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Contrasting Chronic Fatigue Syndrome versus Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

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Abstract

Background—Much debate is transpiring regarding whether chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) are different illnesses. Several prior studies that compared the Fukuda et al. CFS criteria to the Canadian ME/CFS criteria found that the Canadian criteria identified patients with more functional impairments and greater physical, mental, and cognitive problems than those who met Fukuda et al. criteria.[3,4] These samples were located in the Chicago metropolitan area, so the results could not be generalized to other locations. In addition, past studies used a symptom questionnaire that was not specifically developed to tap the Canadian criteria.

Purpose—The present comparative study of CFS and ME/CFS criteria was intended to correct the methodological problems of prior studies.

Methods—This article used data from three distinct samples to compare patients who met criteria for the ME/CFS Canadian clinical case definition [1] to those who met the Fukuda et al. CFS case definition.[2]

Results—Findings indicated that fewer individuals met the Canadian criteria than the Fukuda et al. criteria. Those who met the Canadian criteria evidenced more severe symptoms and physical functioning impairment

Conclusions—Future research should continue to compare existing case definitions and determine which criteria best select for this illness.

Keywords

chronic fatigue syndrome; myalgic encephalomyelitis/chronic fatigue syndrome; Fukuda criteria; Canadian clinical criteria

Fukuda et al.'s widely used case definition for chronic fatigue syndrome (CFS) [2] employs polythetic criteria, i.e., a set of symptoms in which not all need to be present to make a diagnosis. More specifically, the Fukuda et al. criteria only require four of eight core symptoms. However, patients do not need to have what appear to be critical CFS symptoms such as post-exertional malaise and memory and concentration problems.[1] In addition, this case definition has been characterized as lacking operational criteria and guidelines to assist health care professionals in its interpretation and application.[5,6]

The term myalgic encephalomyelitis (ME) was used prior to the term CFS.[7–10] Maes, Twisk and Johnson [11] used the Fukuda et al. criteria to define two subtypes of patients: those who met the Fukuda et al. criteria and reported post-exertional malaise (N = 49, defined as ME) and those who met the Fukuda et al. criteria but did not report post-exertional malaise (N = 58, defined as CFS). This study indicated that the group who reported post-exertional malaise had more severe symptoms and immune dysfunction.

Following the creation of the Fukuda et al. criteria, a definition of the illness was developed called the Canadian ME/CFS clinical case definition.[1] Unlike the polythetic approach of the Fukuda et al. criteria, the Canadian criteria require the presence of specific symptoms, such as post-exertional malaise. The Canadian criteria have not been widely adopted by researchers and clinicians, in part due to the large number of symptoms (seven) for which the diagnosing physician must check. The original Holmes et al. criteria [12] for CFS were criticized for requiring 8 symptoms, as this might have led to identifying cases with somatization rather than CFS. By comparison, the Fukuda et al. criteria only require 4 symptoms. Unfortunately, all of these definitions were created through consensus rather than empirical methods, leading to uncertainty regarding their validity.

Jason et al. [3] compared persons meeting the Canadian criteria, the Fukuda et al. criteria, and people experiencing chronic fatigue explained by psychiatric reasons. The Canadian criteria, in contrast to the Fukuda et al. criteria, selected cases with less psychiatric comorbidity, more physical functioning impairment, more fatigue and weakness, and more neuropsychiatric and neurological symptoms. In an effort to better operationalize the Canadian criteria, Jason et al. [13] specified explicit rules for determining ME/CFS status using this case definition. Using this more precise method to operationalize the Canadian criteria, Jason et al. [4] compared those who met the Canadian criteria to those who met only the Fukuda et al. criteria without meeting the Canadian criteria. Findings indicated that the Canadian criteria identified individuals with more severe symptoms and greater functional disability than those who met only the Fukuda criteria.

In a later study, Jason et al. [14] compared the Canadian criteria with a different set of empiric CFS criteria developed by Reeves et al. [15] that were based on the Fukuda et al. criteria. The authors used data mining with decision trees to determine which survey items were able to best identify patients with CFS. Jason et al. [14] found that the Reeves et al. criteria were able to correctly identify 79% of the CFS cases, whereas the Canadian criteria were able to detect 87% of the cases. In addition, the Canadian criteria selected items representing higher frequency symptoms [16] that are cardinal features of the illness, including the inability to concentrate, post-exertional malaise, and unrefreshing sleep, whereas the Reeves et al. criteria did not identify these items.

One limitation of the studies reviewed above [3,13,14] was that individuals were identified for inclusion in the samples by meeting the polythetic Fukuda et al. criteria. The subset of each sample who met the more stringent Canadian criteria was then compared to the remaining group of individuals who met only the Fukuda et al. criteria. In addition, the samples were located in the Chicago metropolitan area, so similar results might not occur in other locations. Finally, these studies used the CFS Questionnaire, which was not developed for the specific purpose of identifying the Canadian criteria. In contrast, the DePaul Symptom Questionnaire (DSQ) [13] was developed to assess both the Fukuda et al. and Canadian criteria. The present study examined two US-based samples and one sample from Great Britain, each with a different case ascertainment method, in order to identify potential differences in symptomatology and functioning between CFS and Canadian criteria cases.

