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# Contrasting Case Definitions: The ME International Consensus Criteria vs. the Fukuda et al. CFS Criteria

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## Abstract

This article contrasts the Myalgic Encephalomyelitis International Consensus Criteria (ME-ICC) (Carruthers et al., 2011) with the Fukuda et al. (1994) CFS criteria. Findings indicated that the ME-ICC case definition criteria identified a subset of patients with more functional impairments and physical, mental and cognitive problems than the larger group of patients meeting the Fukuda et al. (1994) criteria. The sample of patients meeting ME-ICC criteria also had significantly greater rates of psychiatric comorbidity. These findings suggest that utilizing the ME-ICC may identify a more homogenous group of individuals with severe symptomatology and functional impairment. Implications of the high rates of psychiatric comorbidity found in the ME sample are discussed.

The Fukuda et al. (1994) case definition for chronic fatigue syndrome (CFS) requires an individual to experience six or more months of chronic fatigue of a new or definite onset that is not substantially alleviated by rest, not the result of ongoing exertion, and results in substantial reductions in occupational, social, and personal activities. The Fukuda et al. case definition uses a polythetic approach for assessing symptomatology. This type of approach means that not all definitional symptoms need to be present for a diagnosis to be made. Because the Fukuda et al. criteria only requires four symptoms out of a possible eight, critical CFS symptoms such as post-exertional malaise, and memory and concentration problems are not required of all patients.

The term Myalgic Encephalomyelitis (ME) was used prior to the term CFS (Acheson, 1959). ME was first described in literature of the 1930s, where an outbreak of Epidemic Neuromysthenia in L.A. County was called “atypical poliomyelitis” because of its resemblance to polio (Gilliam, 1938; Hyde, 2007). In 1956, an anonymous editorial in an issue of the Lancet coined the term benign Myalgic Encephalomyelitis (Anonymous Editorial, 1956). It was called ‘benign’ because the illness did not lead to patient death. Later, Ramsay (1988) published a case definition for this disease using the term Myalgic Encephalomyelitis (ME) and the term benign was dropped due to the seriousness of the disability created by the illness (Hyde, Goldstein, & Levine, 1992).

Later, a clinical case definition was developed utilizing the term ME/CFS (Carruthers et al., 2003). These criteria became known as the 2003 Clinical Canadian ME/CFS case definition,

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and unlike the polythetic approach of the Fukuda et al. (1994) criteria, they required the occurrence of specific ME/CFS symptoms. For example, these criteria specified 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. These criteria also required the presence of neurocognitive dysfunction. Jason and colleagues (2004) compared persons meeting the 2003 Clinical Canadian case definition (Carruthers et al.), persons meeting the Fukuda et al. criteria and persons with psychiatrically explained chronic fatigue. The Canadian ME/CFS criteria, in contrast to the Fukuda et al. criteria, selected cases with less psychiatric comorbidity, more physical functional impairment, more fatigue/weakness and more neuropsychiatric and neurological symptoms. Jason and colleagues (2006) later used the Canadian case definition model to develop a pediatric case definition for ME/CFS. Jason, Porter et al. (2010) found that the Fukuda et al. criteria were less sensitive than the Pediatric ME/CFS criteria developed in 2006 in identifying pediatric ME/CFS cases.

Several of the individuals who were involved in creating the 2003 Canadian ME/CFS criteria, as well as other scientists and clinicians, have recently published what they refer to as the International Consensus Criteria for Myalgic Encephalomyelitis (ME-ICC) (Carruthers et al., 2011). These authors indicated that the impact of the illness must result in a 50% or greater reduction of a patient's premorbid activity level for a diagnosis of ME-ICC. In addition, a person must have symptoms from four domains to meet criteria: Post-Exertional Neuroimmune Exhaustion; Neurological Impairment; Immune, Gastro-intestinal and Genitourinary Impairments; and Energy Production/Transportation Impairments. No empirical studies to date been published on this case definition.

In the present exploratory study, those meeting the ME-ICC criteria were compared to those only meeting the Fukuda et al. (1994) criteria, referred to as the Fukuda CFS group throughout the paper. It was hypothesized that the ME-ICC case definition would identify individuals with more serious symptomatology and greater functional disability than those only meeting the Fukuda criteria.

