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Clinical Criteria Versus a Possible Research Case Definition in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis

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Abstract

Background—The Institute of Medicine (IOM) recently developed clinical criteria for what had been known as chronic fatigue syndrome (CFS). Given the broad nature of the clinical IOM criteria, there is a need for a research definition that would select a more homogenous and impaired group of patients than the IOM clinical criteria. At the present time, it is unclear what will serve as the research definition.

Purpose—The current study focused on a research definition which selected homebound individuals who met the four IOM criteria, excluding medical and psychiatric co-morbidities.

Methods—Our research criteria were compared to those participants meeting the IOM criteria. Those not meeting either of these criteria sets were placed in a separate group defined by 6 or more months of fatigue. Data analyzed were from the DePaul Symptom Questionnaire and the SF-36. Due to unequal sample sizes and variances, Welch's *F* tests and Games-Howell *post hoc* tests were conducted.

Results—Using a large database of over 1,000 patients from several countries, we found that those meeting a more restrictive research definition were even more impaired and more symptomatic than those meeting criteria for the other two groups.

Conclusion—Deciding on a particular research case definition would allow researchers to select more comparable patient samples across settings, and this would represent one of the most significant methodologic advances for this field of study.

Keywords

myalgic encephalomyelitis; chronic fatigue syndrome; case definitions

Since the mid-1990s, researchers had been using what has been known as the Fukuda et al. [1] chronic fatigue syndrome (CFS) case definition. McManimen et al. [2] reviewed 53 articles that used the Fukuda et al. [1] definition and found the following reported ranges of rates of key symptoms: post-exertional malaise: 25–100%; neurocognitive deficits: 16–100%; and unrefreshing sleep: 16–100%. It is at least possible that this variability was due to lack of the requirement for key symptoms.

If about 4% of the population has 6 or more months of persistent and relapsing fatigue [3], then when using the Fukuda et al. [1] definition, some estimate that about half of this 4% of individuals have CFS (cf. 2.54% met criteria for the Reeves et al. [4] and 2.6% for Wessely et al. [5]). However, other researchers indicate much lower prevalence numbers using Fukuda et al. [1] CFS definition (.24% [6] and .42% [3]). There very well may be two groups of patients, those with chronic fatigue that have more lifestyle and psychological problems causing their illness versus a smaller group that does not have these etiologic conditions.

Over the past 15 years, several other case definitions have emerged. The Clinical Canadian Consensus criteria (CCC) [7] required seven symptoms including post-exertional malaise and neurocognitive impairment. In comparing this newer case definition to the older Fukuda et al. [1] case definition, Jason et al. [8] utilized three different samples of patients, each collected through a different case ascertainment method. Whereas 87 to 96% of the samples met the Fukuda et al. [1] case definition, only 73 to 77% met the CCC criteria. So, it appears that the CCC selects a smaller group of patients with more symptoms and impairment.

The Institute of Medicine (IOM) [9] has recently proposed clinical criteria for what had been known as chronic fatigue syndrome (CFS). These clinical criteria include the following 4 symptoms: substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social or personal activities; post-exertional malaise; unrefreshing sleep; and at least one of the two following symptoms: cognitive impairment or orthostatic intolerance. In addition, the new clinical case definition regard most other illnesses as comorbid rather than exclusionary, unless another disease fully explains the critical symptoms above. However, because the IOM criteria have few exclusionary conditions, Jason et al. [10] found that the prevalence rate would be 2.8 times as great as the rate found when the Fukuda et al. [1] definition. For example, 47% of a sample of individuals with melancholic depression met IOM criteria. It appears that these IOM [9] clinical case definition bring in a larger group of patients, even though core symptoms are identified. However, it is possible that many with fatigue and somatic symptoms due to lifestyle problems or psychiatric conditions also meet such criteria. Thus although the absence of the usual definitional exclusions in the IOM was apparently intended to give clinicians flexibility in diagnosis, the definition loses its precision as a result.

A prior study by Jason et al. [11] examined 4 groups of patients, those with just 6 or more months of fatigue was one group. Another group consisted of those with medical or psychiatric reasons for their fatigue. A third group met more specific criteria that have been posited by the IOM report, Canadian Clinical Case criteria, ME-ICC case definition and a more empiric approach. Unlike the IOM criteria, this more specific case definition did not provide a choice between cognitive impairment and orthostatic intolerance, but only specified the former. Patients with these characteristics were more functionally impaired than those meeting just chronic fatigue criteria. Finally, those meeting even more restrictive ME case definition as proposed by Ramsay (1988) [12], identified a smaller and even more impaired group. However, that study used a modified IOM criteria, and it is important to assess comparisons using what has been published as the IOM clinical case definition. Another study [13] compared the IOM [9] criteria to the Fukuda et al. [1], but the Fukuda et al. definition will probably not serve as the research case definition in the future, given the types of problems identified with it including not requiring core symptoms.