Method

Research Participants

The *DePaul Sample* consisted of an international convenience sample of adults who self-identified as having CFS, ME/CFS or ME. The *SolveCFS BioBank Sample* included participants who had been diagnosed by a licensed physician who specialized in the illness. Finally, the *Newcastle Sample* consisted of patients referred to the Newcastle-upon-Tyne Royal Victoria Infirmary from primary care, and these patients were given a complete medical workup. Therefore, the three samples were constructed using varied methods of patient ascertainment, and these methods represent the current techniques available for recruiting patients into studies.

DePaul Sample—To be eligible for inclusion in the DePaul sample, an individual needed to be between the ages of 18 and 65, capable of reading and writing English, and have a self-reported current diagnosis of CFS, ME/CFS or ME. Following approval by DePaul University's Institutional Review Board, participants were recruited from a variety of sources, including posting on internet forums, visiting support groups, re-contacting individuals who had participated in the DePaul University's studies in the past and had indicated interest in future studies, and contacting individuals who had emailed the team's address in the past with interest in future studies.

Participants were given three options for completing the surveys: an electronic survey, a hard-copy survey, or a verbal survey over the telephone. All participants were given the opportunity to complete these surveys at home or in person at the Center for Community Research at DePaul University. The first 100 individuals who completed the survey received a \$5.00 gift card to Amazon.com for their participation.

SolveCFS BioBank Sample—Data from the SolveCFS BioBank were de-identified and shared with the DePaul Research Team by the CFIDS Association of America. The SolveCFS BioBank has clinical information and blood samples on a sample of individuals (N = 242) who were diagnosed by a licensed physician specializing in CFS, ME/CFS, and ME. The sample used in the present study included only those over 18 years of age. Participants were recruited by the CFIDS Association of America through their website, other social networking devices, internet forums, and physician referral. All participants who met eligibility criteria completed a written informed consent process before being included in the sample. Participants completed the study measures electronically or by hard copy.

Newcastle Sample—Participants in the third sample were identified by primary care physicians who referred patients with a suspected diagnosis of CFS for a complete medical assessment at the Newcastle-upon-Tyne Royal Victoria Infirmary clinic. At the infirmary, a comprehensive medical history and examination was performed by an experienced consultant physician. Those who met eligibility criteria completed a written informed consent process before being included in the sample. They completed the study measures by hard copy.

Measures

The DePaul Symptom Questionnaire (DSQ)—Participants from the three samples completed the DePaul Symptom Questionnaire (DSQ) [13], a self-report measure consisting of items related to the dimensions of both the Canadian and Fukuda et al. case definitions (see Table 3 for a description of these items). Participants were asked to rate each symptom's frequency over the past 6 months on a 5-point Likert scale for which 0=none of the time, 1=a little of the time, 2=about half the time, 3=most of the time, and 4=all of the time.

Likewise, participants were asked to rate each symptom's severity over the past 6 months on a 5-point Likert scale for which 0=symptom not present, 1=mild, 2=moderate, 3=severe, and 4=very severe. Ratings of both frequency and severity needed to be 2 or higher in order to qualify a symptom to meet case definition criteria (see below for more details). The current study was the first to use the DSQ.

The development of the DSQ was based upon the CFS Questionnaire [17], which evidenced good inter-rater and test-retest reliability and was able to sensitively distinguish among individuals with CFS, individuals with Major Depressive Disorder, and healthy controls.[18] To facilitate comparison with the CFS Questionnaire, the DSQ frequency and severity scores were multiplied by 25 to create a 100-point scale. These 100-point frequency and severity scores were then averaged to obtain a composite score for each symptom. The DSQ was specifically developed to assess both the Fukuda et al. and Canadian criteria.

Functional status

Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36 or RAND Questionnaire): The SF-36 is a 36-item self-report measure of functional status related to health.[19] A higher score indicates better health or less impact of health on functioning. An example of a question on this form follows: Does your health now limit you in these activities? Walking one block (Yes, limited a lot; Yes, limited a little; No, not limited at all). Test construction studies for the SF-36 have shown adequate internal consistency, significant discriminant validity among subscales, and substantial differences between patient and non-patient populations in the pattern of scores.[20]

Case Definitions

CFS Case Definition—A case of CFS is defined by Fukuda et al. [2] as the presence of the following criteria: (1) clinically evaluated, unexplained, persistent or relapsing chronic fatigue that is of new or definite onset (has not been lifelong); 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 (2) the concurrent occurrence of four or more core symptoms, all of which must have persisted or recurred during six or more consecutive months of illness.[2,p.956]

Canadian Clinical ME/CFS Case Definition—The Canadian clinical ME/CFS case definition [1] specifies that post-exertional malaise must occur with a loss of physical or mental stamina, rapid muscle or cognitive fatigability, usually taking 24 hours or longer to recover. In addition, two or more neurological/cognitive manifestations must be present (e.g., confusion, impairment of concentration and short-term memory). Unrefreshing sleep or poor sleep quantity or rhythm disturbance must be reported, as well as a significant degree of arthralgia and/or myalgia. Finally, one symptom from two of the following categories must be present: autonomic manifestations (e.g., neurally mediated hypotension, light headedness), neuroendocrine manifestations (e.g., recurrent feelings of feverishness, cold extremities), and immune manifestations (e.g., recurrent sore throats). In order to assess all of the symptoms mentioned in the Carruthers et al. [1] article, 54 items were used.

