

Examining those Meeting IOM Criteria Versus IOM Plus Fibromyalgia

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Abstract

The Institute of Medicine (IOM) recently developed clinical criteria for chronic fatigue syndrome (CFS). There might be additional criteria that could select a more homogenous and impaired group of patients, particularly those with pain. The current study focused on criteria which involved meeting the four IOM criteria, excluding medical and psychiatric co-morbidities, along with having fibromyalgia (FM). Findings indicated that those meeting the IOM clinical criteria plus FM were more impaired on a wide variety of symptoms and functional areas than those meeting on the IOM criteria or those with just 6 months of fatigue. The implications of using such research criteria are discussed.

Keywords: Myalgic Encephalomyelitis; Chronic Fatigue Syndrome; Fibromyalgia; Case Definitions

Introduction

For the past few decades, researchers had been using what have been known as the Fukuda., et al. [1] research case definition for chronic fatigue syndrome (CFS). However, recently, the Institute of Medicine [2] has proposed clinical criteria for what had been known as CFS. These clinical criteria include: 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 criteria regard most other illnesses as comorbid rather than exclusionary, unless another disease fully explains the critical symptoms above. This new criteria has been named Systemic Exertion Intolerance Disease (SEID), but there has not been much support for this term among the patient community [3]. Because the IOM [2] report stated that within five years, there would be a need to report on any new developments with the IOM criteria, it is important to use the IOM criteria in data based studies, even if the IOM is only a clinical set of criteria.

There have been a few studies that have begun this process. For example, Jason, Sunnquist, Brown, Newton, Strand, and Vernon [4] compared the IOM [2] criteria to the Fukuda., *et al.* [1]. However, because there are few exclusionary conditions with the IOM criteria, Jason, Sunnquist, Kot, and Brown [5] estimated the prevalence rate would be 2.8 times as great as the rate found with the Fukuda., *et al.* [1] CFS criteria. Two other studies have compared the IOM [2] criteria to other criteria. In one study, the IOM [2] criteria were compared to the Canadian Consensus Criteria [6], and Jason, McManimen, Sunnquist, Brown, Newton, and Strand [7] found that those meeting the CCC criteria in contrast to the IOM criteria were significantly more impaired on a wide variety of symptoms and functional areas. In another study, Jason, Sunnquist, Brown, Newton, Strand, Vernon [4] 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.

Few studies have compared the IOM criteria to other chronic illnesses. One study compared those meeting the IOM criteria to those that were homebound, and the homebound group were even more impaired on a variety of outcome measures [8]. Given the relatively recent publication of the IOM clinical criteria, there have been no publications that have compared the IOM clinical criteria to those with IOM plus pain such as in fibromyalgia. It is very possible that as pain is not one of the core symptoms required to meet IOM criteria, those with FM as well as the IOM clinical criteria could represent a more impaired group of patients with both disorders.

Using prior CFS case definitions, there are a number of studies that have compared CFS and FM. Schaefer [9], for example, found that women with CFS reported significantly more trouble staying asleep than women with FM. Bombardier and Buchwald [10] found that patients diagnosed with both CFS and FM were substantially more disabled than patients with either condition alone. Brown and Jason [11] also found that individuals with CFS and comorbid FM demonstrated more symptom severity and functional impairment than individuals with CFS alone. Estimates have varied, from 20 - 70% of patients with FM meeting the criteria for CFS, and about 35 - 75% of patients with CFS also having FM [12,13]. However, in a community-level epidemiological study, of those individuals with CFS, only 15.6% met criteria for FM, and of individuals with FM, only 22.7% were also diagnosed with CFS [14]. Studies with higher co-morbid rates were recruited from primary or tertiary care settings, and such individuals may have more severe symptoms and higher rates of diagnostic comorbidity.

In the current study, we hypothesized that those meeting the IOM plus FM criteria would be more symptomatic and have more functional limitations than those just meeting the IOM [2] clinical criteria. In addition, we hypothesized that those who do not meet the IOM or IOM plus FM criteria, but had 6 or more months of fatigue, would be less impaired.

Method

Participants

DePaul Sample: Participants were recruited through several different outlets to take the online DePaul Symptom Questionnaire (DSQ) [15]. 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 home-makers; 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: 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 [15]. 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 [6]. 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, and 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. 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 has evidenced good test-retest reliability among both patient and control groups [16]. A factor analysis of these symptoms resulted in a three-factor solution, and these factors evidenced good internal consistency [17]. Strand., *et al.* [18] found a sensitivity of 98% when comparing the agreement between a physicians' diagnosis of ME/CFS using the Canadian Consensus Criteria [6] and the DSQ's assessment of this case definition. Murdock, *et al.* [19], an independent group using the DSQ, found that it demonstrated excellent internal reliability, and that among patient-reported symptom measures, it optimally differentiated between patients and controls. The DSQ is available in the shared library of Research Electronic Data Capture (REDCap) [20], 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 [21]. 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 [22].

Case Definitions

IOM [2] 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 six 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.

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(items included: dizziness, feeling unsteady on one's 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.

In order to fulfill 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.)", responding 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 respondent 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.* [23] 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.

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Fibromyalgia Group (FM): To meet criteria for this group, we first selected all those who met the above IOM criteria. Next, we included in dividuals who indicated they had been diagnosed with FM. These individuals were not included in the IOM criteria defined above. We next 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.* [6] 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: We explored differences between the three illness groups for functionality and symptoms. 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. 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. 44.7% (n = 542) met the IOM criteria, and this group is referred to as the IOM group. 30.2% (n = 366) met the IOM criteria and had been diagnosed with Fibromyalgia, and this group is referred to as the FM group. The remaining 25.1% (n = 304) did not meet the IOM [2] criteria, and is referred to as the Chronic Fatigue (CF) group. As shown in Table 1, there were no significant differences for race and education level. Age was significantly different between subgroups, F(2, 1096) = 18.67, p < 0.001. Post-hoc analyses showed significant differences between the CF group and the other two groups, p < 0.05. There was a significant difference for gender, χ^2 (2) = 19.20, p < .001, marital status χ^2 (4) = 16.62, p < 0.01, and education χ^2 (4) = 23.00, p < .001. Thus, age, marital status, education, and gender were controlled for in subsequent analyses. Work status was also significantly differently diffe

