.2%) (2.5%–12.4%)	18/264 (6.8%) (4.1%–10.6%)	χ^2 (1)=0.05; $p = .82$

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue.

TABLE 5. Prevalence of Anxiety Disorders Among Cases With CFS and Persons With ISF

	CFS	ISF	Comparison
	n Affected/Total (%) (95% Exact Confidence Limits)	*n* Affected/Total (%) (95% Exact Confidence Limits)	
Anxiety disorders			
Current	51/111 (45.9%) (36.5%–55.7%)	91/258 (35.3%) (29.5%–41.4%)	χ^2 (1) = 3.7; p = .05
Lifetime	69/112 (61.6%) (51.9%–70.6%)	121/258 (46.9%) (40.7%–53.2%)	χ^2 (1) = 6.8; $p < .05$
Panic disorder			
Current	3/112 (2.7%) (0.6%–7.6%)	4/262 (1.5%) (0.4%–3.9%)	p = .35
Panic disorder without agoraphobia			
Lifetime	15/111 (13.5%) (7.8%–21.3%)	19/261 (7.3%) (4.4%–11.3%)	χ^2 (1) = 3.64; p = .06
Panic disorder with agoraphobia			
Lifetime	7/111 (6.3%) (2.6%–12.6%)	5/261 (1.9%) (0.6%–4.4%)	χ^2 (1) = 4.81; $p < .05$
Agoraphobia			
Current	4/113 (3.5%) (2.0%–11.3%)	6/264 (2.3%) (0.8%–4.9%)	p = .35
Lifetime	6/112 (5.4%) (1.0%–8.8%)	7/264 (2.7%) (1.1%–5.4%)	χ^2 (1) = 1.73; p = .19
Social phobia			
Current	9/112 (8.0%) (3.7%–14.7%)	9/263 (3.4%) (1.6%–6.4%)	χ^2 (1) = 3.66; p = .06
Lifetime	12/111 (10.8%) (5.7%–18.1%)	16/263 (6.1%) (3.5%–9.7%)	χ^2 (1) = 2.52; p = .11
Specific phobia			
Current	10/113 (8.8%) (4.3%–14.1%)	22/263 (8.4%) (5.3%–11.7%)	χ^2 (1) = 0.02; p = .88
Lifetime	14/112 (12.5%) (7.0%–20.1%)	26/263 (9.9%) (6.6%–14.2%)	χ^2 (1) = 0.56; p = .45
Obsessive-compulsive disorder			
Current	6/112 (5.4%) (2.0%–11.3%)	8/264 (3.0%) (1.3%–5.9%)	χ^2 (1) = 1.19; p = .26
Lifetime	8/112 (7.1%) (3.1%–13.6%)	11/264 (4.2%) (2.1%–7.3%)	χ^2 (1) = 1.45; p = .23
Posttraumatic stress disorder			
Current	17/113 (15.0%) (9.0%–23.0%)	29/263 (11.0%) (7.5%–15.5%)	χ^2 (1) = 1.19; p = .28
Lifetime	42/112 (37.5%) (28.5%–47.2%)	56/263 (21.3%) (16.5%–26.7%)	χ^2 (1) = 10.69; p = .001
Generalized anxiety disorder			
Current	24/112 (21.4%) (13.8%–29.0%)	24/263 (9.1%) (5.9%–13.3%)	χ^2 (1) = 10.65; p = .001
Anxiety GMC			
Current	0/113 (0%) (N/A)	0/264 (0%) (N/A)	N/A
Lifetime	0/112 (0%) (N/A)	1/263 (0.4%) (0.01%–2.1%)	p = .70
Substance-induced anxiety			
Current	0/112 (0%) (N/A)	1/264 (0.4%) (0.01%–2.1%)	p = .70
Lifetime	0/111 (0%) (N/A)	2/262 (0.8%) (0.1%–2.7%)	p = .49
Anxiety NOS			
Current	12/113 (10.6%) (4.9%–16.3%)	33/262 (12.6%) (8.8%–17.2%)	χ^2 (1) = 0.29; p = .59
Lifetime	12/112 (10.7%) (5.0%–16.4%)	37/261 (14.2%) (10.2%–19.0%)	χ^2 (1)=0.82; p = .36
Hypochondriasis			
Current	2/113 (1.8%) (0.2%–6.3%)	2/262 (0.8%) (0.1%–2.7%)	p = .35

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue; GMC = due to general medical condition; NOS = not otherwise specified. Fisher's Exact Test was used when cell sizes were <5.