Two other studies have compared the IOM [9] criteria to other case definitions. In one study, the IOM [9] criteria were compared to the CCC [7]; Jason et al. [14] found that those meeting the CCC case definition in contrast to the IOM criteria were significantly more impaired on a wide variety of symptoms and functional areas. In another study, Jason et al. [13] examined the IOM case definition compared to a four item empiric criteria, and findings indicated that the four item empiric criteria identified a smaller, more functionally limited and symptomatic group of patients.

If a consensus develops to use the IOM clinical criteria, there is a need to identify a set of more homogenous research case definition. There are several choice points including using one of the current case definitions, such as the CCC [7], the ME-ICC [15], or the empiric criteria [16]. In the current study, we made more concerted efforts to develop a set of research case definition that identifies more severely impaired patients. A study by Pheby and Saffron [17] focused on severely ill patients with ME and CFS, which were identified on the basis of whether they were housebound or bedbound and had a Barthel score of less than 60% [18], which is an objective measure of physical disability. However, we preferred to use as an outcome measure rather than one of the selection criteria.

In the current study, we decided to focus on housebound patients to determine our research case definition, reflecting a group that has not often been studied [19]. Of the few investigations that have focused on this group of patients, most had small sample sizes or investigated patients across multiple illnesses [20–22]. However, one previous study with an adequate sample size did compare patients with CFS who were housebound versus those who were not housebound [23]. Findings indicated that those who were housebound have more impairment on functional and symptom severity outcomes. However, that investigation did not compare the new IOM [9] criteria or those who only had chronic fatigue and did not meet these criteria. We hypothesized that those meeting our research case definition (being housebound, meeting IOM criteria, and not having medical or exclusionary illnesses) would be a smaller group that was more symptomatic and had more functional limitations than those meeting the IOM [9] clinical case definition. In addition, we hypothesized that those

who do not meet the clinical or research case definitions, but had 6 or more months of fatigue, would be less impaired than those meeting the clinical or research criteria.

Method

Participants

DePaul Sample—Participants were recruited through several different outlets to take the online DePaul Symptom Questionnaire (DSQ) [24]. Links and descriptions of the survey were posted to support group websites, national foundations, research forums, and social media outlets. Social media outlets included Facebook groups and pages and twitter pages. A total of 364 people with ME or CFS participated in the study. The study obtained approval from the DePaul Institutional Review Board.

This sample was 88.2% female and 11.8% male. They were predominantly White/Caucasian (97.0%) with 0.8% identifying as Asian and 2.2% as “Other.” Almost half of the sample was married or living with a partner (49.2%); 2.8% were separated; 2.5% were widowed; 16.9% were divorced; the remaining 28.7% were never married. Only 21.8% of the participants were working; 49.2% were on disability; 1.7% were students; 4.7% were homemakers; 11.7% were retired; the remaining 10.9% were unemployed. With regard to education level, 10.8% completed high school or less; 19.6% completed at least one year of college; 28.2% held a standard college degree; 41.4% had a graduate or professional degree. The mean age of these participants was 49.1 ($SD = 13.2$).

BioBank (2016)—The BioBank sample was gathered by Solve ME/CFS Initiative. All participants were recruited by physicians and had been diagnosed by a specialist with ME or CFS. A total of 508 people with a diagnosis of ME or CFS participated in this study. This sample was 76.9% female and 23.1% male. The majority were married (60.0%); 0.8% were separated; 2.0% were widowed; 14.9% were divorced; 22.2% were never married. Most of the sample was White/Caucasian (97.7%) with 0.4% identifying as African-American, 0.2% as Asian, 0.2% as American Indian, and 1.4% as “Other.” For work status, 46.1% were on disability; 1.8% were students; 2.0% were homemakers; 14.1% were retired; 15.4% were unemployed; 20.5% were working. In regards to education, 4.7% completed high school or less; 25.6% completed at least one year of college; 69.7% had a standard college degree. The mean age of participants was 54.6 ($SD = 12.4$).

Newcastle Sample—Participants in the Newcastle sample had been diagnosed with ME or CFS by an experienced physician after a comprehensive medical history and examination at the Newcastle-upon-Tyne Royal Victoria Infirmary. After written informed consent, a total of 97 participants completed study measures by hard copy. This sample was 99.0% Caucasian and 1.0% multiracial. They were predominantly female (82.5%). Of this sample, 37.5% of participants were working and 30.2% were on disability. With regard to education level, 20.9% had a graduate or professional degree; 29.7% had a college degree; 24.2% had completed at least one year of college; 14.3% had a high school degree; and 11.0% had not completed high school. The average age of the sample was 45.6 ($SD = 14.0$).