## Method

### Participant Recruitment

Participants were recruited from a variety of sources in the Chicago metropolitan area, including physician referrals. One hundred and fourteen individuals diagnosed with CFS according to the Fukuda et al. (1994) criteria were recruited and enrolled in the study. All data in the current study are from baseline measures of a larger, longitudinal, randomized controlled trial of non-pharmacological interventions (see Jason et al., 2007 for more details). Participants received $75 for completing the baseline interviews.

At initial screening, all participants were required to be at least 18 years of age, not pregnant, able to read and speak English, and considered to be physically capable of attending the scheduled sessions. Persons who used wheelchairs and those who were bedridden or housebound were excluded due to the practical difficulties of keeping therapy appointments required beyond baseline. Referrals to local physicians who treat CFS and to support groups were provided for those individuals who did not these requirements.

Following an informed consent procedure, prospective participants were initially screened for CFS using a structured questionnaire. The study was approved by the DePaul University Institutional Review Board.

## Measures

**The CFS Questionnaire—**This screening scale was initially validated by Jason and colleagues. (1997). This scale is comprised of demographic, health status, medication usage, and symptomatology questions, and it assesses for the 8 definitional symptoms of CFS (Fukuda et al., 1994). Hawk, Jason, and Torres-Harding (2007) revised this CFS Questionnaire and administered the questionnaire to three groups (CFS, Major Depressive Disorder, and healthy controls). The revised instrument, which was used in the present study, evidences good test-retest reliability and has good sensitivity and specificity.

The CFS Questionnaire was designed to assess for CFS as specified by Fukuda et al. (1994). For each symptom, participants were asked to indicate if the symptom had been present for 6 months or longer, if the symptom began before the onset of their fatigue or health problems, and how often the symptom is experienced (0 = never, 1 = seldom, 2 = often/usually, 3 = always). Participants were also asked to rate the severity of each symptom they endorsed on a scale of 0 to 100, where 0 = no problem and 100 = the worst problem possible. This is a numerical rating scale, which has been shown to be a consistently valid measure of symptom intensity, particularly for pain intensity (Jensen & Karoly, 1992). In assessing case definitional symptoms, items were designed to measure the eight core CFS symptoms (i.e., impaired memory or concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, new headaches, unrefreshing sleep, and post-exertion malaise) as specified by the Fukuda et al. case definition.

Both the frequency and severity of a symptom provides a more complete understanding of its impact. Therefore, a new scale was developed, combining frequency and severity ratings on the CFS Questionnaire to create one composite score. Scores were obtained by multiplying the frequency score by 33.3 so that the scale ranged from 0–100, which was comparable to the severity rating. Then the transposed frequency rating was multiplied by the severity rating, and the product was divided by 100 to yield a total score representing frequency and severity, that ranged from 0–100, with higher scores indicating more impairment.

Kroenke (2003) found that patients with CFS who experienced a greater number of symptoms were more likely to have a psychiatric diagnosis. Our data set contained 13 of the 15 symptom variables used in Kroenke's (2003) study including stomach pain; pain in arms, legs, or joints; menstrual cramps or other problems with your period; headaches; chest pain; dizziness; feeling your heart pound or race; shortness of breath; pain or problems during sexual intercourse; constipation, loose bowels, or diarrhea; nausea, gas, or indigestion; feeling tired or having low energy; and trouble sleeping. Back pain and fainting spells were the two Kroenke variables not included.

**Psychiatric Interview—**A semi-structured psychiatric interview, the Structured Clinical Interview for DSM-IV (SCID; Spitzer, Williams, Gibbon, & First, 1995) was administered

in order to establish Axis I psychiatric diagnoses. The professionally administered SCID allows for clinical judgment in the assignment of symptoms to psychiatric or medical categories, a crucial distinction in the assessment of symptoms that overlap between CFS and psychiatric disorders, e.g., fatigue, concentration difficulty, and sleep disturbance (Friedberg & Jason, 1998). A psychodiagnostic study (Taylor & Jason, 1998) validated the use of the SCID in a sample of patients with CFS. Because CFS is a diagnosis of exclusion, prospective participants were screened for identifiable psychiatric and medical conditions that may explain CFS-like symptoms.

After the initial interview was completed, the participants' information was reviewed to ensure that they met all eligibility requirements. If an individual was eligible for the study, a medical appointment was set up. Conversely, if an individual was not eligible, we discussed with him or her alternate treatment options.