TABLE 6. Prevalence of Eating Disorders Among Cases With CFS and Persons With ISF

	CFS	ISF	Comparison
	n Affected/Total (%) (95% Exact Confidence Limits)	*n* Affected/Total (%) (95% Exact Confidence Limits)	
Eating disorders			
Current	5/112 (4.5%) (1.5%–10.1%)	7/264 (2.7%) (1.1%–5.4%)	χ^2 (1) = 0.84; p = .36
Lifetime	10/113 (8.8%) (4.3%–15.7%)	12/264 (4.5%) (2.4%–7.8%)	χ^2 (1) = 2.67; p = .10
Anorexia—lifetime	3/113 (2.7%) (0.6%–7.67%)	2/264 (0.8%) (0.1%–2.7%)	p = .16
Bulimia—lifetime	0/113 (0%) (N/A)	2/264 (0.8%) (0.1%–2.7%)	p = .49
Binge eating			
Current	5/112 (4.5%) (1.5%–10.1%)	7/264 (2.7%) (1.1%–5.4%	χ^2 (1) = 0.84; p = .36
Lifetime	8/113 (7.1%) (3.1%–13.5%)	8/264 (3.0%) (1.3%–5.9%)	χ^2 (1) = 3.19; p = .07

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue. Fisher's Exact Test was used when cell sizes were <5.

TABLE 7. Age-Standardized Prevalence Rates in Hundreds, Represented as Percent, Among Cases With CFS and Persons With ISF

Comorbidity	CFS (%)	ISF (%)
Affective disorders—current	29.2	22.6
Affective disorders—lifetime	84.8	53.2
Anxiety disorders—current	47.3	33.9
Anxiety disorders—lifetime	61.7	44.2
Eating disorders—current	4.6	3.2
Eating disorders—lifetime	10.2	4.6
Substance disorder—lifetime	31.5	26.2

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue.

TABLE 8. Odds Ratios for Having Any Type of Psychiatric Disorders

	CFS (% With Diagnosis)	ISF (% With Diagnosis)	OR (95% CI)
Current psychiatric disorders (yes/no) OR	56.64	44.70	1.62 (1.04–2.52)
Current psychiatric disorders (yes/no) Adjusted OR[a]			1.60 (1.02–2.52)
Lifetime psychiatric disorders (yes/no) OR	89.38	78.79	2.27 (1.16–4.42)
Lifetime psychiatric disorders (yes/no) Adjusted OR[b]			2.19 (1.12–4.29)

CFS = chronic fatigue syndrome; ISF = insufficient symptoms or fatigue; OR = odds ratio; CI = Confidence Interval.

[a] Adjusted for age, sex, race (White/non-White), geographic strata; p value for Hosmer and Lemeshow Goodness-of-Fit Test is 0.24.

[b] Adjusted for age, sex, race (Black/non-Black), geographic strata; p value for Hosmer and Lemeshow Goodness-of-Fit Test is 0.36.

standardized rates are similar to nonstandardized rates reported in Tables 2 to 6, with the exception of current affective disorders in the ISF group (22.6% age-standardized versus 12% nonstandardized rates).

Sixty-four persons with CFS (57%) had at least one current psychiatric diagnosis, in contrast to 118 persons with ISF (45%) (χ^2 (1) = 4.52; p = .03), whereas the number of current psychiatric diagnoses in both groups ranged from 0 to 8 (CFS: median = 1, mean = 1.2, standard deviation (SD) = 1.4, range = 0–7; ISF: median = 0, mean = 0.7, SD = 1.1, range = 0–8). CFS cases were 62% more likely to have at least one current psychiatric disorder compared with the ISF group ($OR_{unadjusted}$ = 1.62; 95% CI = 1.04–2.52) (Table 8). Adjustment for demographic factors (age, sex, race/ethnicity, and geographic strata) did not alter the OR appreciably. The likelihood of having CFS increased 34% with each additional current psychiatric diagnosis ascribed to a person (OR = 1.34, 95% CI = 1.12–1.61).