Norway Sample 1—In a separate article, Strand [25] discusses aspects of using the DSQ with a Norway sample. The DSQ was translated into Norwegian by two researchers, and retranslated by a professional translator. The retranslated version was then discussed by the two researchers to reach a consensus on the final version. Individuals with CFS were invited to participate in a randomized controlled trial of a CFS self-management program. Participants were recruited from four mid-sized towns in southern Norway, two suburbs of Oslo, and some surrounding communities. Recruitment sources included: healthcare professionals, the waiting list for a patient education program, and CFS patient organizations. Information about the study was disseminated through brochures and personal communication. In addition, study announcements for participants were placed on the Oslo University Hospital website.

Participants were required to be older than 18 years of age and diagnosed with CFS by a physician or medical specialist. In addition, participants could not be pregnant and needed to be physically able to attend the self-management program. Those who were interested in participation were given additional information by telephone. Participants completed a consent form that provided permission to request confirmation of their CFS diagnosis from their physician or medical specialist. The study gained approval from the Regional Committee for Medical Research Ethics (Health Region North) and the Privacy Ombudsman for Research at Oslo University Hospital. Of the 176 participants, 175 were included in this study; one participant was excluded due to missing data.

This sample was 86.8% female and 13.2% male. Almost all participants were Caucasian (99.4%); one participant selected 'Other' when asked about race. Only 9.7% of participants were working, while 84.0% were on disability. Regarding education, 9.9% of participants had a graduate or professional degree, 40.1% a standard college degree, 41.9% a high school degree, and the remainder had not completed high school. The mean age of the sample was 43.4 years ($SD = 11.7$).

Norway Sample 2—Participants were recruited from an inpatient medical ward for severely ill patients as well as from the outpatient clinic at a multidisciplinary CFS/ME Center. To be eligible for inclusion, participants needed to be between 18 and 65 years old and capable of reading and writing Norwegian. Individuals with a suspected diagnosis of CFS were referred for evaluation and completed the study measures. All participants took part in a comprehensive medical history interview and a detailed medical examination conducted by experienced consultant physicians and a psychologist. The examinations were conducted to rule out exclusionary medical and psychiatric conditions. Participants completed a written informed consent, and the study measures were completed by hard copy. The project gained approval from the Privacy Ombudsman for research at Oslo University Hospital. Of the 64 total participants, 63 were included in this study; one was excluded due to missing data.

This sample was 82.5% female and 17.5% male. The majority of the sample identified as Caucasian, but 1.6% identified as Asian, and 3.3% as 'Other.' Most participants (76.2%) were on disability, while 19.0% were working. With regard to education, 11.1% held a graduate or professional degree; 25.4% held a standard college degree; 46.0% had a high

school degree; and 17.5% had not completed high school. The mean age of the sample was 34.9 years ($SD = 11.6$).

Measures

The DePaul Symptom Questionnaire

All participants completed the DePaul Symptom Questionnaire (DSQ), a self-report measure of ME and CFS symptomatology, demographics, and medical, occupational and social history [24]. This measure was developed to classify individuals by a variety of ME and CFS case definitions, but the list of 54 symptoms was based upon a revised approach to the Clinical Canadian criteria [7]. Participants rate each symptom's frequency over the past six months on a 5-point Likert scale: 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 rate each symptom's severity over the past six months on a 5-point Likert scale: 0=symptom not present, 1=mild, 2=moderate, 3=severe, 4=very severe. Frequency and severity scores were multiplied by 25 to create 100-point scales. The 100-point frequency and severity scores for each symptom were averaged to create one composite score per symptom. The DSQ has evidenced good test-retest reliability among both patient and control groups [26]. A factor analysis of these symptoms resulted in a three-factor solution, and these factors evidenced good internal consistency [27]. Subsequently, domain composite scores for these factors were created by taking the 100-point score for each symptom's frequency and severity within the domain and averaging them for one 100-point domain composite score. The DSQ is available in the shared library of Research Electronic Data Capture (REDCap) [28], hosted at DePaul University: <https://redcap.is.depaul.edu/surveys/?s=tRxytSPVVw>

Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36 or RAND Questionnaire)

The SF-36 measures the impact of participants' health on physical and mental functioning [29]. The measure results in eight subscales: Physical Functioning, Role Physical, Bodily Pain, General Health, Social Functioning, Mental Health, Role Emotional, and Vitality. Higher subscale scores indicate less impairment. The SF-36 evidences strong psychometric properties, including good internal consistency and discriminant validity [30].