	CF	IOM	FM	
	(n = 304)	(n = 542)	(n = 366)	
	M (SD)	M (SD)	M (SD)	Sig.
Age	52.10 (13.93)ª	47.26 (13.99) ^{ab}	52.31 (12.06) ^b	***
	% (n)	% (n)	% (n)	
Gender				***
Female	81.2 (238)	78.1 (417)	89.4 (321)	
Male	18.8 (55)	21.9 (117)	10.6 (38)	
Marital Status				**
Married or living with partner	53.2 (157)	55.0 (293)	57.1 (206)	
Separated, Widowed, or Divorced	18.3 (54)	14.4 (77)	22.4 (81)	
Never married	28.5 (84)	30.6 (163)	20.5 (74)	
Work Status				***
On disability	36.8 (107)	52.7 (267)	60.8 (216)	
Not working	36.1 (105)	24.5 (124)	24.8 (88)	
Working	27.1 (79)	22.9 (116)	14.4 (51)	
Education				***
High school or less	13.4 (39)	22.9 (121)	14.7 (53)	
Partial college	17.8 (52)	15.3 (81)	23.8 (86)	
College Degree	68.8 (201)	61.7 (326)	61.5 (222)	
Race				
White/Caucasian	98.5 (261)	96.6 (345)	97.9 (320)	
Non-white	1.5 (4)	3.4 (12)	2.1 (7)	
Ethnicity				
Hispanic	3.0 (8)	1.7 (6)	2.2 (7)	
Non-Hispanic	97.0 (257)	98.3 (348)	97.8 (316)	

Table 1: Demographics for the CF, IOM and FM illness groups (N = 1,212). ** p<.01, *** p<.001, Similar letters denote significant differences

SF-36: For the SF-36, as shown in Table 2, there were significant differences between the groups for all subscales. Post-hoc analyses showed the FM group was significantly more impaired than the IOM group for Physical Functioning, Bodily Pain, General Health, Role Emotional and Mental Health. In addition, the FM group in comparison to the CF group was significantly more impaired on all the SF-36 subscales. Finally, post-hoc analyses showed the IOM group was significantly more impaired than the CF group on all subscales except for Role Emotional and Mental Health. These results suggest the CF group had higher overall functioning levels and the FM group has the lowest overall functioning levels.

	CF	IOM	FM	
	(n = 225)	(n = 483)	(n = 339)	
	M (SD)	M (SD)	M (SD)	Sig.
Physical Functioning	49.21 (25.67) ^{ab}	35.68 (22.24) ^{ac}	28.09 (20.11) ^{bc}	***
Role Physical	12.57 (27.12) ^{ab}	3.86 (12.66)ª	2.73 (8.49) ^b	***
Bodily Pain	51.91 (23.85) ^{ab}	42.93 (23.80) ^{ac}	28.20 (18.97) ^{bc}	***
General Health	31.68 (18.50) ^{ab}	26.77 (15.10) ^{ac}	24.44 (15.00) ^{bc}	***
Vitality	23.70 (19.27) ^{ab}	13.81 (13.02) ^a	11.10 (12.07) ^b	***
Social Functioning	41.33 (28.27) ^{ab}	24.38 (20.34) ^a	23.30 (20.69) ^b	***
Role Emotional	70.55 (41.31) ^a	69.81 (41.75) ^b	60.45 (44.30) ^{ab}	***
Mental Health	71.43 (18.69) ^a	68.47 (18.25) ^b	65.59 (20.32) ^{ab}	**

Table 2: SF-36 subscale means for the CF, IOM and FM illness groups (N = 1,047).** p < 0.01, *** p < 0.001, Similar letters denote significant differences

Symptom and Domain Composites: As shown in Table 3, the FM group had significantly more severe symptom composite scores compared to the IOM group in the following domains: Sleep, Neurocognitive, Immune, Neuroendocrine, Pain, and Autonomic. Additionally, the FM group had significantly more severe symptom composite scores compared to the CF group in all seven domains. Finally, the IOM group had significantly more severe symptom composite scores compared to the CF group in all seven domains. These results indicate that the FM group experienced the symptoms more severely and more frequently than the IOM and CF groups.