**Medical Assessment of CFS—**The physician screening evaluation included an in-depth medical and neurological history and a general and neurological physical examination. The evaluation also included a structured instrument, a modified version of the CFS Questionnaire (Komaroff et al., 1996). This instrument assesses signs, symptoms, and medical history to rule out other disorders. Relevant medical information was gathered to exclude possible other medical causes of chronic fatigue, including exposure histories to tuberculosis, AIDS, and non-AIDS sexually transmitted diseases. Information on prescribed and illicit drug use was also assessed and recorded. Finally the histories of all symptoms related to CFS were gathered. To be diagnosed with the Fukuda et al. criteria, participants were required to experience persistent or relapsing fatigue for a period of six or more months concurrent with at least 4 of 8 specific core symptoms that did not predate the illness. Twenty-four additional individuals who were screened were excluded for a variety of reasons (i.e., lifelong fatigue, less than 4 Fukuda definitional symptoms, BMI > 45, melancholic depression or bipolar depression, alcohol or substance abuse disorder, autoimmune thyroiditis, cancer, lupus, rheumatoid arthritis).

Laboratory tests included a chemistry screen (which assesses liver, renal, and thyroid functioning), complete blood count with differential and platelet count, erythrocyte sedimentation rate, arthritic profile (which includes rheumatoid factor and antinuclear antibody), hepatitis B, Lyme disease screen, HIV screen and urinalysis. A tuberculin skin test was also performed. The project physician performed a detailed medical examination to detect evidence of diffuse adenopathy, hepatosplenomegaly, synovitis, neuropathy, myopathy, cardiac or pulmonary dysfunction. These laboratory tests in the battery were used to rule out other illnesses (Fukuda et al., 1994); in other words, they are used as exclusionary criteria rather than as inclusionary criteria.

## Functional status

**Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) or RAND Questionnaire—**The SF-36 is a broad-based 36 item self-report measure of functional status related to health (Ware & Sherbourne, 1992). 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 (McHorney, Ware, Lu, & Sherbourne, 1994) have shown adequate internal consistency, significant discriminant validity among subscales, and substantial differences between patient and non-patient populations in the pattern of scores. The SF-36 has also indicated sufficient psychometric properties as a measure of functional status in a CFS population (Buchwald, Pearlman, Umali, Schmaling, & Katon, 1996).

### Cognitive Test

The Trailmaking Test is a sub-test included in the Halstead-Reitan Battery (Reitan & Tarshes, 1959). This test contains "parts" A and B. Both are presented on an 8″ × 11″ page. Part A consists of 25 circles scattered about the page, each containing a number, 1 through 25. The examinee is instructed to connect the numbers, in order, as quickly as they can, without skipping any. Part B contains circles with numbers, 1 through 13, and letters, A through L. The examinee is instructed to connect the numbers and letters in order, alternating numbers and letters (1-A-2-B, etc.), as quickly as they can. Both parts are timed, and while the participant does not lose points for making errors, they are notified when they make an error, and instructed to correct their error, thus slowing progress and increasing total time. Total time required to complete each part is recorded. Higher completion times indicate more difficulties finishing the task. This test yields information concerning the cognitive domains of attention, visual scanning with speed of eye-hand coordination, and speed of information processing. Part B also considers the ability of the individual to alternate between two sets of stimuli, an executive function requiring multi-tasking. Reliability coefficients of the trailmaking test have been variable, ranging from .60–.90.

### Heart Rate

As part of the medical examination, participants had their heart rate taken while lying down, and then while standing up for a period of ten minutes. Heart rate recordings were taken every two minutes. For this study a selection of these recordings were used to reduce redundancy in the data reported. The following three recordings were used: Lying down, two minutes after standing, and 10 minutes after standing.

### Fukuda et al. (1994) CFS Case Definition

A case of chronic fatigue syndrome is defined by Fukuda et al. (1994) 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 definitional symptoms, all of which must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue (Fukuda et al., 1994, p.956). All 114 participants met the Fukuda CFS case definition as this was required for original study inclusion.