Statistics—Across all three samples, all but one participant who met the Canadian criteria also met the Fukuda et al. criteria; therefore, two independent groups were created for comparison purposes. Participants who met the Canadian criteria (referred to as the ME/CFS group) were compared to participants who met the Fukuda case definition but did *not* meet the Canadian criteria (referred to as the CFS group). MANOVAs were used to compare the ME/CFS and CFS groups within the DePaul and BioBank samples. MANOVAs could not be used for the Newcastle sample comparisons due to the smaller sample size and violations

of MANOVA assumptions; thus, individual ANOVAs were conducted for each symptom. Due to the number of comparisons and associated risk of Type I error, results significant at the $p < 0.01$ level can be interpreted with more confidence than those significant at the $p < 0.05$ level.

Results

Description of Samples

DePaul Sample—Of the original 217 individuals who completed the DSQ in the DePaul sample, 189 participants were included in the present study. Twenty-eight participants were excluded due to endorsing lifelong fatigue or exclusionary medical or psychological conditions that preclude a diagnosis of CFS based on the Fukuda et al. case definition.

Demographically, the sample of 189 participants was 83.5% female and 16.5% male (See Table 1). 97.9% of the sample identified as Caucasian, 0.5% as Asian, and the remaining 1.6% identified as “Other.” 55.3% of the sample stated that they were currently on disability, with only 12.8% of the sample working part- or full-time. With regard to education level, 39.9% of the sample held a professional degree; 35.6% held a standard college degree; 17.6% attended college for at least one year; and 6.9% completed high school or had a GED. The mean age of the sample was 51.6 ($SD = 11.2$).

BioBank Sample—The BioBank sample was 98.3% Caucasian, 0.8% Asian, and 0.8% of the sample identified as “Other.” With regard to gender, 73.4% of the sample was female. Only 12% of the sample was working part- or full-time, with 64.7% on disability. Regarding education level, 24.4% of the sample held a graduate or professional degree; 43.2% completed college; 20.7% had completed some college; 11.2% had a high school degree or GED; and 0.4% refused to answer. The average age of the sample was 49.7 ($SD = 12.8$).

Newcastle Sample—A total of 96 participants were included in the Newcastle sample (4 participants were excluded for morbid obesity or endorsing lifelong fatigue). The sample was 99% Caucasian and 1% multiracial, and 81.3% of participants were female. Of this sample, 36.1% of participants were working either part- or full-time, and 30.2% were on disability. With regard to education level, 18.8% had a graduate or professional degree; 28.1% had a college degree; 20.8% had completed at least one year of college; 13.5% had a high school degree; and 11.5% had not completed high school. The average age of the sample was 46 ($SD = 14.2$).

Demographics

Table 1 presents demographic data for the ME/CFS and CFS groups from the three samples, as well as data on other domains such as illness onset. There were two significant demographic differences between these groups. In the BioBank sample, the ME/CFS group contained a significantly larger percentage of participants who reported being on disability compared to the CFS group [$\chi^2(7, N = 224) = 25.22, p < 0.01$]. In the Newcastle sample, the ME/CFS group had significantly higher education levels compared to the CFS group [$p = 0.04$, two-tailed Fisher's exact test].

Functional Status

Table 2 presents data from the SF-36. For the DePaul sample, the MANOVA indicated that the ME/CFS group was significantly different from the CFS group [Wilks' Lambda = 0.82, $F(8, 170) = 4.79, p < 0.001$]. The univariate tests revealed that the ME/CFS group had significantly worse Physical Functioning [$F(1, 177) = 4.92, p = 0.03$] and Bodily Pain [$F(1, 177) = 35.21, p < 0.001$] scores than the CFS group. The BioBank MANOVA also revealed

a significant difference between the ME/CFS and CFS groups [Wilks' Lambda = 0.82, $F(8, 213) = 5.94$, $p < 0.001$] on the SF-36. Univariate tests showed significantly worse scores for the ME/CFS group compared to the CFS group for the following subscales: Physical Functioning [$F(1, 220) = 14.40$, $p < 0.001$], Bodily Pain [$F(1, 220) = 28.10$, $p < 0.001$], General Health [$F(1, 220) = 8.21$, $p = 0.01$], Social Functioning [$F(1, 220) = 24.14$, $p < 0.001$], Mental Health [$F(1, 220) = 4.21$, $p = 0.04$], and Vitality [$F(1, 220) = 17.36$, $p < 0.001$]. Finally, for the Newcastle sample, individual ANOVAs revealed significantly worse scores for the ME/CFS group for the following subscales: Physical Functioning [$F(1, 81) = 6.43$, $p = 0.01$], Bodily Pain [$F(1, 81) = 5.71$, $p = 0.02$], General Health [$F(1, 80) = 12.63$, $p < 0.01$], and Social Functioning [$F(1, 81) = 5.38$, $p = 0.02$].