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Need to any aluly47.72 (31.46)56.33 (30.33)50.10 (29.47)8Trouble falling asleep44.39 (31.62)55.71 (34.74)6.124 (28.77)8Touble staying asleep41.62 (30.43)43.23 (31.33)51.03 (30.44)8Sleep ald ay, awake all night12.55 (24.33)13.50 (23.53)13.91 (23.53)8Muscreoxenitive25.26 (23.91)30.41 (24.99)65.71 (24.94)15.71 (24.94)15.71 (24.94)Muscle waches25.26 (23.91)30.41 (24.99)65.71 (24.94)15.71 (24.94)15.71 (24.94)Sensitivity to noise45.49 (30.24)50.51 (24.94)65.71 (24.94)15.71 (24.94)15.71 (24.94)Sensitivity to noise15.41 (24.94)50.51 (24.94)67.72 (24.94)15.71 (24.94)15.71 (24.94)Difficulty membering thing15.81 (28.47)70.73 (23.61)63.72 (25.97)16.71 (24.94)15.71 (24.94)Difficulty night the right word25.82 (25.93)70.72 (25.91)27.71 (25.91)15.71 (24.94)15.71 (24.94)15.71 (24.94)Difficulty night the right word25.92 (27.91)64.72 (23.94)16.71 (24.94)15.71 (24.94) <td>Sleep</td> <td>43.29 (19.68)^{ab}</td> <td>51.13 (16.61)^{ac}</td> <td>56.34 (16.26)^{bc}</td> <td>***</td>	Sleep	43.29 (19.68) ^{ab}	51.13 (16.61) ^{ac}	56.34 (16.26) ^{bc}	***
Trouble failing asleep44.99 (31.62)53.96 (30.61)61.42 (28.27)8.88Trouble staying asleep49.80 (30.90)55.17 (30.47)6.28 (28.27)8.89Waing ourp4.162 (30.31)15.87 (35.31)19.90 (70.05)8.81Sheep all ay, awkal anight12.85 (24.33)30.34 (24.90)6.57 (12.87)8.81Musce twitches48.92 (30.21)52.92 (27.09)6.57 (24.72)8.81Sussitivity to noise48.92 (30.21)52.93 (27.00)6.37 (24.00)8.81Sensitivity to noise52.40 (23.30)50.33 (21.90)8.82 (20.90)8.81Diffculty remembering thing51.44 (28.43)6.17 (24.00)8.62 (20.90)8.81Diffculty noing the thing35.53 (27.37)47.06 (25.50)8.81 (23.90)8.81Diffculty noing the thing35.63 (27.37)47.06 (25.50)8.81 (23.90)8.91Diffculty noing the thing35.63 (27.37)4.81 (23.40)8.818.81Diffculty noing the thing35.63 (27.37)4.81 (23.40)8.918.91Diffculty noing the thing35.41 (27.37)5.21 (27.40)8.918.91Diffculty noing the thing35.41 (27.37)5.21 (27.40)8.918.91Diffculty noing the thing35.91 (27.37)5.31 (27.53)<	Unrefreshing sleep	63.24 (26.57) ^{ab}	82.97 (15.51) ^a	84.48 (14.69) ^b	***
Number of the strep of the s	Need to nap daily	47.72 (31.46) ^{ab}	56.53 (30.83)ª	59.10 (29.47) ^b	***
Waking up early4.42 (30.43)4.4.3 (31.13)5.108 (30.41)4Sleep all day, awake all night1.285 (24.84)1.58 (23.33)1.99 (27.05)6.54 (15.47)4Nuccoreognitive4.90 (30.75)5.54 (15.47)6.706.54 (15.47)6.70Musche wakeness4.92 (30.23)5.03 (13.07)6.54 (23.08)6.716.716.71Sensitivity to bright lights3.74 (30.23)5.05 (30.31)6.36 (20.09)6.716.716.71Difficulty rememering things5.36 (27.07)6.54 (23.09)6.71 <td>Trouble falling asleep</td> <td>44.39 (31.62)^{ab}</td> <td>53.96 (30.51)^{ac}</td> <td>61.34 (28.76)^{bc}</td> <td>***</td>	Trouble falling asleep	44.39 (31.62) ^{ab}	53.96 (30.51) ^{ac}	61.34 (28.76) ^{bc}	***
Sleep all alay, awake all night12.85 (24.80)13.81 (23.53)18.99 (27.05)4Nucrocgnitive4.30 (20.75)52.56 (12.42)57.85 (13.87)4Muscle twitches52.56 (23.93)50.91 (27.00)65.41 (27.20)1Sensitivity to orige45.49 (30.26)57.40 (28.54)63.91 (23.03)4Sensitivity to bright lights31.41 (20.32)50.33 (23.10)50.62 (20.30)1Difficulty argentening52.02 (29.33)70.73 (23.06)71.09 (23.13)4Difficulty night eng throw73.82 (26.27)50.82 (27.00)63.72 (23.00)1Difficulty night eng throw53.52 (27.37)57.82 (25.33)44Difficulty night eng throw73.83 (26.00)63.72 (23.00)63.72 (23.00)1Difficulty night eng throw53.62 (27.37)57.82 (27.00)63.72 (23.00)11Difficulty night eng throw73.83 (26.07)52.82 (23.30)111Difficulty night eng throw53.62 (27.01)52.82 (27.00)62.82 (27.00)111Difficulty night eng throw45.72 (27.7)57.82 (27.00)63.12 (27.00)1111Difficulty night eng throw45.72 (27.7)57.82 (27.00)63.12 (27.00)111111111111111111111111111111111111 </td <td>Trouble staying asleep</td> <td>49.80 (30.90)^{ab}</td> <td>55.17 (30.47)^{ac}</td> <td>62.82 (28.27)^{bc}</td> <td>***</td>	Trouble staying asleep	49.80 (30.90) ^{ab}	55.17 (30.47) ^{ac}	62.82 (28.27) ^{bc}	***
Neurocognitive40.30 (20.75)52.65 (16.24)57.85 (15.87)6Muscle twitches25.26 (23.93)30.41 (24.99)65.45 (24.72)6Sensitivity to noise45.49 (30.20)50.31 (20.31)50.31 (20.31)5Sensitivity to noige51.41 (24.34)60.71 (24.00)60.72 (22.00)6Difficulty remembering things51.84 (28.43)60.71 (24.07)60.72 (22.00)6Difficulty nembering things32.56 (27.37)61.71 (24.07)60.72 (22.00)6Difficulty networking things33.56 (27.37)62.71 (26.43)52.82 (33.98)6Difficulty networking thing35.65 (26.64)44.81 (26.43)52.82 (33.98)6Difficulty networking thing15.47 (26.09)46.72 (23.98)66Lass of depth perception15.47 (26.09)16.82 (24.78)16.9216.92Southers stion/attention24.94 (27.37)57.82 (25.40)52.82 (23.98)6Southers stion/attention24.94 (27.73)57.82 (25.40)52.82 (23.98)16.92Southers stion/attention24.94 (27.73)57.82 (25.40)52.82 (23.98)16.92Southers stion/attention24.94 (27.73)51.92 (27.93)16.92Southers stio	Waking up early	41.62 (30.43) ^a	44.32 (31.13) ^b	51.08 (30.41) ^{ab}	**