### ME-ICC Case Definition

The International Consensus Criteria for ME (Carruthers et al., 2011) state that symptom severity impact must result in a 50% or greater reduction of a patient's premorbid activity level for a diagnosis. There are four major symptom groupings and each are described below. To meet criteria, a person must have Post-Exertional Neuroimmune Exhaustion. Within the Neurological Impairment area, a patient must have at least one symptom from three of the following four symptom categories 1. neurocognitive impairments (e.g., difficulty processing information, short-term memory loss), 2. pain, 3. sleep disturbance, and 4. neurosensory, perceptual and motor disturbances (e.g. inability to focus vision, sensitivity to light, muscle weakness, feeling unsteady on feet). The third category is Immune, Gastro-intestinal and Genitourinary Impairments, and there needs to be at least one symptom from three of the following five symptom categories: 1. flu-like symptoms, 2. susceptibility to viral infections with prolonged recovery periods, 3. gastro-intestinal tract (e.g., nausea, abdominal pain), 4. genitourinary (e.g., urinary urgency), and 5. sensitivities to food, medications, odors or chemicals. The final category is Energy Production/Transportation Impairments, and there needs to be at least one symptom from one of the following four symptom categories: 1. cardiovascular (e.g. orthostatic intolerance), 2. respiratory (e.g. labored breathing), 3. loss of thermostatic stability (e.g. subnormal body temperature), and 4. intolerance of extremes of temperature.

Because the symptom data for the present study were collected before the development of the ME-ICC criteria, the study was unable to assess for one symptom from the category of Immune, Gastro-intestinal and Genitourinary Impairments, "susceptibility to viral infections with prolonged recovery periods." Therefore, to meet ME-ICC criteria for the present study, an individual only had to have one symptom from *two* of the five Immune, Gastro-intestinal and Genitourinary Impairments category, rather than one symptom from three of the five as specified by Carruthers et al. (2011). Of the 114 participants, 74 met the ME-ICC criteria.

## Results

### Demographics

Table 1 presents demographic data for the ME-ICC (n=74) versus Fukuda et al. (1994) CFS group who did not meet the ME-ICC criteria (n=39) conditions. Due to missing data, 1 participant could not be classified using the ME-ICC criteria and was excluded from the comparison. There were no significant demographic differences between these groups. However, as expected, the ME-ICC condition had significantly more reports of sudden onset. The ME-ICC condition had significantly higher current psychiatric comorbidity rates (61.5%) than the Fukuda et al. (1994) CFS condition (27%) [$x^2$ (1, $N$ = 113) = 12.79, $p$ = .001].

### Functional Status

Table 2 presents data from the SF-36. Using a MANOVA, the ME-ICC group was significantly different than the Fukuda et al. (1994) CFS group [Wilks Lambda = .78, $F$(8, 100) = 3.60, $p$ = .001]. Upon examination of the univariate tests, the ME-ICC condition had significantly worse scores than the Fukuda et al. (1994) CFS group on the following four

subscales: Physical Functioning [$F(1, 109) = 11.40$, $p = .001$], Bodily Pain [$F(1,108) = 21.92$, $p < .001$], Vitality [$F(1, 108) = 4.30$, $p = .04$], and Social Functioning [$F(1, 108) = 10.02$, $p < .01$]. A significant difference between the ME-ICC and Fukuda et al., (1994) CFS groups was not found for the Role Physical, General Health, Mental Health, and Role Emotional subscales.

Of interest was that the Role Emotional and Mental Health subscales were not significantly different between the two groups, although the ME-ICC group had significantly higher rates of current psychiatric comorbidity.

## Symptoms

Table 3 lists the Fukuda et al. (1994) symptoms, as well as the ME-ICC (Carruthers et al., 2011) symptoms that were significantly different between the ME-ICC group and the Fukuda et al. (1994) CFS group. The symptoms are categorized into the following groups: Post-Exertional Malaise, Neurological Impairments, Neurological Impairments, Immune/ Gastrointestinal/Genitourinary Impairments, and Energy Production/Transportation Impairments, and use the combined frequency × severity 0–100 scale. These tables only specify the symptoms from the ME-ICC criteria that were significantly different between the two groups. Symptoms that were not significantly different were not included in the table. As is evident, the ME-ICC group had significantly worse scores on 53 items, and most items were significant at the $p < .01$ level. For the majority of items that were not significantly different and not included in the table, 31 items, the ME-ICC group had directionally worse scores than the Fukuda et al. (1994) CFS group.