Case Definitions

IOM [9] Clinical Criteria—To meet criteria, patients have to have a substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest. However, for the purposes of this study, these participants could not be housebound.

Post-exertional malaise items included: soreness after mild activity, feeling drained or sick after mild activity, minimum exercise makes you tired, a dead or heavy feeling after exercise, and feeling mentally tired after the slightest effort. Patients would need to meet either the Neurocognitive domain (items included: difficulty paying attention, difficulty

expressing thoughts, problems remembering, absent-mindedness, can only focus on one thing at a time, slowness of thought, and difficulty understanding) or the Orthostatic Intolerance (OI) domain including at least one of the following: dizziness, feeling unsteady on ones feet, disturbed balance, irregular heartbeat, chest pain, and shortness of breath. Sleep dysfunction symptoms included: unrefreshing sleep, problems staying asleep, problems falling asleep, waking up early, and need to nap daily. Frequency and severity criteria as recommended by the IOM report were used. Finally, these patients must have had a substantial reduction in functioning as measured by meeting at least two of the three following criteria on the SF-36: Role Physical score ≥ 50 , Social Functioning score ≥ 62.5 , and Vitality score ≥ 35 .

In order to fulfill not having lifelong fatigue, the person would have to respond in the following manner to these three questions: responding yes to “Have you always had persistent or recurring fatigue/energy problems, even back to your earliest memories as a child? (By persistent or recurring, we mean that the fatigue/energy problems are usually ongoing and constant, but sometimes there are good periods and bad periods.)”. In addition, the respondent would have to indicate that their problem with fatigue/energy began during childhood or adolescence, and that their fatigue/energy problems developed over a period of three years or more. Regarding the criteria of “fatigue is not substantially alleviate by rest,” if a person indicated that the person’s problem with fatigue/energy entirely went away with rest, they would be excluded. For the item involving “fatigue is the result of excessive exertion,” Hu et al. [31] found that long working hours are correlated with burnout when working over 40 hours per week and is even stronger when working over 60 hours per week. Therefore, individuals who indicated that combined work related activities or household activities involved 60 or more hours a week, for the past 4 weeks, would be considered exclusionary.

Research Criteria—To meet our full criteria, participants were required to be housebound and to meet IOM criteria. We excluded cases if their fatigue/symptoms were due to other medical problems, medications, or psychiatric conditions excluded by the Fukuda et al. [1] and Carruthers et al. [7] case definitions. For example, we excluded individuals from this category if they mentioned that their illness was psychological or primarily psychologically caused. Methods of obtaining this information did vary by sample, as for samples with a physician diagnosis (Newcastle and Norway) would be obtained after a medical examination, whereas with those who just completed the DSQ for the DePaul sample, symptoms were obtained by self-report.

Chronic Fatigue (CF)—The first category refers to those with chronic fatigue, which involves 6 or more months of fatigue but does not include individuals classified by the two categories above.

Statistical Analysis—All statistical analyses were performed by the DePaul group. In order to explore the differences between the three illness groups, differences in functionality and symptoms between housebound and not housebound groups were compared. Due to unequal sample sizes and variances, Welch’s *F* tests and Games-Howell *post hoc* tests were conducted to compare the RAND-36 scores and 100-point symptom scores of these groups

(age and gender were controlled for as covariates and as the results were similar without these covariates, we present results without the covariates). A chi square analysis was performed on measures pertaining to dichotomous variables.

Results

Demographics

There was a total of 1,212 participants in this study. 58.4% ($n = 708$) met the IOM criteria, but were not homebound. This group is referred to as the IOM subgroup. 16.5% ($n = 200$) met the IOM criteria and were homebound. This group is referred to as the Research subgroup. The remaining 25.1% ($n = 304$) did not meet the IOM [9] criteria. This group is referred to as the Chronic Fatigue subgroup. As shown in Table 1, there were no significant differences for marital status, education level, race, or ethnicity. Age was significantly different between subgroups, $F(2, 1096) = 4.72, p < .01$. Post-hoc analyses showed the Chronic Fatigue group was significantly older than the other two subgroups, $p < .05$. There was a significant difference for Gender, $\chi^2(2) = 6.46, p < .05$, with the research group have a higher percentage of females. Thus, Age and Gender were controlled for in subsequent analyses. Work status was also significantly different, $\chi^2(10) = 87.14, p < .001$, with the Research subgroup having more individuals on disability. However, it was determined that this significance was a result of the Research case definition criteria, and it was considered an outcome variable.