Nuscle watches25.26 (23.39)30.31 (24.99)30.47 (23.66)8Muscle watchess48.92 (30.21)57.90 (27.84)6.54 (24.72)6Sensitivity to noise37.14 (30.23)50.31 (30.12)5.30 (20.33)7Sensitivity to bright lights37.14 (30.23)6.717 (24.00)67Difficulty remembering things51.20 (29.35)7.073 (23.00)7.03 (23.01)7Difficulty and retartion42.12 (29.37)6.737 (20.00)6.737 (23.00)7Difficulty understanding things33.56 (27.37)47.06 (25.27)5.877 (24.63)8Difficulty understanding things32.87 (26.60)4.837 (20.72)6.257 (29.33)7South to focus vision/tattents34.74 (27.74)10.85 (27.21)6.25 (27.33)7South to focus vision/tattents4.147 (27.74)10.85 (27.21)10.81 (27.21)1South to focus vision/tattents4.147 (27.40)13.147 (28.10)11South to focus vision/tattent2.947 (27.23)13.147 (28.10)11South to focus vision/tattent2.947 (27.13)13.147 (2	Sleep all day, awake all night	12.85 (24.86) ^a	13.58 (23.53) ^b	18.99 (27.05) ^{ab}	***
Muscle weakness48.92 (30.21)52.92 (27.07)65.54 (24.72)7Sensitivity to onise57.44 (30.23)50.53 (30.31)53.63 (20.08)77Sensitivity to bright lights51.84 (28.43)50.83 (30.11)53.63 (20.08)77Difficulty membering things52.20 (29.35)70.73 (23.60)53.97 (21.57)77Difficulty finding the right word47.18 (27.47)50.83 (24.16)63.74 (27.37)77Difficulty finding the right word45.21 (29.37)62.73 (26.09)63.74 (23.98)77Difficulty finding the right word23.83 (26.66)44.83 (26.47)52.24 (23.98)77Difficulty finding the right word23.83 (26.67)44.83 (26.47)52.24 (23.98)77Solong the finding23.84 (26.47)52.82 (23.98)477Absent-mindens45.71 (27.69)52.82 (23.98)777Absent-mindens45.71 (27.69)52.82 (23.98)777Solong that particip24.94 (27.49)52.82 (23.98)777Absent-mindens45.71 (27.69)52.82 (23.98)777 <td>Neurocognitive</td> <td>40.30 (20.75)^{ab}</td> <td>52.56 (16.24)^{ac}</td> <td>57.58 (15.87)^{bc}</td> <td>***</td>	Neurocognitive	40.30 (20.75) ^{ab}	52.56 (16.24) ^{ac}	57.58 (15.87) ^{bc}	***
Sensitivity to noise45.49 (30.26)7.40 (30.37)8.39 (20.30)8.30 (20.30)8.30Sensitivity to bright lights51.84 (28.43)60.77 (24.07)6.72 (24.00)6.70Difficulty nembering things52.20 (29.33)70.70 (23.52)50.72 (23.00)6.70Difficulty nuderstanding things35.56 (27.37)70.70 (25.52)50.87 (24.33)6.70Difficulty understanding things32.56 (27.37)70.70 (25.52)50.87 (24.39)6.70Difficulty understanding things32.36 (26.37)70.87 (25.20)6.22 (23.98)6.70Difficulty understanding things32.36 (26.37)70.87 (25.20)6.22 (24.78)70.70Disout of the preception15.47 (26.09)70.80 (25.40)70.80 (25.40)70.80Somens of thought29.40 (24.20)70.80 (27.40)70.8070.80Somentor29.40 (24.20)70.80 (24.78)70.8070.80Somentor29.40 (24.20)70.80 (26.40)70.8070.80Perer10.45 (17.60)70.80 (26.40)70.8070.80Somentor20.70 (27.70)70.80 (26.40)70.8070.80Nagentaping and the precesson70.80 (27.80)70.80 (27.80)70.80Somentor20.70 (27.80)70.80 (27.80)70.8070.80Somentor20.70 (27.80)70.80 (27.80)70.8070.80Somentor20.70 (27.80)70.80 (27.80)70.8070.80Somentor20.70 (27.80)70.80 (27.80)70.8070.80Somentor20.	Muscle twitches	25.26 (23.93)ª	30.34 (24.99) ^b	36.47 (23.66) ^{ab}	***
Sensitivity to bright lightsSi.7.14 (30.2.3)Si.3.3 (3.0.31)Si.3.6 (2.0.0.3)IDifficulty remembering thingsSi.2.0 (29.3.5)7.0.7 (3.2.0.0)7.0.0 (3.3.1.3)IDifficulty funding the right word47.1.8 (28.7.3)V.7.0 (2.3.0.0)V.7.0 (2.3.1.3)V.7.0Difficulty funding the right wordV.7.1.8 (2.7.3.7.0)V.7.0 (2.3.0.0)V.7.0 (2.3.0.0)V.7.0Difficulty understanding thingsV.7.1.6 (2.7.3.7.0)V.7.0 (2.3.0.0)V.7.0V.7.0 (2.3.0.0)V.7.0Difficulty understanding thingsV.7.1.6 (2.7.7.0)V.7.1.6 (2.7.0.0)V.7.1.6 (2.7.1.0)V.7.1.6 (2.7.1.0) <td>Muscle weakness</td> <td>48.92 (30.21)^{ab}</td> <td>59.29 (27.09)^{ac}</td> <td>65.54 (24.72)^{bc}</td> <td>***</td>	Muscle weakness	48.92 (30.21) ^{ab}	59.29 (27.09) ^{ac}	65.54 (24.72) ^{bc}	***
Difficulty memehering things51.84 (28.43)66.17 (24.07)69.72 (22.00)***Difficulty paying attention52.20 (29.35)70.73 (23.06)71.09 (23.13)***Difficulty finding the right word47.18 (28.74)59.88 (24.16)63.79 (21.57)***Difficulty understanding things33.56 (27.37)47.06 (25.27)60.47 (22.34)***Only able to focus ono enting46.21 (20.97)61.62 (20.97)66.47 (22.34)***Loss of elpt perception15.47 (26.09)19.55 (22.00)62.52 (23.30)***Sourness of thought43.14 (28.74)56.22 (24.01)59.54 (24.84)***Absent-mindedness44.57 (27.75)57.82 (25.40)63.21 (24.84)***Sort thoat29.40 (24.20)31.41 (28.74)81.03 (18.44)****Ferer16.65 (21.97)18.17 (28.65)******Funder/swollen lymp hondes24.00 (23.01)18.27 (27.54)\$**Sort thoat20.01 (21.90)14.16 (23.90)***Fuer16.65 (21.97)18.17 (28.74)\$**Sort thoat20.07 (30.01)82.77 (23.74)\$**Sort thoat20.07 (30.01)14.17 (28.94)\$**\$**Sort that20.07 (20.71)14.16 (23.95)\$**\$**Sort appetite20.87 (27.72)21.48 (23.95)\$**\$**Sort appetite21.89 (27.91)21.48 (23.95)\$**\$**Cold limbs21.41 (23.91)21.41 (23.91)\$**\$**Sort appetite21.8	Sensitivity to noise	45.49 (30.26) ^{ab}	57.40 (28.54) ^{ac}	63.91 (26.38) ^{bc}	***