## Heart Rate and Cognitive Measure

Table 4 presents data on heart rate lying down and standing, and the Trailmaking A and B cognitive measure. Findings from a MANOVA revealed a significant overall effect of ME-ICC vs. Fukuda et al. (1994) CFS groups on the three heart rate measures [Wilks' Lambda = 0.90, $F(3, 108) = 4.20$, $p = .007$]. Univariate findings indicate that the ME-ICC group had significantly higher heart rates than the Fukuda et al. (1994) CFS group when lying down [$F(1, 110) = 10.18$, $p = .002$], two minutes after standing [$F(1, 110) = 4.92$, $p = .03$], and 10 minutes after standing [$F(1, 110) = 8.24$, $p = .005$].

For the Trailmaking A and B test, no significant overall effect was found for ME-ICC vs. the Fukuda et al. (1994) CFS group on the two measures [Wilks' Lambda = .98, $F(2, 110) = 1.15$, $p = .32$]. However, the ME-ICC group had directionally higher completion times for both Trailmaking tasks.

## Symptoms and Psychiatric Comorbidity

When we examined those individuals with five or fewer of the 13 Kroenke symptoms, 13 out of 48 (27%) individuals had a current psychiatric diagnosis, whereas among those individuals with 6 or more symptoms, 31 out of 65 (48%) had a current psychiatric diagnosis [$x^2$ (1, N = 113) = 4.93, $p < .05$]. Those who met the ME-ICC classification had a mean of 7.72 of these Kroenke symptoms, whereas those that met the Fukuda et al. (1994)

CFS criteria had significantly fewer with a mean of only 5.35 symptoms [$t(111) = -5.49$, $p < .001$].

## Discussion

The present study compared the ME International Consensus Criteria (ME-ICC) (Carruthers et al., 2011) with the Fukuda et al. CFS criteria (1994) utilizing a tertiary care sample of individuals diagnosed with CFS as defined by Fukuda et al. (1994). Since the illness became formally recognized as CFS in the late 1980s following reports of cluster outbreaks in Nevada (Buchwald et al., 1992) and New York (Bell, Bell & Cheney, 1994), there has been considerable debate about the Fukuda et al. (1994) criteria. To date, the ME-ICC represents the most recent consensus case definition published. However, the Fukuda et al. case definition remains the most widely utilized criteria. In the current study, the ME-ICC case definition criteria identified a subset of patients with more functional impairments and physical, mental and cognitive problems than the larger group of patients meeting the Fukuda et al. (1994) criteria. In addition, higher rates of psychiatric co-morbidity were found in the ME-ICC condition, a finding that might have been influenced by requiring a higher number of symptoms to meet the ME-ICC case definition.

These findings are comparable to a study by Jason, Brown, Clyne, Bartgis, Evans, and Brown (2012), who found significantly higher current psychiatric comorbidity rates for those meeting the 2003 Canadian ME/CFS criteria versus Fukuda et al. (1994) CFS criteria, but there were not significant differences between Fukuda CFS and an alternative ME criteria (ME-C). These different ME criteria (ME-C), specified in Jason, Brown et al.'s (2012) paper, require a sudden onset, post-exertional malaise, at least one neurocognitive symptom, and at least one autonomic symptom, and is based on some of the original work from Ramsay and other theorists in the 1980s and 1990s. This Jason, Brown et al. (2012) study used specific symptom frequency and severity criteria, as in the present study, whereas a prior study (Jason et al., 2004) that compared Fukuda et al. to the Clinical Canadian criteria (Carruthers et al., 2003) used only occurrence of symptoms. It is probable that by applying symptom frequency and severity thresholds, the 2003 Canadian ME/CFS criteria as well as the ME-ICC criteria selected a more seriously impaired group of patients with ME/CFS, and that their impairments were across a broad array of both physical and mental health areas (Jason, Brown et al., 2012).

Of interest, on the SF-36 measure of disability, in the Jason, Brown et al. (2012) study, the 2003 Canadian ME/CFS criteria group was significantly worse than the Fukuda CFS comparison group on the Role Emotional and Mental Health subscales. However there was not a significant difference between the ME-C and Fukuda CFS groups on these subscales. Likewise, the present study indicated that there was no significant difference on these subscales between the ME-ICC and Fukuda CFS groups. For all other SF-36 subscales in both studies, the group meeting ME criteria (either ME-C or ME-ICC) had directionally worse scores when compared to the group meeting ME/CFS criteria or CFS criteria. However, the ME-ICC group did have more psychiatric co-morbidity than the Fukuda et al. (1994) group. It is possible that the ME-C criteria which only require a sudden onset, post-exertional malaise, at least one neurocognitive symptom, and at least one autonomic

symptom, identify individuals with fewer emotional and mental health problems. Recently, Maes, Twisk & Johnson (2012) demonstrated that when individuals with Fukuda defined CFS are separated into two groups, CFS with post-exertional malaise and CFS without post-exertional malaise, those with post-exertional malaise had more severe symptoms and more immune abnormalities than those without. When additional symptoms are required, individuals with more physical *and* psychiatric impairment may be selected for. However, post-exertional malaise may need to be considered as a hallmark, required symptom.