In summary, all samples showed significantly worse Physical Functioning and Bodily Pain scores for the ME/CFS group. In addition, both the BioBank and Newcastle samples showed significantly worse General Health and Social Functioning scores for the ME/CFS group. Only the BioBank sample showed significantly worse scores for the ME/CFS group for the Mental Health and Vitality subscales. No significant differences were found in any of the samples for the Role Physical or Role Emotional subscales.

Table 3 lists the Fukuda et al. and Canadian criteria symptoms. The symptoms are categorized into the following groups: Fatigue, Post-Exertional Malaise, Sleep, Pain, Neurological, Autonomic, Neuroendocrine, and Immune, based on the symptom categories described in the Canadian criteria. All MANOVAs for the DePaul and BioBank samples were significant, and univariate tests revealed that the ME/CFS group had significantly worse scores for 51 of the 54 symptoms analyzed in the DePaul sample and for all 54 items in the BioBank sample. The Newcastle ME/CFS group had significantly worse scores for 28 of the 54 items compared to the CFS group. Across all three samples, most of the significant items were significant at the $p < 0.001$ level. For those items that were not significantly different, the ME/CFS group had directionally worse scores than the CFS group, with the exception of two items in the Newcastle sample (problems falling asleep and alcohol intolerance).

Discussion

Considerable debate has transpired regarding whether ME/CFS and CFS represent different illnesses, [21] as well as whether the criteria that designate these illnesses select different types of patients.[3,13,14] Different names (ME, CFS, and ME/CFS) and criteria [1,2,8,12,15,22,23] have been used to characterize the illness. By using three distinct data sets from different case ascertainment methods, the current study minimized selection bias, and consistent findings indicated that the ME/CFS criteria, when compared to the CFS criteria, selected a group of patients who had more severe functional impairments and symptoms.

The current study also determined the percentage of patients who met the different case definition criteria. For the Fukuda et al. case definition, 96.3% of the DePaul sample, 92.6% of the BioBank sample, and 86.5% for the Newcastle sample met criteria. For the Canadian criteria, 77.2% of the DePaul sample, 72.7% of the BioBank sample, and 72.9% of the Newcastle sample met criteria. These consistent findings across the three data sets suggest that about three fourths of those within disparate samples meet the case definition for ME/CFS, whereas the Fukuda et al. criteria identify a larger group of patients. In this study, considerable overlap existed in participants who met the CFS and ME/CFS case definitions. In all three samples, only one participant met the ME/CFS case definition but did not meet the CFS case definition. This trend is important to note in discussions regarding whether

CFS and ME/CFS are different illnesses, as, based on the data used for this study, the ME/CFS group appears to be a subset of the CFS group.

In order to achieve high levels of diagnostic reliability for a case definition, it is important to specify the domains or symptoms that must be assessed, as well as to provide specific ways of asking about these domains or symptoms using standardized questionnaires.[24] Even if the symptoms are well specified, a failure to carefully operationalize how the symptoms should be measured will compromise the diagnostic process. The present study, for example, suggests that about three quarters of patients in three distinct samples met the ME/CFS criteria. However, the original Canadian criteria did not specify whether the required symptoms needed to meet specific frequency and severity thresholds. In the Jason et al. [4] study, using a sample that was recruited for a non-pharmacologic treatment trial, over 90% of the sample met the ME/CFS criteria when just occurrence of symptoms was required rather than employing frequency and severity cutoffs. Fluge et al. [25] also found that over 90% of their sample met both CFS and ME/CFS criteria, yet it is unclear how the research team operationalized the ME/CFS criteria. In a different sample in the Jason et al. [4] study, only 50% met the ME/CFS criteria when the symptom frequency and severity cutoffs specified by Jason et al. [13] were employed. However, the current study suggests that about 75% of patients meet the ME/CFS criteria, as this percentage was replicated across three samples when the DSQ was used as the assessment instrument.

Measurement factors might explain this difference, as the DSQ used in the current study was specifically developed to assess the symptoms of ME/CFS whereas the Jason et al. [4] study used the CFS questionnaire, an older symptom assessment measure that was not developed to tap the ME/CFS symptoms. This same issue also may have occurred in a study by Pheby et al., [26] who found that 97% of their participants met the Fukuda et al. criteria, while only 53% met the Canadian criteria. Clearly, it is important to use questionnaires that adequately measure the symptoms of the case definition used, as efforts to assess symptoms that surveys were not initially intended to measure can introduce validity challenges.

For the SF-36 measures in Table 2, participants with ME/CFS had more physical functioning problems and bodily pain than those with CFS. However, for the scales related to mental and emotional functioning, the only significant difference occurred in the BioBank sample for the Mental Health subscale. In addition, for the symptoms listed in Table 3, the ME/CFS group reported worse symptom scores than the CFS group. Specifically, the ME/CFS group reported significantly worse scores for 51 items in the DePaul sample, all 54 items in the BioBank sample, and 28 items in the Newcastle sample. These data suggest that the ME/CFS case definition, which requires more cardinal features of this illness, such as post-exertional malaise, selected a more impaired group. This finding is also supported by the Maes, Twisk and Johnson study [11] described above, which compared those who met the Fukuda et al. criteria and also reported post-exertional malaise to those who met the Fukuda et al. criteria but did not report post-exertional malaise. This study found that the participants with post-exertional malaise had more severe symptoms and more immune abnormalities.