SF-36

For the SF-36, as shown in Table 2, there were significant differences between the groups for all subscales, $p < .05$, except Role Emotional subscale, $p > .05$. Post-hoc analyses showed the Research group was significantly different from the Chronic Fatigue group on all subscales except for Role Emotional. Additionally, the Research group was significantly different from the IOM group on the Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, and Social Functioning subscales. Finally, the IOM group had significantly worse functioning than the Chronic Fatigue group on all subscales except Role Emotional and Mental Health. These results suggest the Chronic Fatigue group has higher overall functioning levels and the Research group has the lowest overall functioning levels.

Symptom and Domain Composites

As shown in Table 3, the Research group has significantly higher symptom composite scores compared to the other two subgroups in the following domains: Post-Exertional Malaise, Sleep, Neurocognitive, Immune, Neuroendocrine, Pain, and Autonomic. Additionally, the IOM group has significantly higher symptom composite scores compared to the Chronic Fatigue group in all seven domains. These results indicate that the Research group is experiencing the symptoms more severely and more frequently than the IOM and Chronic Fatigue groups.

Illness Characteristics

There are several additional differences between the three subgroups as shown in Table 4. The percent reduction in hours spent on activities for household, social, family, and work

activities was significantly higher for the Research group compared to the IOM and Chronic Fatigue group. Additionally, the reduction was higher for the IOM group compared to the Chronic Fatigue group. This suggests that, although these individuals had substantial reductions in activities, their reductions were not as large as the IOM and Research groups. There was a significant difference for length of illness onset, $\chi^2(14) = 42.60, p < .001$, suggesting that the Research group is more likely to have a sudden illness onset of within 24 hours. The course of illness was significantly different, $\chi^2(10) = 62.59, p < .001$, with more individuals in the Research group selecting “Constantly getting worse” to describe their illness. The duration of symptom exacerbation following effort was significantly different, $\chi^2(10) = 45.75, p < .001$, with more lengthy symptom exacerbation for the Research group. Similarly, there was a significant difference in fatigue that is relieved by rest, $\chi^2(6) = 87.43, p < .001$, with those in the Research group having fatigue less relieved by rest.

Discussion

The study’s major finding was that when using a research criteria that involved meeting the IOM [9] criteria, excluding those with psychiatric and medical conditions, and being homebound, a group of patients were identified that had more disability; more functional impairment on physical functioning, role physical, bodily pain, general health, vitality and social functioning; and more impairment on symptoms than the IOM criteria group. In addition, this more impaired group was more likely to have an illness course described as constantly getting worse, and had larger reductions in hours spent on a variety of activities. Clearly, the research criteria group in this study was both smaller and more impaired in a wide variety of areas.

Another interesting findings was that those who only had chronic fatigue but did not meet the IOM criteria had considerably better functioning on almost every measure that was administered. This suggests that it might be worthwhile to categorize this group of less impaired patients in studies, and continue to investigate characteristics of this group. This group might very well represent a larger group of individuals seeking help for their symptoms, as about one out of 20 people seems to have chronic fatigue, versus much smaller percentages for those meeting CFS or ME criteria [32]. Even though this group is not as impaired, they still need to be both diagnosed and treated with respect and care by medical personnel. But the differences in chronic fatigue and IOM clinical and research criteria might also help us better understand why some non-pharmacologic interventions may have some success with patients who are less impaired [33, 34]. It is of importance for researchers to clearly designate their ways of classifying patients in order to determine therapeutic outcomes for clinical studies with these different groups of patients.

There is considerable ongoing discussion regarding the case criteria to use. With the release of the IOM’s [9] clinical criteria, it was clear that these criteria would not be used as a research case definition. Due to this, it is possible that many researchers will continue to use the Fukuda et al. [1] case definition as a research criteria. However, it is also possible that some may now begin using the IOM [9] clinical criteria for research purposes, or as in the present study, identify a smaller more impaired group of patients who are homebound. Others might select other characteristics, such as research criteria that include those meeting

IOM and also having Fibromyalgia or Multiple Chemical Sensitivities. Alternatively, the research community might select one set of research criteria, either an empirically based one (though not the Reeves et al. [35] criteria), the Myalgic Encephalomyelitis-International Consensus Criteria (ME-ICC), the Canadian Consensus Criteria (CCC), the Ramsay Criteria, or the IOM clinical criteria with more extensive and concretely specified exclusions.

One limitation of the present study is the lack of diversity with regards to race in all samples. In addition, the aggregation of different samples could represent a limitation of the study. However, it does provide a more generalizable view of the data, but these samples may include individuals who are especially motivated and able to take part in research. Because severely ill housebound patients have difficulty accessing medical care, our recruitment methods may not include the most severely ill of patients or those who do not have access to the Internet. Future research may include home visits to recruit these patients. There were significant differences between the DePaul, Biobank, Newcastle, and Norway samples with regards to mean age and gender. When age and gender was controlled for, similar results occurred. The heterogeneity of the samples with regards to age and gender increases generalizability of the findings.