Katon and Russo (1992) have argued that a requirement of more symptoms to meet criteria could inadvertently select for individuals with psychiatric problems. Similarly, Kroenke (2003) found similar results examining 15 variables within a fatigued sample. Upon examination of 13 of these 15 variables in the sample, we found that a greater number of symptoms was associated with increased psychiatric comorbidity. In addition, those who met the ME-ICC classification had significantly more Kroenke symptoms than those that met the Fukuda CFS criteria. It should be noted that the first US case definition by Holmes et al. (1988) required patients to report at least 8 of 11 minor symptoms. A major concern raised was that the requirement of eight or more minor symptoms could inadvertently select for individuals with psychiatric problems (Katon & Russo, 1992). The ME-ICC criteria also requires at least 8 symptoms. Thus while the ME-ICC criteria are an improvement over the vague and minimal guidelines of Fukuda and colleagues (1994), it is possible that the ME-ICC criteria select for individuals with increased psychiatric symptoms and functional impairment.

Based on the present analyses, the ME-ICC criteria appear to a select a more functionally impaired and symptomatic group of individuals, with regards to both mental and physical health, when compared to a group who only meet the Fukuda criteria. However, the present study had a number of limitations. The questions used to tap the domains of the ME-ICC were not specifically designed for this purpose, and thus some symptoms were not ideally operationalized. Further, one symptom (susceptibility to frequent viral infections with prolonged recovery periods) could not be included in the classification process. Due to this missing item, it was easier for individuals to meet the Immune, Gastro-intestinal and Genitourinary Impairments category, as participants were only required to have two symptoms rather than three from this category. Additionally, based on the inclusion criteria for the larger study, individuals who were home or bedbound were excluded. These results may not generalize to the subset of individuals who are more severely impaired.

Due to the exploratory nature of the present study, additional studies are needed to establish the differences between patient groups selected with various diagnostic criteria, specifically the ME-ICC criteria (Carruthers et al., 2011). Findings of the present study need to be replicated with larger samples of individuals and with questionnaires that are developed to specifically tap the domains of the ME-ICC. Jason, Evans and colleagues (2010) recently published a symptom inventory, the DePaul Symptom Questionnaire, designed to assess individuals on all published case definitions of ME, ME/CFS and CFS. This measure is now being used internationally, the results of which will potentially yield critical information about the nature of patient groups selected by various diagnostic criteria.

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**Table 1**

Demographics, Psychiatric Characteristics, and Onset Issues (*N*=113)

| | **CFS (*n*=74) *n* (%)** | **ME-ICC (*n*=39) *n* (%)** | **Sig.** |
|---|---|---|---|
| Gender | | | .82 |
| Male | 12 (16.2) | 7 (17.9) | |
| Female | 62 (83.8) | 32 (82.1) | |
| Average Age | *M* (*SD*) | *M* (*SD*) | .81 |
| | 44.1 (12.7) | 43.5 (9.6) | |
| Ethnicity | | | .10 |
| Caucasian | 63 (85.1) | 36 (92.3) | |
| African-American | 2 (2.7) | 3 (7.7) | |
| Latino | 5 (6.8) | 0 (0.0) | |
| Asian-American | 4 (5.4) | 0 (0.0) | |
| Marital Status | | | |
| Married/Living together | 37 (50.7) | 19 (48.7) | .18 |
| Single | 20 (27.4) | 16 (41.0) | |
| Divorced/Separated | 16 (21.9) | 4 (10.3) | |
| Work Status | | | .72 |
| Working full-time | 16 (22.2) | 5 (13.2) | |
| Working part-time | 17 (23.6) | 10 (26.3) | |
| On disability | 16 (22.2) | 10 (26.3) | |
| Unemployed | 23 (31.9) | 13 (34.2) | |
| Educational Level | | | .67 |
| Graduate/Professional degree | 17 (23.0) | 8 (20.5) | |
| Standard college degree | 35 (47.3) | 19 (48.7) | |
| Partial college | 14 (18.9) | 10 (25.6) | |
| High school degree or less | 8 (10.8) | 2 (5.1) | |
| Current psychiatric diagnosis | | | <.001 |
| Yes | 20 (27.0) | 24 (61.5) | |
| No | 54 (73.0) | 15 (38.5) | |
| Mode of illness onset | | | .05 |