Jason et al. [27] factor analyzed symptoms from the Fukuda et al. criteria and compared the results to a second factor analysis that used symptoms from the Canadian criteria. A more interpretable factor structure was identified when using the Canadian criteria. The six factor solution obtained when using the Canadian criteria included items from the following domains: neurocognitive (e.g., slowness of thought), vascular (e.g., dizziness after standing), inflammation (e.g., chemical sensitivities), muscle/joint (e.g., pain in multiple joints), infectious (e.g., sore throat), and sleep/post-exertional (e.g., unrefreshing sleep). Other studies have also found support for dimensions specified in the Canadian criteria.[28,29]

The Fukuda et al. criteria do not include items from the vascular and inflammatory domains, whereas the Canadian criteria do include items from these domains. These findings suggest that the broader group of symptoms included in the Canadian criteria, but not the Fukuda et al. criteria, might be needed to accurately identify critical symptom domains of this illness. However, it is also possible that simply requiring more symptoms selects a more impaired group.

One limitation of the current study was that a structured clinical schedule was not administered to the patients in the three samples; therefore, some participants may have had exclusionary psychiatric illnesses. Psychiatric exclusions were identified through self-report data, and participants who reported an exclusionary illness were excluded from analysis. In a study assessing the accuracy of patient self-report data, Torres-Harding et al. [30] recruited a sample of 23 people diagnosed with CFS (all of whom had been medically and psychiatrically examined). The results of 14 participants' Structured Clinical Interview Schedule confirmed a lifetime diagnosis of a mood, anxiety, or psychotic disorder. Of those 14 patients, 12 (86%) were able to accurately self-report having at least one lifetime disorder, providing evidence for the validity of self-report data for assessing psychiatric comorbidity.

Another limitation is that the Fukuda et al. criteria were developed for research purposes while the Canadian criteria were developed for clinical purposes. For this study, the symptom criteria for both case definitions were operationalized in the same manner so that these case definitions could be meaningfully compared. In addition, the DSQ has not been independently validated, but the prior instrument upon which the DSQ was based had good psychometric properties [18], and the authors are currently collecting test-retest data on the DSQ for both patients and controls.

Over the past decades, there have been both different names (ME, CFS and ME/CFS) and criteria [1,2,8,22,23] used to describe this illness. Other criteria have also been proposed, [e.g., 31,32] but they have not been widely utilized by the research community. The current study compared to the most frequently used Fukuda et al. criteria to the less frequently used Canadian criteria, and findings indicated that the Canadian criteria selected similar percentages of participants and identified a group of patients who had more severe functional impairments and physical and cognitive symptoms in each of the three data sets analyzed. Future research should continue to compare and contrast current case definitions and better operationalize current criteria to reduce criterion variance. In addition, the use of more sophisticated analytic techniques could better determine the critical dimensions of a CFS or ME/CFS case definition.[14]

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Table 1

Demographics, Psychiatric Characteristics, and Onset Issues

	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
	M (SD)	M (SD)		M (SD)	M (SD)		M (SD)	M (SD)	
Age	53.8 (12.5)	50.9 (10.9)		52.3 (12.5)	48.9 (12.7)		50.8 (12.1)	45.0 (13.8)	
Other Demographic Information:	N (%)	N (%)	Sig.	N (%)	N (%)	Sig.	N (%)	N (%)	Sig.
Gender									
Male	9 (25)	22 (15)		15 (31)	45 (26)		3 (23)	13 (19)	
Female	27 (75)	124 (85)		33 (69)	131 (74)		10 (77)	57 (81)	
Race									
Caucasian	36 (97)	142 (98)		46 (96)	175 (99)		13 (100)	69 (99)	
Asian / Pacific Islander	0 (0)	1 (1)		2 (4)	0 (0)		0 (0)	0 (0)	
Other	1 (3)	2 (1)		0 (0)	1 (1)		0 (0)	1 (1)	
Marital status									
Married / Living with partner	20 (54)	82 (58)		28 (58)	100 (57)		7 (54)	37 (53)	
Separated	0 (0)	1 (1)		1 (2)	0 (0)		0 (0)	2 (3)	
Divorced	9 (24)	23 (16)		6 (13)	25 (14)		3 (23)	9 (13)	
Never married	8 (22)	36 (25)		13 (27)	47 (27)		3 (23)	22 (31)	
Widowed	0 (0)	0 (0)		0 (0)	4 (2)		0 (0)	0 (0)	
Work status									
On disability	15 (41)	87 (60)		23 (48)	125 (71)	**	4 (31)	25 (36)	
Student	1 (3)	5 (3)		1 (2)	9 (5)		0 (0)	4 (6)	
Homemaker	2 (5)	7 (5)		8 (17)	4 (2)		0 (0)	1 (1)	
Retired	7 (19)	15 (10)		9 (19)	13 (7)		3 (23)	11 (16)	
Unemployed	7 (19)	15 (10)		0 (0)	2 (1)		0 (0)	5 (7)	
Working part-time ¹	3 (8)	11 (8)					4 (31)	13 (19)	
Working full-time ¹	2 (5)	5 (3)		5 (10)	19 (11)		2 (15)	10 (14)	
Other	0 (0)	0 (0)		2 (4)	4 (2)		0 (0)	0 (0)	
Educational level									
Less than high school	0 (0)	0 (0)		0 (0)	0 (0)		3 (23)	6 (9)	*
High school	1 (3)	12 (8)		6 (13)	20 (11)		0 (0)	12 (18)	
Partial college	3 (8)	29 (20)		6 (13)	40 (23)		5 (38)	12 (18)	
Standard college degree	12 (32)	53 (37)		23 (48)	75 (43)		1 (8)	23 (35)	
Graduate / Professional degree	21 (57)	51 (35)		13 (27)	40 (23)		4 (31)	12 (18)	
	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Psychiatric and Onset Issues:									