Difficulty paying attention52.20 (29.33)70.73 (23.06)71.09 (23.13)8Difficulty finding the right word47.18 (28.74)59.88 (24.16)63.79 (21.57)8Difficulty understanding things33.56 (27.37)47.06 (25.52)50.87 (24.63)8Only able to focus on one thing46.21 (29.37)62.73 (26.09)68.47 (22.34) ^a 8Unable to focus vision/attention15.87 (26.04)56.52 (24.01)59.54 (24.44)8Slowness of thought43.14 (28.74)56.62 (24.01)59.54 (24.44)8Absent-mindedness44.57 (27.75)57.82 (25.04)63.18 (45.12)8Sore throat29.40 (24.20)31.41 (28.09)31.81 (24.51)8Freer10.45 (17.61)16.66 (21.97)18.17 (22.56)8Fuer10.45 (17.61)16.66 (21.97)18.17 (22.56)8Sore throat20.00 (20.32)32.37 (33.79)48.91 (23.01)8Fuer10.45 (17.61)16.16 (21.97)13.16 (21.57)8Fuer10.45 (17.61)36.16 (15.16)11Nagle shage you sick20.00 (20.32)36.90 (23.02)36.90 (23.02)1Neuroendocrine20.79 (27.72)31.19 (16.33)36.91 (23.12)1Negle thosy gain20.90 (22.12)31.20 (22.12)31.101Negle thosy gain20.91 (23.12)31.12 (23.02)11Neuroendocrine20.79 (27.12)31.20 (27.23)31.91 (23.12)1Negle thosy gain20.91 (23.12)31.20 (23.1	Sensitivity to bright lights	37.14 (30.23) ^{ab}	50.53 (30.31) ^{ac}	58.36 (29.08) ^{bc}	***
Difficulty induing the right word47.18 (28.74)59.88 (24.16)61.3961.39Difficulty understanding thick33.56 (27.37)47.06 (25.52)50.87 (24.30)61.39Only able to focus wision/attention32.38 (26.66)44.83 (26.43)52.28 (23.98)61.39Loss of de th perception15.47 (26.09)19.55 (27.00)52.52 (23.93)61.39Sownes of thought43.14 (28.74)56.62 (24.01)52.43 (24.84)61.30Absent-mindentess44.57 (27.57)57.82 (54.00)53.14 (24.84)61.30Sore throat20.40 (24.20)31.41 (25.00)31.81 (24.51)61.30Sore throat20.40 (24.20)31.41 (25.00)14.16 (28.99)61.30Sore throat20.40 (24.20)31.21 (25.00)31.91 (25.10)61.30Fever10.45 (17.61)16.66 (1.97)14.91 (25.62)14.91Suells make you sick32.00 (33.00)32.71 (37.91)14.9114.91Suells make you sick30.01 (21.01)14.91 (23.91)14.9114.91Neght loss/gain30.41 (21.91)14.91 (23.91)14.9114.91Night weats20.70 (27.91)31.91 (23.11)14.9114.91Sue ang Hands10.10 (21.91)14.91 (23.91)14.9114.91Night weats20.72 (27.91)31.91 (24.11)14.9114.91Sue ang Hands20.71 (27.91)14.9114.9114.91Sue ang Hands10.10 (21.91)14.9114.9114.91Night weats20.72 (27.91)14.	Difficulty remembering things	51.84 (28.43) ^{ab}	66.17 (24.07) ^{ac}	69.72 (22.00) ^{bc}	***
Difficulty understanding hings33.50 (7.37)47.06 (25.52)50.87 (24.63)4Only able to focus on one hing46.21 (29.37)62.73 (26.09)64.84 (22.34)4Unable to focus vision/attention32.38 (26.64)44.83 (26.43)52.28 (23.98)4Loss of depth perception15.47 (26.09)19.85 (27.02)62.52 (29.33)4Slowness of thought43.14 (28.74)56.62 (24.01)52.43 (24.84)4Absen-mindedness44.57 (27.57)57.82 (25.04)62.33 (24.78)4Sore thorat29.40 (28.49)31.20 (27.72)41.16 (28.89)4Fender/swollentymp nodes24.60 (25.84)31.20 (27.72)41.16 (28.89)4Fuer10.45 (17.61)16.66 (21.97)81.81 (24.51)4Fuer10.45 (17.61)16.67 (21.72)41.61 (28.89)4Swathg banks pousick32.00 (33.00)82.71 (32.73)8.494Muroendocrine26.97 (16.77)31.91 (16.33)16.81 (15.16)1Neuroendocrine26.97 (16.77)31.91 (16.33)36.91 (21.12)4Neuroendocrine26.97 (16.77)31.91 (16.33)16.81 (15.16)1Night swats20.03 (20.04)14.84 (23.33)36.91 (23.12)1Cold labes10.10 (21.33)31.91 (23.12)11Night swats23.23 (28.19)33.12 (23.12)11Cold labes27.94 (27.83)32.31 (28.12)311Night swats23.73 (27.23)32.31 (28.13)31 </td <td>Difficulty paying attention</td> <td>52.20 (29.35)^{ab}</td> <td>70.73 (23.06)^a</td> <td>71.09 (23.13)^b</td> <td>***</td>	Difficulty paying attention	52.20 (29.35) ^{ab}	70.73 (23.06) ^a	71.09 (23.13) ^b	***
Only able to focus on on thing46.21 (29.37)67.37 (26.90)84.47 (23.49)84.47Unable to focus vision/attention32.38 (26.63)44.83 (24.34)52.28 (23.93)4.81Loss of depth perception15.47 (26.09)50.54 (24.49)4.81Slowness of thought44.57 (27.57)57.28 (25.40)62.32 (24.78)4.81Absent-mindedness44.57 (27.57)57.28 (25.40)62.32 (24.78)4.81Imme26.93 (17.38)31.40 (25.80)31.81 (24.51)4.81Sorthrat24.00 (25.80)31.20 (27.72)41.61 (28.80)4.81Fever10.45 (17.61)16.66 (21.97)41.90 (20.80)4.81Partendorine26.09 (13.00)32.07 (23.70)48.90 (23.00)4.81Smells make you sick32.00 (23.00)32.07 (23.70)48.90 (23.00)4.81Sweating Hands30.04 (23.30)32.07 (25.80)32.17 (25.70)4.81Negati postype26.97 (16.70)31.91 (26.30)32.91 (27.10)4.81Sweating Hands10.01 (21.30)31.91 (23.10)1.814.81Subardi postype27.81 (27.80)32.31 (28.10)31.91 (27.10)4.81System postype27.81 (27.80)32.31 (28.10)32.11 (28.10)31.11Subardi postype27.91 (27.91)32.11 (28.10)32.11 (28.10)31.11 (28.10)31.11System postype27.91 (27.91)32.11 (28.10)32.11 (28.10)31.11 (28.10)31.11 (28.10)31.11 (28.10)31.11 (28.10)31.11 (28.10)31.11 (28.10)31.11	Difficulty finding the right word	47.18 (28.74) ^{ab}	59.88 (24.16) ^{ac}	63.79 (21.57) ^{bc}	***