| | CFS (*n*=74) *n* (%) | ME-ICC (*n*=39) *n* (%) | Sig. |
|---|---|---|---|
| Sudden(less than 1 month) | 19 (26.0) | 16 (44.4) | |
| Gradual | 54 (74.0) | 20 (55.6) | |
| Virus caused illness | | | .51 |
| Agree | 23 (34.3) | 9 (23.7) | |
| Neutral | 26 (38.8) | 18 (47.4) | |
| Disagree | 18 (26.9) | 11 (28.9) | |
| Cause of fatigue | | | .17 |
| Definitely Physical | 30 (42.3) | 12 (30.8) | |
| Mainly Physical | 14 (19.7) | 15 (38.5) | |
| Equally Physical and Psychological | 26 (36.6) | 12 (30.8) | |
| Mainly Psychological | 1 (1.4) | 0 (0.0) | |

**Table 2**

SF-36 subscales (N=113)

| | **CFS** ***n*=74** ***M* (*SD*)** | **ME-ICC** ***n*=39** ***M* (*SD*)** | **Sig.** |
|---|---|---|---|
| Physical functioning | 51.0 (22.63) | 35.64 (23.32) | .001 |
| Role physical | 4.58 (12.18) | 3.84 (12.22) | .76 |
| Bodily pain | 46.65 (21.42) | 27.28 (19.45) | .00 |
| General health | 34.35 (17.52) | 29.25 (17.18) | .14 |
| Vitality | 19.86 (15.26) | 13.85 (13.15) | .04 |
| Social functioning | 45.25 (24.22) | 30.45 (21.99) | .002 |
| Role emotional | 55.40 (44.34) | 46.49 (40.67) | .31 |
| Mental health | 65.13 (17.42) | 60.21 (17.65) | .16 |

**Table 3**

Significantly different symptoms (*N*=113)

| | **CFS** ***n*=74** ***M* (*SD*)** | **ME-ICC** ***n*=39** ***M* (*SD*)** | **Sig.** |
|---|---|---|---|
| **Post-exertional malaise** | 55.58 (25.91) | 70.07 (20.70) | .004 |
| **Neurological Impairments** | | | |
| *Neurocognitive Impairments* | | | |
| Memory/concentration problems | 45.69 (26.19) | 59.23 (23.71) | .01 |
| Slowness of thought | 40.27 (23.49) | 59.39 (24.03) | .001 |
| Absent mindedness | 39.36 (24.61) | 51.66 (23.01) | .02 |
| Confusion/disorientation | 26.63 (21.29) | 46.98 (25.15) | .001 |
| Difficulty reasoning | 25.85 (19.43) | 41.82 (25.06) | .01 |
| Forgetting what you're trying to say | 36.16 (22.87) | 53.15 (22.62) | .001 |
| Difficulty finding the right word | 37.27 (20.14) | 53.15 (22.62) | .01 |
| Difficulty comprehending information | 28.59 (21.12) | 45.47 (21.74) | .002 |
| Need to focus on one thing at a time | 39.23 (29.73) | 61.65 (21.84) | <.001 |
| Frequently lose train of thought | 34.40 (26.29) | 53.28 (21.57) | .001 |
| Trouble expressing thoughts | 27.00 (19.19) | 48.03 (22.35) | <.001 |
| Difficulty retaining information | 35.26 (22.35) | 56.80 (23.38) | <.001 |
| Difficulty recalling information | 35.64 (23.98) | 57.70 (22.97) | <.001 |
| Put words/numbers in the wrong order | 29.40 (19.65) | 40.82 (21.55) | .04 |
| Slow to react | 26.95 (20.97) | 48.95 (16.82) | <.001 |
| Attention deficit | 35.41 (22.78) | 48.88 (24.24) | .05 |
| Poor hand-eye coordination | 27.32 (22.79) | 44.40 (25.00) | .02 |
| *Pain* | | | |
| Muscle pain | 42.47 (27.89) | 63.44 (30.40) | <.001 |
| Pain in multiple joints | 25.31 (27.63) | 58.89 (28.59) | <.001 |
| Headaches | 31.25 (25.99) | 43.63 (28.18) | .02 |
| Eye pain | 27.17 (19.12) | 45.88 (29.52) | .03 |
| Chest pain | 19.70 (14.20) | 31.19 (18.32) | .04 |
| *Sleep Disturbance* | | | |