Lifetime psychiatric diagnosis²

	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
Psychiatric and Onset Issues:	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Yes	14 (38)	64 (44)		<i>Data not available for this sample</i>			6 (46)	28 (40)	
No	23 (62)	82 (56)					7 (54)	42 (60)	
Time period of illness onset									
Within 24 hours	8 (22)	39 (27)		<i>Data not available for this sample</i> ³			0 (0)	6 (9)	
Over 1 week	8 (22)	20 (14)					1 (8)	8 (12)	
Over 1 month	7 (19)	16 (11)					0 (0)	3 (5)	
Over 2–6 months	7 (19)	23 (16)					4 (33)	15 (23)	
Over 7–12 months	1 (3)	9 (6)					2 (17)	8 (12)	
Over 1–2 years	2 (5)	17 (12)					2 (17)	9 (14)	
Over 3 or more years	4 (11)	32 (22)					3 (25)	17 (26)	
Cause of fatigue:									
Definitely physical	33 (92)	109 (75)		<i>Data not available for this sample</i>			5 (50)	38 (59)	
Mainly physical	3 (8)	27 (19)					2 (20)	14 (22)	
Equally physical and psychological	0 (0)	8 (6)					3 (30)	11 (17)	
Mainly psychological	0 (0)	1 (1)					0 (0)	1 (2)	
Definitely psychological	0 (0)	0 (0)					0 (0)	0 (0)	

*
p < 0.05;

**
p < 0.01

¹ Information regarding part-time or full-time work status is not available for the participants in the BioBank sample who indicated that they were working.

² Lifetime psychiatric diagnosis is based on self-report data regarding whether the participant had ever been diagnosed or treated for any of the following: major depression, major depression with melancholic features, bipolar disorder, anxiety, schizophrenia, an eating disorder, or substance abuse.

³ Time period of illness onset was not available for the majority of the BioBank sample, so it was not included in this table.

Table 2

SF-36 Subscales (Higher score indicates less impairment)

	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
	M (SD)	M (SD)		M (SD)	M (SD)		M (SD)	M (SD)	
Physical Functioning	35.6 (19.6)	28.1 (17.9)	*	46.8 (22.9)	33.2 (21.6)	***	49.1 (25.8)	29.6 (25.4)	*
Role Physical	7.4 (20.3)	4.0 (13.5)		3.6 (11.5)	3.3 (12.3)		4.2 (9.7)	9.4 (19.7)	
Bodily Pain	59.3 (24.3)	36.6 (19.7)	***	60.0 (24.8)	41.1 (21.0)	***	45.2 (25.0)	29.5 (21.3)	*
General Health	21.6 (14.6)	24.9 (14.8)		29.8 (17.8)	22.8 (14.2)	**	35.3 (18.9)	20.7 (12.5)	**
Social Functioning	23.3 (21.9)	19.2 (19.2)		42.7 (28.8)	24.0 (21.6)	***	39.4 (20.9)	25.0 (20.5)	*
Mental Health	72.3 (16.5)	71.5 (16.9)		72.2 (13.7)	66.0 (19.6)	*	55.7 (19.8)	61.3 (20.4)	
Role Emotional	76.6 (40.7)	80.8 (36.0)		79.2 (36.8)	68.2 (43.0)		52.8 (46.0)	63.7 (44.1)	
Vitality	15.8 (13.2)	12.2 (13.0)		20.6 (13.7)	12.0 (12.3)	***	21.2 (13.4)	13.5 (14.6)	

*
p < 0.05;**
p < 0.01;***
p < 0.001

Table 3

Symptoms (Higher score indicates more impairment)