Unable to focus vision/attention32.38 (26.63)44.38 (26.43)52.28 (2.3.98)4Loss of depth perception15.47 (26.09)19.85 (27.00)26.25 (29.33)4Slowness of thought43.14 (28.74)56.62 (24.01)59.54 (24.84)4Absent-mindedness44.57 (27.75)57.82 (25.40)62.32 (24.78)4Immune26.93 (17.83)34.80 (18.36)40.13 (18.44)4Sore throat29.40 (24.20)35.14 (25.00)38.18 (24.51)4Tender/swollen lymp nodes24.60 (25.84)31.20 (27.72)41.16 (28.89)4Fver10.45 (17.61)52.38 (26.90)53.51 (26.52)4Smells make you sick32.00 (33.00)36.21 (37.9)48.90 (32.40)4Neuroendocrine26.79 (16.77)34.19 (16.63)36.18 (15.16)4Veight loss/gain30.41 (23.31)36.91 (23.12)44Sweating Hands10.01 (21.39)31.21 (27.20)44Night sweats27.08 (27.08)32.31 (28.81)39.10 (21.19)4Chills or shivers27.41 (27.49)50.35 (30.42)52.73 (27.72)4Night sweats25.41 (25.50)37.41 (27.49)36.16 (27.49)4Alcolo Intolerance30.13 (33.65)35.41 (23.49)44Mucle pain30.13 (33.65)35.71 (27.81)44Night sweats30.31 (23.62)35.71 (27.81)44Reing like you have hight emp30.31 (23.63)35.71 (27.81)54Nigh	Difficulty understanding things	33.56 (27.37) ^{ab}	47.06 (25.52) ^{ac}	50.87 (24.63) ^{bc}	***
Loss of depth perception15.47 (26.00)9.815 (27.20)2.62 (29.33)%Slowness of thought43.14 (28.74)5.62 (24.01)5.954 (24.84)%Absent-mindedness44.57 (27.75)5.782 (25.40)6.23 (24.78)%Immun26.93 (17.83)3.810 (24.51)3.810 (24.51)3.810 (24.51)%Sore throat29.40 (24.20)3.514 (25.80)3.818 (24.51)%%Tender/swollen lymp hodes24.60 (25.84)3.120 (27.72)4.116 (28.89)%%Fuer10.45 (17.61)16.66 (21.97)4.16 (28.89)%%%Fuer3.80 (27.15)3.817 (25.51)4.81%%%Smells make you sick3.200 (33.00)3.827 (33.79)4.840 (32.61)%%Meroendocrine26.07 (16.73)3.41 (16.83)3.420 (15.83)%%Night sock gain3.044 (23.20)3.421 (23.63)3.841 (23.63)%%Night sock gain10.01 (21.93)3.23 (28.11)3.81 (23.61)%%Night sock gain2.541 (25.59)3.51 (36.61)%%%Cold linds4.717 (29.49)3.51 (36.12)%%%Adouble there3.013 (23.61)3.51 (36.61)%%%Feling like you have hight man3.013 (23.61)3.61 (24.91)%%%Alcohol Intolerance3.013 (23.61)3.51 (36.61)%%%%Feling like you have hight for the start for the start for the start for	Only able to focus on one thing	46.21 (29.37) ^{ab}	62.73 (26.90) ^{ac}	68.47 (22.34) ^{bc}	***
Slowneso fthought43.14 (28.74)56.62 (24.01)57.44 (24.84)%Absent-mindedness44.57 (27.75)57.82 (25.40)62.32 (24.78)%Immune26.93 (17.83)34.80 (18.36)40.13 (18.44)%Sore throat29.40 (24.20)35.14 (25.08)31.81 (24.51)%Tender/swollen lymph nodes24.60 (25.84)12.00 (27.72)41.16 (28.89)%Fever10.45 (17.61)16.66 (21.97)18.77 (22.56)%Flu38.05 (27.15)52.38 (26.90)53.51 (26.25)%Smells make you sick32.00 (33.00)38.27 (33.79)48.90 (32.04)%Neuroendocrine26.79 (16.77)34.19 (16.63)36.18 (15.16)%Weight loss/gain30.44 (32.33)36.66 (25.50)24.80 (25.75)%Swating Hands10.01 (21.30)14.84 (23.95)14.38 (22.75)%Odd limbs10.01 (21.30)31.33 (28.11)39.19 (21.10)%Swating Hands10.01 (21.30)32.33 (28.11)39.19 (21.10)%Odd limbs27.84 (25.50)37.41 (27.86)36.10 (27.91)%Swating Hands15.24 (25.50)37.41 (27.86)36.10 (27.91)%Odd limbs25.41 (25.50)37.41 (27.86)31.61 (28.91)%Idity con haves25.27 (16.71)31.10 (24.20)%%Feeling like you have high term33.23 (28.11)31.61 (28.91)%Feeling like you have high term33.13 (33.50)31.61 (28.91)%Muscle pain35	Unable to focus vision/attention	32.38 (26.66) ^{ab}	44.83 (26.43) ^{ac}	52.28 (23.98) ^{bc}	***
Absent-mindedness44.57 (27.5%)57.82 (25.4%)62.23 (24.78)8Immune26.93 (17.83)34.80 (18.36)40.13 (18.44)4***Sore throat29.40 (24.20)35.14 (25.08)31.81 (24.51)4***Tender/swollen lymph nodes24.60 (25.84)31.20 (27.72)41.16 (28.99)4***Fever10.45 (17.61)16.66 (21.97)18.77 (22.56)4***Fuu38.05 (27.15)52.38 (26.90)53.51 (26.25)4***Smells make you sick32.00 (33.00)38.27 (33.79)48.90 (32.44)4***Neuroendocrine26.79 (16.77)34.19 (16.63)61.81 (51.61)4***Weight loss/gain30.44 (32.33)36.96 (34.20)42.70 (35.27)4***Sweating Hands10.01 (21.39)14.84 (23.55)14.38 (22.75)4***Old limbs27.08 (27.08)33.23 (28.81)38.91 (29.11)4***Chills or shivers25.41 (25.50)37.61 (27.44)36.12 (24.90)4***Feeling like you have high temp.22.82 (24.94)32.42 (29.82)31.61 (28.42)4***Feeling like you have low temp.23.07 (26.22)25.77 (16.81)4***Feiling like you have low temp.35.27 (18.27)35.13 (36.03)1****Feiling like you have low temp.35.27 (28.21)31.51 (36.03)5****Feiling like you have low temp.35.77 (28.82)35.13 (36.03)4****Feiling like you have low temp.23.07 (26.23)35.13 (36.03)4*****Feiling like you have low temp.35.77 (Loss of depth perception	15.47 (26.09) ^a	19.85 (27.20) ^b	26.25 (29.33) ^{ab}	***
Immune26.93 (17.33)34.80 (18.36)40.13 (18.44)4***Sore throat29.40 (24.20)35.14 (25.08)31.81 (24.51)4***Tender/swollen lymph nodes24.60 (25.84)31.20 (27.72)41.16 (28.89)4***Fever10.45 (17.61)16.66 (21.97)18.77 (22.56)4***Fuu38.05 (27.15)52.38 (26.90)53.51 (26.25)4***Smells make you sick20.07 (30.00)38.27 (33.79)48.90 (32.44)4***Weight loss/gain30.44 (32.33)36.96 (34.20)4.77 (35.27)**4***Sweating Hands10.01 (21.39)14.84 (23.55)14.38 (22.75)4***Sweating Hands27.08 (27.09)32.32 (28.14)38.11 (28.17)**4***Chills or shivers27.94 (27.94)32.32 (28.14)31.41 (28.14)**4***Guilinbs27.94 (27.94)32.32 (28.14)31.61 (28.14)**4***Feiling like you have high temp.21.24 (27.49)31.61 (28.14)**4***Feiling like you have high temp.22.82 (28.44)31.30 (28.17)**31.51 (36.01)**4***Fulling like you have light32.32 (28.14)31.51 (36.01)**31.41 (28.14)**31.41 (28.14)**31.41 (28.14)**31.41 (28.14)**31.41 (28.14)**31.41 (28.14)**31.41 (28.14)***31.41 (28.14)***31.41 (28.14)***31.41 (28.14)***31.41 (28.14)***31.41 (28.14)****31.41 (28.14)*****31.41 (28.14)************************************	Slowness of thought	43.14 (28.74) ^{ab}	56.62 (24.01) ^a	59.54 (24.84) ^b	***