It is important for the field to make decisions about clinical and research case definitions. Certainly, the research case definition described in this article is one of many that could be selected. However, having clearly defined diagnostic categories would help with estimating the prevalence of the illness, identifying biomarkers with consistency, and determining which treatments help patients. In addition to a need to reach consensus on common data elements (i.e., measures and scales), deciding which research case definition to use would allow researchers to select more comparable patient samples across settings, and this would represent one of the most significant methodologic advances for this field of study.

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Table 1

Demographics for each illness subgroup (N = 1,212)

	Chronic Fatigue (n = 304)	IOM (n = 708)	Research (n = 200)	
	M (SD)	M (SD)	M (SD)	Sig.
Age	52.10 (13.93) ^{ab}	49.59 (13.12) ^a	48.36 (14.62) ^b	**
	% (n)	% (n)	% (n)	
Gender				*
Female	81.2 (238)	81.0 (566)	88.7 (172)	
Male	18.8 (55)	19.0 (133)	11.3 (22)	
Marital Status				
Married or living with partner	53.2 (157)	57.0 (397)	51.8 (102)	
Separated	2.4 (7)	1.7 (12)	0.5 (1)	
Widowed	3.4 (10)	1.7 (12)	1.0 (2)	
Divorced	12.5 (37)	14.6 (102)	14.7 (29)	
Never married	28.5 (84)	25.0 (174)	32.0 (63)	
Work Status				***
On disability	36.8 (107)	50.7 (341)	75.1 (142)	
Student	3.8 (11)	2.4 (16)	1.6 (3)	
Homemaker	3.4 (10)	3.3 (22)	0.0 (0)	
Retired	18.6 (54)	10.0 (67)	6.3 (12)	
Unemployed	10.3 (30)	10.5 (71)	11.1 (21)	
Working	27.1 (79)	23.2 (156)	5.8 (11)	
Education				
High school or less	13.4 (39)	18.6 (129)	23.0 (45)	
Partial college	17.8 (52)	18.6 (129)	19.4 (38)	
College degree	68.8 (201)	62.8 (435)	57.7 (113)	
Race				
White/Caucasian	98.5 (261)	97.7 (517)	95.5 (148)	
Non-white	1.5 (4)	2.3 (11)	4.5 (7)	
Ethnicity				
Hispanic	3.0 (8)	2.1 (11)	1.3 (2)	
Non-Hispanic	97.0 (257)	97.9 (514)	98.7 (150)	

*
 $p < .05$,**
 $p < .01$,***
 $p < .001$

Table 2

SF-36 subscale means for the IOM Homebound research criteria (N = 1,152)

	Chronic Fatigue (n = 245)	IOM (n = 707)	Research (n = 200)	
	M(SD)	M (SD)	M (SD)	Sig.
Physical Functioning	48.99(26.34) ^{ab}	37.06(21.13) ^{ac}	16.28(15.63) ^{bc}	***
Role Physical	13.44(28.52) ^{ab}	3.90(11.79) ^{ac}	1.79(7.80) ^{bc}	***
Bodily Pain	51.50(24.31) ^{ab}	39.12(22.22) ^{ac}	28.28(24.52) ^{bc}	***
General Health	31.99(19.08) ^{ab}	27.29(15.68) ^{ac}	21.22(12.73) ^{bc}	***
Vitality	23.59(19.55) ^{ab}	13.67(12.66) ^{ac}	10.37(13.72) ^{bc}	***
Social Functioning	41.55(28.59) ^{ab}	27.07(20.51) ^{ac}	12.31(16.17) ^{bc}	***
Role Emotional	69.42(41.77)	65.91(42.55)	64.96(45.12)	
Mental Health	70.64(19.22) ^a	67.83(18.38)	65.86(20.28) ^a	*

*
 $p < .05$,**
 $p < .01$,***
 $p < .001$,

Similar letters denote significant differences

Table 3

Composite means for the IOM Homebound research criteria (N = 1,212)