	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
	M (SD)	M (SD)		M (SD)	M (SD)		M (SD)	M (SD)	
Fatigue	70.7 (22.5)	81.5 (13.2)	**	68.6 (20.3)	83.8 (13.6)	***	68.8 (10.0)	80.7 (14.8)	**
Post-exertional malaise									
Dead, heavy feeling after starting to exercise	52.5 (33.3)	72.2 (26.7)	***	59.9 (29.1)	76.0 (24.0)	***	48.9 (26.5)	74.3 (23.6)	**
Next-day soreness after non-strenuous activities	67.5 (23.7)	76.1 (19.3)	*	51.4 (29.8)	75.7 (22.5)	***	42.7 (29.4)	77.0 (19.1)	**
Mentally tired after slightest effort	48.9 (28.2)	66.5 (22.7)	***	42.9 (27.1)	64.8 (25.9)	***	51.1 (33.3)	69.8 (23.0)	
Minimum exercise makes you tired	65.4 (28.0)	78.5 (21.4)	**	59.9 (28.1)	79.4 (20.7)	***	51.0 (27.9)	74.6 (27.0)	***
Physically drained / sick after mild activity	67.9 (26.0)	73.0 (23.5)		56.3 (26.9)	76.1 (23.4)	***	43.8 (34.3)	69.7 (23.7)	*
Sleep									
Unrefreshing sleep	66.0 (25.6)	81.6 (18.8)	***	68.0 (21.5)	83.9 (18.1)	***	74.0 (18.0)	84.8 (15.9)	*
Need to nap during each day	48.0 (31.9)	52.0 (30.1)		44.5 (34.5)	59.5 (32.0)	**	40.6 (31.6)	52.9 (33.5)	
Problems falling asleep	41.0 (31.0)	63.9 (30.4)	***	43.6 (31.4)	64.0 (30.0)	***	57.3 (28.9)	51.6 (33.4)	
Problems staying asleep	47.7 (27.0)	65.0 (30.4)	**	39.2 (26.5)	58.1 (29.9)	***	40.6 (24.5)	51.7 (32.9)	
Waking up early in the morning	34.4 (29.6)	51.7 (33.7)	**	27.3 (23.8)	49.0 (32.8)	***	38.5 (25.3)	46.5 (32.9)	
Sleeping all day / staying awake all night	9.4 (24.4)	18.4 (27.6)		6.1 (18.4)	20.6 (28.2)	**	10.4 (19.1)	19.0 (25.9)	
Pain									
Muscle pain	35.6 (23.2)	67.5 (23.7)	***	43.1 (25.6)	69.7 (25.6)	***	51.9 (22.2)	77.5 (20.5)	***
Pain in multiple joints	25.8 (28.5)	56.5 (31.8)	***	34.0 (28.4)	62.9 (30.7)	***	42.3 (31.3)	72.5 (25.0)	***
Eye pain	9.8 (21.4)	38.0 (27.5)	***	10.9 (16.8)	30.2 (28.6)	***	31.7 (23.2)	41.8 (28.1)	
Chest pain	12.5 (21.4)	29.0 (24.5)	**	14.1 (17.8)	29.1 (26.2)	***	17.7 (24.7)	30.1 (25.2)	
Bloating	21.2 (21.3)	50.5 (26.7)	***	19.1 (20.8)	42.8 (29.6)	***	21.9 (26.2)	46.8 (31.5)	*
Abdomen / stomach pain	18.2 (19.8)	42.7 (24.7)	***	15.4 (21.5)	43.1 (29.6)	***	12.5 (18.5)	45.9 (31.3)	***
Headaches	29.5 (21.2)	53.4 (24.3)	***	36.4 (23.3)	52.2 (25.8)	***	44.8 (15.5)	63.0 (25.0)	**
Neurocognitive									
Muscle twitches	18.9 (23.2)	34.5 (25.4)	**	19.4 (79.5)	36.1 (26.9)	***	19.8 (20.3)	41.8 (31.3)	**
Muscle weakness	42.4 (29.5)	66.4 (24.6)	***	47.8 (27.3)	68.9 (25.5)	***	50.0 (25.0)	69.8 (24.3)	*
Sensitivity to noise	43.6 (29.2)	66.1 (25.9)	***	46.7 (30.1)	63.5 (28.6)	**	39.8 (29.5)	57.0 (32.5)	
Sensitivity to bright lights	39.4 (32.5)	61.8 (26.6)	***	43.1 (33.6)	60.3 (28.0)	**	40.6 (28.3)	54.6 (29.9)	
Problems remembering things	52.3 (20.1)	69.3 (21.2)	***	51.7 (27.4)	71.1 (22.7)	***	59.4 (25.1)	72.3 (21.5)	
Difficulty paying attention for long periods of time	61.0 (29.1)	75.3 (23.3)	**	46.4 (25.9)	60.2 (24.8)	**	62.5 (21.7)	77.0 (20.6)	*
Difficulty expressing thoughts	46.2 (23.7)	65.8 (22.4)	***	47.2 (26.9)	67.4 (23.5)	***	54.2 (26.8)	64.5 (25.0)	
Difficulty understanding things	32.6 (25.0)	50.8 (21.4)	***	36.9 (26.8)	52.8 (26.1)	***	46.9 (20.7)	56.9 (28.4)	
Can only focus on one thing at a time	53.0 (34.4)	72.9 (24.2)	***	53.3 (27.9)	64.5 (27.9)	*	53.1 (24.5)	68.7 (25.2)	
Unable to focus vision / attention	36.7 (29.1)	52.5 (23.2)	**	25.0 (23.8)	46.8 (27.5)	***	43.8 (24.1)	52.7 (26.5)	
Loss of depth perception	13.3 (27.4)	28.2 (31.6)	*	11.5 (19.6)	26.1 (30.9)	***	13.6 (27.6)	32.0 (33.1)	
Slowness of thought	43.2 (27.4)	62.4 (21.3)	***	46.1 (25.7)	60.0 (28.0)	**	45.8 (20.9)	60.9 (25.5)	
Absent-mindedness	43.2 (30.3)	64.2 (24.0)	***	45.8 (27.2)	63.4 (28.3)	***	43.8 (25.3)	66.1 (26.3)	**