A total of 101 persons with CFS (89%) had at least one lifetime psychiatric diagnosis compared with 208 persons with ISF (79%) (χ^2 (1) = 6.01; p = .01), and the frequency in both groups ranged from 1 to 8 (CFS: median = 2, mean = 2.4, SD = 1.6; ISF: median = 1, mean = 1.7, SD = 1.5). CFS cases were more than twice as likely to have at least one psychiatric comorbidity sometime during their lifetime as the ISF group ($OR_{unadjusted}$ = 2.27, CI = 1.16–4.42) (Table 8). Again, adjustment for covariates had negligible effects on the OR. The likelihood of having CFS increased 32% with each additional lifetime psychiatric diagnosis (OR = 1.32, 95% CI = 1.14–1.52).

All participants were asked whether they had been seeking treatment from a psychiatrist, psychologist, or counselor during the previous 6 months. Despite the high rates of psychiatric comorbidity in both groups, only 11 persons with CFS (9.8%) (of 112 who responded to this question) and 25 persons with ISF (9.5%) (of 264 who responded to this question) had

sought treatment. Of these 11 CFS cases, six (54.5%) subjects had at least one current psychiatric comorbidity, in contrast to 57 of the nontreatment-seeking CFS cases (59.4%). In the ISF group, 15 persons (60%) who sought treatment had at least one current psychiatric comorbidity, in contrast to 104 (45.2%) who did not seek treatment. Of those who reported having seen a psychiatrist, psychologist, or counselor during the previous 6 months, 10 out of 11 CFS cases reported one to six visits during this time frame, and only one case reported >6 visits (12 visits). Twenty persons with ISF reported one to six visits during the previous 6 months, and five reported >6 visits.

We also queried participants about their current psychotropic medications and examined two broad categories: antidepressants and sedatives. Antidepressants (tricyclic antidepressants, specific serotonin reuptake inhibitors) were used in the 2 weeks preceding the visit to the clinic by 41 of the CFS group (36.3%) and 48 of the ISF group (18.2%). Thus, persons with CFS were significantly more likely than persons with ISF to use antidepressants (OR = 2.43, 95% CI = 1.46–4.05). Twenty persons with CFS (17.7%) reported using sedatives compared with only 18 with ISF (6.8%). Thus, persons with CFS were significantly more likely to use sedatives than those with ISF (OR = 2.76, 95% CI = 1.38–5.52). The reported indications for use of sedatives were equally sleep problems or anxiety (or both) and did not differ between the two groups.

DISCUSSION

The current study demonstrates that individuals diagnosed with CFS or subsyndromic unwellness (i.e., ISF) have high rates of both current and lifetime psychiatric disturbance. Almost 60% of persons with CFS fulfilled the criteria for at least one current psychiatric diagnosis, and almost 90% had at least one lifetime psychiatric condition. In the ISF group, the rates were slightly lower but still very high with >45% having a current psychiatric diagnosis and almost 80% having a lifetime psychiatric comorbidity. Further analyses showed that the likelihood of having CFS, i.e., fulfilling the full case-defining criteria for CFS, increased by >30% with each additional psychiatric diagnosis (both current and lifetime).

Our findings are in accord with several previous studies in primary and tertiary care samples on the comorbidity of psychiatric conditions in CFS. Wood et al. detected psychiatric disorders in 41% of a group fulfilling the Oxford criteria for CFS (10). Buchwald and colleagues (13) reported that 35% of a total of 255 patients (including both CFS cases diagnosed according to CDC 1988 criteria and those with chronic fatigue) had a current psychiatric disorder and 82% had a lifetime psychiatric disorder (based on DSM-III-R criteria). In CFS patients fulfilling the CDC 1994 criteria, current DSM-III-R diagnoses were present in 77.4% and lifetime diagnoses were present in 81.1% (14). In a case-series study, a 45% prevalence of lifetime DSM-IV axis I disorders was reported in a CFS group (16).