	Chronic Fatigue (n = 304)	IOM (n = 708)	Research (n = 200)	
	M(SD)	M(SD)	M(SD)	Sig.
Post-Exertional Malaise	58.94(25.16) ab	69.96(16.33) ac	85.24(12.68) bc	***
Minimum exercise makes you tired	62.79(27.67) ab	73.47(21.07) ac	90.04(15.25) bc	***
Next day soreness or fatigue	60.60(26.54) ab	70.19(20.24) ac	87.25(15.40) bc	***
Drained after mild activity	57.71(29.43) ab	68.64(20.91) ac	86.63(14.09) bc	***
Dead, heavy feeling after exercise	61.11(30.92) ab	71.72(25.24) ac	85.08(23.46) bc	***
Mentally tired after slightest effort	52.87(28.05) ab	66.01(21.76) ac	77.48(20.34) bc	***
Sleep	45.66(20.43) ab	52.33(16.53) ac	59.23(17.98) bc	***
Unrefreshing sleep	65.11(26.63) ab	82.84(15.19) ac	87.63(14.77) bc	***
Trouble falling asleep	46.82(31.92) ab	54.62(30.25) ac	68.25(28.38) bc	***
Trouble staying asleep	52.06(31.30) ab	57.18(29.71) a	64.65(30.41) b	***
Need to nap daily	50.04(31.15) ab	58.11(29.20) a	58.50(33.77) b	***
Waking up early	44.43(30.84) a	45.95(31.14)	51.87(31.33) a	**
Sleep all day, awake all night	14.92(26.29) a	14.66(24.37) b	22.27(29.06) ab	**
Neurocognitive	42.42(21.58) ab	53.19(15.59) ac	62.11(16.5) bc	***
Difficulty paying attention	54.86(29.04) ab	70.18(22.85) ac	78.05(21.12) bc	***
Only able to focus on one thing	48.39(29.34) ab	62.54(25.04) ac	75.51(22.91) bc	***
Problems remembering things	53.85(28.41) ab	66.26(22.86) ac	73.62(23.16) bc	***
Muscle weakness	51.08(30.34) ab	59.59(26.06) ac	72.55(25.12) bc	***
Sensitivity to noise	47.61(30.52) ab	58.42(27.82) ac	69.25(25.68) bc	***
Difficulty finding the right word	48.72(28.35) ab	60.42(22.67) ac	67.75(24.18) bc	***
Absent-mindedness	46.85(27.97) ab	58.07(24.63) ac	66.58(26.82) bc	***
Slowness of thought	45.06(29.35) ab	56.26(23.86) ac	64.38(25.40) bc	***
Sensitivity to bright lights	39.93(30.88) ab	52.35(29.56) ac	61.44(29.91) bc	***
Difficulty understanding things	35.72(27.89) ab	46.44(24.15) ac	57.00(27.33) bc	***
Unable to focus vision/attention	34.89(27.77) ab	45.69(25.57) ac	55.58(25.83) bc	***
Muscle twitches	26.82(24.87) ab	31.56(24.04) ac	39.06(26.96) bc	***
Loss of depth perception	17.00(27.21) ab	22.57(28.06) a	25.88(30.11) b	**
Immune	28.84(19.32) ab	35.44(18.28) ac	42.69(18.69) bc	***
Flu	40.14(27.68) ab	50.56(25.96) ac	59.69(27.70) bc	***
Smells make you sick	34.57(33.37) ab	39.76(32.56) ac	53.16(33.65) bc	***
Sore throat	30.67(25.17) ab	35.28(25.14) a	41.06(24.66) b	***
Tender/sore lymph nodes	26.13(26.92) ab	34.82(28.06) a	37.19(30.47) b	***