Sore throat29.40 (24.20)35.14 (25.08)31.81 (24.51)***Tender/swollen lymph nodes24.60 (25.84)*31.20 (27.72)*41.16 (28.89)****Fever10.45 (17.61)*16.66 (21.97)*18.77 (22.56)****Flu38.05 (27.15)*52.38 (26.90)53.51 (26.25)****Smells make you sick32.00 (33.00)*38.27 (33.79)*48.90 (32.04)****Neuroendocrine26.79 (16.77)*34.19 (16.63)*36.18 (15.16)****Weight loss/gain30.44 (32.33)36.96 (34.20)*42.70 (35.27)****Loss of apetite18.90 (22.44)*24.60 (25.55)28.48 (25.12)****Sweating Hands10.01 (21.39)14.84 (23.95)14.38 (22.75)***Cold limbs41.77 (29.49*50.35 (30.42)52.73 (27.72)****Chills or shivers25.41 (25.50)*37.61 (27.44)*36.21 (24.90)****Feeling like you have high temp.22.82 (24.94*)32.42 (29.28*)33.16 (28.42*)***Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)***Jaint pain53.77 (28.08)51.03 (3.65)79.35 (18.61)****Muscle pain53.77 (28.09*)51.08 (31.74)*50.57 (16.81)****Joint pain44.23 (33.05*51.08 (31.74)*50.45 (28.81)*****Headaches38.00 (25.64)*51.70 (26.49)*51.10 (24.29)*****Bloating38.50 (29.04)*42.07 (27.64)*51.61 (26.94)*****H	Absent-mindedness	44.57 (27.75) ^{ab}	57.82 (25.40) ^{ac}	62.23 (24.78) ^{bc}	***
Tender/swollen lymph nodes24.60 (25.84) th 31.20 (27.72) ^{sc} 41.16 (28.89) th ***Fever10.45 (17.61) th 16.66 (21.97) ^{sc} 18.77 (22.56) ^{sc} ***Flu38.05 (27.15) th 52.38 (26.90) ^{sc} 53.51 (26.25) ^{sc} ***Smells make you sick32.00 (33.00)38.27 (33.79) ^{sc} 48.90 (32.04) ^{sc} ***Neuroendocrine26.79 (16.77) th 34.19 (16.63) ^{sc} 36.18 (15.16) ^{sc} ***Weight loss/gain30.44 (32.33)36.96 (34.20) ^{sc} 42.70 (35.27) ^{sc} ***Loss of appetite18.90 (22.44) ^{sc} 24.60 (25.55)28.48 (25.12) ^{sc} ***Sweating Hands10.01 (21.39)14.84 (23.95)14.38 (22.75)***Cold limbs10.01 (21.39)50.35 (30.42)52.73 (27.72)***Cold limbs10.01 (21.39)35.31 (32.68) ^{sc} ******Cold limbs14.77 (29.49) ^{sc} 50.35 (30.42)52.73 (27.72)***Chills or shivers25.41 (25.50) ^{sc} 37.61 (27.44)36.21 (24.90)***Feeling like you have high temp.23.07 (26.82)32.42 (29.28)33.16 (28.42)***Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)***Muscle pain53.77 (28.00 ^{sh} 51.08 (17.48)55.57 (16.81) ^{sc} ***Joint pain44.23 (30.50)51.08 (37.44)36.01 (27.85) ^{sc} ***Iotin pain44.23 (30.50)51.08 (37.44)36.01 (27.85) ^{sc} ***Bloating36.07 (27.81) ^{sc} 36.01 (27.8	Immune	26.93 (17.83) ^{ab}	34.80 (18.36) ^{ac}	40.13 (18.44) ^{bc}	***
Fever10.45 (17.61)**16.66 (21.97)*18.77 (22.56)*****Flu38.05 (27.15)**52.38 (26.09)**53.51 (26.25)******Smells make you sick32.00 (33.00)**38.27 (33.79)**48.90 (32.04)*******Neuroendocrine26.79 (16.77)***34.19 (16.63)**36.18 (15.16)*******Weight loss/gain30.44 (32.33)***36.96 (34.20)***42.70 (35.27)*******Loss of appetite18.90 (22.44)***24.60 (25.55)***28.48 (25.12)********Sweating Hands10.01 (21.39)***14.38 (22.75)*************************************	Sore throat	29.40 (24.20) ^a	35.14 (25.08)	38.18 (24.51) ^a	***
Flu38.05 (27.15)**52.38 (26.09)**53.51 (26.25)******Smells make you sick32.00 (33.00)**38.27 (33.79)**48.90 (32.04)*******Neuroendocrine26.79 (16.77)***34.19 (16.63)***36.18 (15.16)*******Weigh loss/gain30.44 (32.33)***36.96 (34.20)****24.70 (35.27)*********Loss of apetite18.90 (22.44)***24.60 (25.55)*****28.48 (25.12)************************************	Tender/swollen lymph nodes	24.60 (25.84) ^{ab}	31.20 (27.72) ^{ac}	41.16 (28.89) ^{bc}	***
Smells make you sick32.00 (33.00)*38.27 (33.79)*48.90 (32.04)******Neuroendocrine26.79 (16.77)**34.19 (16.63)**6.18 (15.16)******Weight loss/gain30.44 (32.33)36.96 (34.20)**42.70 (35.27)******Loss of appetite18.90 (22.44)**24.60 (25.55)**28.48 (25.12)******Sweating Hands10.01 (21.39)14.84 (23.95)14.38 (22.75)****Old limbs27.08 (27.08)33.23 (28.81)*38.91 (29.11)******Cold limbs41.77 (29.49)**50.35 (30.42)52.73 (27.22)******Chills or shivers25.41 (25.50)**37.61 (27.44)36.21 (24.90)******Hot/cold for no reason38.11 (28.27)**48.21 (27.86)**33.16 (28.42)******Feeling like you have high temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)****Jachoh intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)****Muscle pain53.77 (28.80)**61.30 (26.55)**54.********Joint pain44.23 (33.05)20.47 (28.31)**54.*******Bloating38.50 (29.04)**23.47 (23.81)**31.10 (24.20)*******Readense38.00 (25.64)**37.49 (28.27)**31.10 (24.20)*******Muscle pain16.06 (20.29)**23.47 (23.81)**51.51 (24.98)*******Ipint pain24.97 (27.64)**50.51 (24.98)*********Bloating38.00 (25.64)**50.58 (26.20)**51.21 (24.98)*********** </td <td>Fever</td> <td>10.45 (17.61)^{ab}</td> <td>16.66 (21.97)ª</td> <td>18.77 (22.56)^b</td> <td>***</td>	Fever	10.45 (17.61) ^{ab}	16.66 (21.97)ª	18.77 (22.56) ^b	***