Although most previous studies show similarly high prevalence rates of psychiatric comorbidity, the current study extends the existing literature in a significant manner. All of the above-mentioned studies assessed CFS patients from primary or specialized healthcare services. This approach is susceptible to a significant patient selection bias in that individuals with psychosocial problems might use primary or tertiary care institutions more often than persons identified from the general population (29). Considering the overlap between symptoms and high comorbidity rates between CFS and irritable bowel syndrome (IBS) (30), it might be interesting to compare findings of psychiatric comorbidity in these two conditions. Two population-based studies found high rates of psychiatric comorbidity in IBS cases (31,32). However, the rates were lower than in our study of CFS. It might be assumed that the differences in prevalence rates between our study and population-based studies in IBS most likely reflect different methodological approaches. Future studies might want to compare directly CFS and IBS in one study regarding psychiatric comorbidity.

An additional difference between our study and previous studies is the fact that studies published before 1994 and some time later used the CDC 1988 criteria, which by definition specifically excluded all psychiatric conditions for the diagnosis of CFS. Therefore, most of these studies were performed in subjects with chronic fatigue, i.e., varying length of presence of impairing fatigue. However, the criteria for chronic fatigue in these earlier studies and the 1994 criteria for CFS vary markedly. Moreover, in most studies of CFS, adherence to the 1994 criteria and adequate assessment of the criteria might not have been thorough, because most of the published papers failed to report details on medical examinations, psychiatric exclusionary conditions, and other factors outlined by the International CFS Research Group (23). Finally, the studies differed in their use of structured assessment instruments for psychiatric diagnoses.

Our study diverges from other studies in that it also included a group of chronically fatigued subjects who did not fulfill the criteria for a CFS diagnosis because they had an insufficient number of symptoms or insufficient fatigue severity. We were able to show that, with each additional current and lifetime psychiatric diagnosis, the likelihood of having CFS increased by >30%. This might indicate that having a psychiatric comorbidity was associated with an increased probability of the presence of sufficient symptom load and severity to receive a full diagnosis of CFS compared with fulfilling the criteria for subsyndromic CFS. Support for this notion comes from a previous study showing that psychiatric comorbidity increased linearly with the number of lifetime medically unexplained physical symptoms in patients with chronic fatigue (18). The idea of a spectrum of severity and its relationship to psychiatric illness in medically unexplained symptoms, as previously described (33,34), is intriguing and warrants further investigation.

The prevalence of comorbid psychiatric conditions in cases with CFS is alarmingly high, especially in light of our finding that individuals with CFS did not seek adequate treatment for their psychiatric symptoms. Less than 10% saw a mental

healthcare specialist in the 6 months preceding the study, despite the fact that almost 60% of individuals with CFS suffered from a clinically relevant psychiatric condition. Alternatively, CFS patients are treated by their individual practitioners. For an explanation of why CFS patients with severe psychiatric distress do not seek mental health care, it might be instructive to consider "perceived barriers" to accessing health services. Recently (35), we showed that about 34% of CFS cases reported accessibility barriers to healthcare utilization and 19% reported belief barriers. The latter include fear of stigma, fear of confronting the health problems, and fear that other people would think that they are "crazy." Also, persons suffering from CFS tend to seek medical explanations for their symptoms and often deny any psychological component to their illness (36,37). This could explain low rates of psychiatric care-seeking in a population of severely affected individuals. Comparisons of broad categories of psychiatric conditions indicate that affective disorders seem to be more prevalent in CFS than in ISF, whereas the two groups did not substantially differ in other categories. This suggests that CFS might particularly be associated with an increased occurrence of depressive symptoms.

Our results need to be considered in light of some limitations. Due to the cross-sectional nature of the current study, we were not able to address the question of whether psychiatric illness preceded CFS or developed after CFS. Also, it needs to be considered that a variety of psychiatric conditions are exclusionary in the diagnosis of CFS. Prevalence of exclusionary conditions, such as major depressive disorder of the melancholic subtype, psychotic disorders, current substance abuse and dependence, and severe eating disorders like bulimia and anorexia nervosa, was therefore not included.

In conclusion, the high prevalence of psychiatric conditions in cases of CFS identified from the general population is an important finding that will help explain the impact of CFS on functional capacity, well-being, and suffering. Also, our findings suggest that individuals with CFS are likely undertreated for psychiatric illness and therefore healthcare experts are urged to take appropriate steps. Both physicians and psychiatric specialists need to be aware of the high prevalence of psychiatric conditions in CFS and need to have tools to address these conditions in their CFS patients. Specifically, future treatment studies should take into account the presence of psychiatric comorbidity, as therapeutic outcome might be heavily influenced by the additional burden exerted by psychiatric illness.

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