	DePaul Sample			Solve CFS BioBank Sample			Newcastle Sample		
	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.	CFS	ME/CFS	Sig.
	M (SD)	M (SD)		M (SD)	M (SD)		M (SD)	M (SD)	
Autonomic									
Bladder problems	11.1 (21.7)	34.8 (33.1)	***	12.8 (23.6)	35.0 (34.4)	***	21.6 (26.9)	31.3 (33.0)	
Irritable bowel problems	23.3 (25.2)	51.1 (30.3)	***	20.6 (27.2)	50.0 (32.4)	***	27.1 (29.6)	54.0 (33.9)	*
Nausea	18.4 (20.8)	35.5 (23.5)	***	14.2 (18.4)	37.9 (26.5)	***	22.9 (14.9)	40.2 (26.7)	**
Feeling unsteady on feet	24.7 (24.2)	45.7 (25.7)	***	21.1 (22.6)	42.6 (25.6)	***	30.2 (18.0)	49.8 (29.0)	**
Shortness of breath	22.2 (25.4)	42.6 (25.2)	***	20.0 (23.0)	43.0 (28.3)	***	23.9 (14.2)	37.7 (28.6)	*
Dizziness / fainting	29.9 (26.1)	40.5 (24.6)	*	19.7 (19.9)	40.6 (28.4)	***	35.0 (19.4)	46.4 (30.3)	
Irregular heart beats	16.7 (22.0)	34.6 (27.3)	***	18.1 (23.2)	30.1 (25.3)	**	21.9 (25.6)	36.8 (32.3)	
Neuroendocrine									
Losing / gaining weight without trying	24.3 (32.9)	42.2 (33.9)	**	22.3 (30.1)	38.1 (35.7)	**	26.0 (27.9)	50.0 (35.1)	*
No appetite	13.9 (18.6)	25.1 (24.6)	*	10.6 (19.0)	24.3 (24.6)	**	11.4 (23.4)	31.3 (30.8)	*
Sweating hands	2.0 (6.9)	13.6 (22.1)	***	3.5 (14.0)	12.6 (22.6)	**	4.5 (10.1)	24.1 (30.3)	***
Night sweats	17.6 (22.3)	38.4 (31.5)	***	15.5 (23.7)	38.8 (31.5)	***	14.8 (18.4)	38.4 (30.5)	**
Cold limbs	38.9 (29.1)	55.1 (30.3)	**	18.8 (24.8)	48.5 (31.6)	>***	48.9 (27.1)	52.3 (34.5)	
Chills / shivers	17.9 (22.0)	39.9 (27.8)	***	14.1 (19.6)	34.2 (28.3)	***	21.9 (26.2)	39.1 (30.5)	
Feeling hot / cold for no reason	34.1 (24.8)	55.4 (28.4)	***	22.8 (24.9)	49.1 (29.9)	***	43.2 (27.6)	57.0 (28.7)	
Feeling like you have a high temperature	16.2 (18.8)	35.3 (31.0)	***	13.0 (19.3)	32.7 (29.3)	***	18.8 (28.4)	44.1 (31.6)	*
Feeling like you have a low temperature	15.2 (21.3)	31.7 (30.3)	**	11.5 (19.4)	26.3 (27.9)	***	15.0 (31.6)	25.7 (29.8)	
Alcohol intolerance	37.2 (37.9)	51.7 (39.6)	*	22.2 (31.9)	35.3 (39.3)	*	47.7 (28.9)	46.8 (38.1)	
Immune									
Sore throat	20.1 (17.0)	39.7 (23.6)	***	27.7 (19.7)	37.1 (25.9)	*	26.1 (31.4)	44.6 (28.4)	
Tender lymph nodes	25.7 (23.7)	46.0 (28.7)	***	26.3 (25.4)	45.1 (27.6)	***	20.5 (21.8)	41.5 (30.1)	*
Fever	6.3 (14.8)	17.0 (21.0)	**	7.4 (15.6)	17.6 (23.7)	**	4.5 (10.1)	24.8 (26.8)	***
Flu-like symptoms	32.3 (23.4)	58.1 (24.8)	***	27.7 (28.1)	54.1 (29.3)	***	31.3 (28.0)	58.6 (25.7)	**
Sensitivity to smells/foods/medications/chemicals	25.7 (33.9)	62.2 (32.4)	***	28.7 (32.5)	53.2 (35.1)	***	22.9 (33.2)	49.1 (36.6)	*

*
p < 0.05;

**
p < 0.01;

p < 0.001