	Chronic Fatigue (n = 304)	IOM (n = 708)	Research (n = 200)	
	M(SD)	M(SD)	M(SD)	Sig.
Fever	11.88(19.56) ^{ab}	16.58(21.63) ^{ac}	21.31(24.32) ^{bc}	***
Neuroendocrine	28.43(18.05) ^{ab}	34.38(15.68) ^{ac}	39.84(18.17) ^{bc}	***
Feeling hot/cold for no reason	40.11(28.89) ^{ab}	49.24(26.21) ^a	57.19(29.19) ^b	***
Cold limbs	42.90(30.04) ^{ab}	50.34(29.24) ^a	55.50(29.99) ^b	***
Losing/gaining weight	32.02(32.61) ^{ab}	37.75(34.06) ^a	46.65(36.97) ^b	***
Alcohol intolerance	31.57(34.35) ^a	35.05(35.03)	43.38(38.52) ^a	*
Feeling like you have a high temp.	24.63(25.99) ^{ab}	31.90(27.51) ^a	40.26(33.57) ^b	***
Feeling chills or shivers	27.64(26.73) ^{ab}	37.38(25.73) ^a	39.57(30.41) ^b	***
Night sweats	29.04(28.01) ^{ab}	35.96(28.93) ^a	37.81(30.58) ^b	***
No appetite	20.75(24.01) ^{ab}	24.70(24.59) ^{ac}	33.50(28.43) ^{bc}	***
Feeling like you have a low temp.	23.38(27.22)	26.85(27.31)	25.00(29.19)	
Sweating hands	11.17(22.16)	14.18(22.95)	19.50(27.56)	
Pain	36.63(19.28) ^{ab}	45.41(17.60) ^{ac}	51.36(19.50) ^{bc}	***
Muscle pain	54.87(29.27) ^{ab}	67.62(24.68) ^{ac}	72.93(27.08) ^{bc}	***
Joint pain	46.36(33.36) ^{ab}	57.97(30.14) ^a	61.69(33.35) ^b	***
Headaches	39.32(25.71) ^{ab}	49.91(25.13) ^{ac}	60.38(26.91) ^{bc}	***
Bloating	39.63(29.28) ^{ab}	45.43(28.41) ^a	48.19(29.48) ^b	**
Stomach pain	33.60(27.95) ^{ab}	39.98(27.41) ^{ac}	47.25(30.03) ^{bc}	***
Eye pain	24.34(26.12) ^{ab}	30.68(27.49) ^{ac}	40.00(30.80) ^{bc}	***
Chest pain	17.70(22.54) ^{ab}	26.06(23.62) ^a	28.96(25.30) ^b	***
Autonomic	30.04(18.72) ^{ab}	36.89(16.71) ^{ac}	45.60(19.69) ^{bc}	***
Unsteady on your feet	33.54(27.87) ^{ab}	40.58(26.20) ^{ac}	55.56(29.25) ^{bc}	***
Irritable bowel problems	38.53(34.02) ^{ab}	46.52(31.94) ^a	51.70(33.40) ^b	***
Dizziness or fainting	30.73(27.24) ^{ab}	38.49(25.59) ^{ac}	50.56(27.97) ^{bc}	***
Shortness of breath	29.18(26.56) ^{ab}	37.31(26.37) ^{ac}	46.34(30.08) ^{bc}	***
Nausea	25.95(24.51) ^{ab}	31.81(24.83) ^{ac}	42.06(28.44) ^{bc}	***
Bladder problems	27.71(30.80) ^{ab}	33.48(31.73) ^a	36.68(34.29) ^b	**
Irregular heartbeats	24.17(25.52) ^{ab}	29.64(26.14) ^a	35.50(29.40) ^b	***

*
 $p < .05$,

**
 $p < .01$,

 $p < .001$,

Similar letters denote significant differences

Table 4

Illness characteristics for the IOM Homebound research criteria (N = 1,212)

	Chronic Fatigue (n = 304)	IOM (n = 708)	Research (n = 200)	
	M(SD)	M(SD)	M(SD)	Sig.
Illness duration	11.5(8.88)	10.8(9.20)	11.4(9.69)	
Reduction in hours spent on activities				
Household	46.3(32.14) ^a	50.0(28.57) ^b	74.3(24.11) ^{ab}	***
Social	63.3(30.04) ^{ab}	71.4(25.20) ^{ac}	82.4(24.76) ^{bc}	***
Family	56.6(34.72) ^a	60.6(32.24) ^b	74.2(29.84) ^{ab}	***
Work	78.3(32.70) ^{ab}	85.2(27.34) ^{ac}	97.5(10.34) ^{bc}	***
	% (n)	% (n)	% (n)	
Onset length				***
Within 24 hours	15.4(46)	16.5(113)	23.1(45)	
Over 1 week	13.1(39)	12.1(83)	10.3(20)	
Over 1 month - 2 years	35.2(105)	50.2(344)	44.6(87)	
Over 3+ years	35.6(106)	21.3(146)	22.1(43)	
Illness course				***
Constantly getting worse	16.9(51)	15.4(108)	33.3(66)	
Constantly improving	5.3(16)	1.1(8)	0.5(1)	
Persisting	12.6(38)	16.7(117)	17.7(35)	
Relapsing and remitting	10.6(32)	9.3(65)	6.1(12)	
Fluctuating	54.2(163)	57.5(403)	42.4(84)	
Duration of worsened symptoms after effort				***
1 hour or less	1.8(5)	0.9(6)	2.1(4)	
2–3 hours	9.6(26)	4.7(32)	2.1(4)	
4–10 hours	9.6(26)	9.8(67)	1.0(2)	
11–13 hours	2.2(6)	4.1(28)	1.0(2)	
14–23 hours	11.8(32)	15.0(103)	10.9(21)	
More than 24 hours	65.1(177)	65.6(451)	82.9(160)	
Fatigue goes away with rest				***
Entirely	3.4(10)	0.0(0)	0.0(0)	
Partially	53.9(160)	46.0(326)	25.0(50)	
Not improved by rest	41.8(124)	54.0(382)	75.0(150)	

*
 $p < .05$,**
 $p < .01$,***
 $p < .001$,

Similar letters denote significant differences