| | CFS *n*=74 *M* (*SD*) | ME-ICC *n*=39 *M* (*SD*) | Sig. |
|---|---|---|---|
| Unrefreshing sleep | 64.66 (27.97) | 83.62 (17.73) | <.001 |
| Need to nap during each day | 48.19 (28.09) | 62.22 (24.53) | .02 |
| Difficulty falling asleep | 46.48 (34.54) | 64.68 (29.60) | .02 |
| Difficulty staying asleep | 52.32 (31.17) | 66.03 (26.49) | .04 |
| *Neurosensory, Perceptual & Motor Disturbances* | | | |
| Muscle weakness | 29.55 (26.19) | 55.97 (30.33) | <.001 |
| Unsteady on feet | 24.60 (18.46) | 42.48 (26.66) | .001 |
| Legs weak | 37.68 (25.93) | 54.74 (25.76) | .01 |
| Arms weak | 38.78 (25.68) | 52.60 (26.57) | .03 |
| Neck weak | 29.40 (19.65) | 40.82 (21.55) | .04 |
| **Immune, Gastrointestinal & Genitourinary Impairments** | | | |
| *Flu-like Symptoms* | | | |
| Tender/sore lymph nodes | 10.34 (15.91) | 28.29 (27.63) | <.001 |
| Flu-like symptoms | 36.78 (23.55) | 56.71 (26.02) | .002 |
| *Gastrointestinal tract* | | | |
| Gastrointestinal symptoms | 43.47 (29.21) | 61.22 (33.09) | .02 |
| Upset stomach | 29.82 (25.99) | 44.57 (26.43) | .02 |
| Nausea | 10.24 (16.94) | 24.98 (25.17) | <.001 |
| Frequent urination | 45.51 (33.66) | 63.87 (26.75) | .04 |
| *Sensitivities* | | | |
| Sensitivity to alcohol | 12.26 (26.02) | 23.99 (35.62) | .05 |
| **Energy Production/Transportation Impairments** | | | |
| *Cardiovascular* | | | |
| Dizziness | 25.59 (18.43) | 43.13 (24.79) | .001 |
| Light headedness | 25.68 (18.64) | 39.64 (24.91) | .01 |
| Dizzy moving head | 25.72 (18.09) | 41.94 (29.44) | .05 |
| *Loss of thermostatic stability* | | | |
| Fever and chills | 18.33 (24.59) | 29.29 (27.20) | .03 |
| Chilled or shivery | 25.74 (19.81) | 46.53 (24.10) | <.001 |
| Hot or cold spells | 30.65 (22.84) | 45.65 (23.87) | .01 |

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| | CFS *n*=74 *M* (*SD*) | ME-ICC *n*=39 *M* (*SD*) | Sig. |
|---|---|---|---|
| Feeling like you have a high temp. | 25.71 (17.66) | 44.42 (28.51) | .003 |
| Feeling like you have a low temp. | 20.67 (24.06) | 41.69 (29.30) | .004 |
| Affected by daily weather change | 48.29 (27.49) | 70.09 (21.92) | .001 |

**Table 4**

Heart rate and cognitive measures (*N*=113)

| | **CFS** ***n*=74** ***M* (*SD*)** | **ME-I** ***n*=39** ***M* (*SD*)** | **Sig.** |
|---|---|---|---|
| HR lying down | 74.71 (10.54) | 82.74 (15.99) | .002 |
| HR standing minute 2 | 87.41 (14.62) | 94.49 (18.55) | .03 |
| HR standing minute 10 | 88.07 (14.27) | 96.10 (13.81) | .01 |
| Trailmaking A | 29.03 (10.90) | 32.27 (15.13) | .19 |
| Trailmaking B | 49.70 (16.46) | 55.64 (27.88) | .16 |