Neuroendocrine26.79 (16.77)**34.19 (16.63)**36.18 (15.16)******Weight loss/gain30.44 (32.33)a36.96 (34.20)**42.70 (35.27)*****Loss of appetite18.90 (22.44)**24.60 (25.55)**28.48 (25.12)******Sweating Hands10.01 (21.39)14.84 (23.95)14.38 (22.75)****Sight sweats27.08 (27.08)*33.23 (28.81)**38.91 (29.11)******Cold limbs41.77 (29.49)**50.35 (30.42)*52.73 (27.72)*****Chills or shivers25.41 (25.50)**37.61 (27.44)*36.21 (24.90)*****Hot/cold for no reason38.11 (28.27)**48.21 (27.86)*33.16 (28.42)*****Feeling like you have high temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)****Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)****Joint pain35.22 (18.72)42.18 (17.88)*52.57 (16.81)******Iount pain53.77 (28.80)*61.30 (26.55)*54.***Iount pain22.99 (25.02)29.47 (28.32)*36.01 (27.85)******Bloating38.50 (29.04)*42.70 (27.64)*50.45 (28.81)******Iteadaches38.00 (25.64)*50.58 (26.20)**51.2 (24.98)******Iteadaches38.00 (25.64)**50.58 (26.20)**51.3 (30.18)******Iteadaches38.00 (25.64)**50.58 (26.20)**51.3 (30.18)******Iteadaches38.00 (25.64)**50.58 (26.37)**51.51 (24.98)****** </td <td>Flu</td> <td>38.05 (27.15)^{ab}</td> <td>52.38 (26.90)^a</td> <td>53.51 (26.25)^b</td> <td>***</td>	Flu	38.05 (27.15) ^{ab}	52.38 (26.90) ^a	53.51 (26.25) ^b	***
Weight loss/gain30.44 (32.33)a36.96 (34.20)b42.70 (35.27)b***Loss of appetite18.90 (22.44)b24.60 (25.57b28.48 (25.12 bb)***Sweating Hands10.01 (21.39)b14.84 (23.95)14.38 (22.75)b***Night sweats27.08 (27.08)b33.23 (28.81b)b38.91 (29.11 bb)***Cold limbs41.77 (29.49)bb50.35 (30.42)b52.73 (27.72)b***Chills or shivers25.41 (25.50)bb37.61 (27.44b)b36.21 (24.90)bb***Hot/cold for no reason38.11 (28.27)bb32.42 (29.28b)bb33.16 (28.42b)bb***Feeling like you have high temp.22.82 (24.94b)bb32.42 (29.28bb33.16 (28.42b)bb***Feeling like you have low temp.23.07 (26.82bb25.74 (28.34bbb25.71 (16.81bbbb***Muscle pain35.22 (18.72bbbbb51.08 (31.74bbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbb	Smells make you sick	32.00 (33.00) ^a	38.27 (33.79) ^b	48.90 (32.04) ^{ab}	***
Loss of appetite18.90 (22.44)*24.60 (25.55)*28.48 (25.12)******Sweating Hands10.01 (21.39)14.84 (23.95)14.38 (22.75)1Night sweats27.08 (27.08)*33.23 (28.81)*38.91 (29.11)******Cold limbs41.77 (29.49)**50.35 (30.42)*52.73 (27.72)*****Chills or shivers25.41 (25.50)**37.61 (27.44)*36.21 (24.90)*****Feeling like you have high temp.22.82 (24.94)**32.42 (29.28)*33.16 (28.42)*****Feeling like you have high temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)****Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)****Muscle pain53.77 (28.80)**61.30 (26.55)**********Joint pain44.23 (33.05)51.08 (31.74)*69.61 (26.03)******Eye pain22.99 (25.02)*29.47 (28.32)*36.10 (27.85)******Bloating38.50 (29.04)*42.07 (27.64)*50.45 (28.81)******Stomach pain32.40 (28.12)*37.29 (28.29)*46.21 (26.60)******Headaches38.00 (25.64)**50.58 (26.20)**55.12 (24.98)******Bladter problems37.15 (33.96)*42.46 (32.78)*35.90 (31.42)******Nausea24.95 (24.27)*31.75 (26.37)*35.96 (25.07)******Nausea24.95 (24.27)*31.75 (26.37)**35.96 (25.07)******Nausea24.95 (24.27)*31.75 (26.37)**35.96 (25.07)****** </td <td>Neuroendocrine</td> <td>26.79 (16.77)^{ab}</td> <td>34.19 (16.63)^{ac}</td> <td>36.18 (15.16)^{bc}</td> <td>***</td>	Neuroendocrine	26.79 (16.77) ^{ab}	34.19 (16.63) ^{ac}	36.18 (15.16) ^{bc}	***
Sweating Hands 10.01 (21.39) 14.84 (23.95) 14.38 (22.75) Night sweats 27.08 (27.08) ^a 33.23 (28.81) ^b 38.91 (29.11) ^b *** Cold limbs 41.77 (29.49) ^{bb} 50.35 (30.42) ^a 52.73 (27.72) ^b *** Chills or shivers 25.41 (25.50) ^{ab} 37.61 (27.44) ^{ab} 36.21 (24.90) ^{bb} *** Hot/cold for no reason 38.11 (28.27) ^{ab} 48.21 (27.86) ^{ac} 53.05 (25.65) ^{bc} *** Feeling like you have high temp. 22.82 (24.94) ^{ab} 32.42 (29.28) ^a 33.16 (28.42) ^b *** Feeling like you have low temp. 23.07 (26.82) 25.74 (28.34) 26.60 (26.78) *** Alcohol intolerance 30.13 (33.65) 37.43 (35.87) 35.51 (36.03) *** Muscle pain 53.77 (28.80) ^{ab} 61.30 (26.55) ^{ac} 79.35 (18.73) ^{bc} *** Ioint pain 44.23 (33.05) ^a 51.08 (31.74) ^b 69.61 (26.03) ^{ab} *** Eye pain 22.99 (25.02) ^a 29.47 (28.32) ^b 36.01 (27.85) ^{bb} *** Bloating 38.50 (29.04) ^a 42.07 (27.64) ^b 50.45 (28.81) ^{bb} <	Weight loss/gain	30.44 (32.33)a	36.96 (34.20) ^b	42.70 (35.27) ^{ab}	**
Night sweats27.08 (27.08)*33.23 (28.81)*38.91 (29.11)*b****Cold limbs41.77 (29.49)*b50.35 (30.42)*52.73 (27.72)*b****Chills or shivers25.41 (25.50)*b37.61 (27.44)*b36.21 (24.90)*b****Hot/cold for no reason38.11 (28.27)*b48.21 (27.86)*c53.05 (25.65)*c****Feeling like you have high temp.22.82 (24.94)*b32.42 (29.28)*b33.16 (28.42)*b****Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)1Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)1Pain35.22 (18.72)42.18 (17.88)*c52.57 (16.81)*c***Muscle pain53.77 (28.80)*b61.30 (26.55)*c79.35 (18.73)*c***Joint pain44.23 (33.05)51.08 (31.74)*c69.61 (26.03)*b***Eye pain22.99 (25.02)*c29.47 (28.31)*c31.10 (24.20)*c***Bloating38.50 (29.04)*c37.29 (28.29)*c46.21 (26.60)*c***Stomach pain32.40 (28.12)*c37.29 (28.29)*c46.21 (26.60)*c***Headaches38.00 (25.64)*c55.58 (26.20)*c55.12 (24.98)*c***Mutonomic28.45 (18.00)*c36.28 (17.88)*c41.52 (16.94)*c***Irritable bowel problems37.15 (33.96)*c42.46 (32.78)*c35.33 (30.18)*c***Bladder problems27.76 (30.59)*c29.48 (32.16)*c38.59 (25.07)*c***Nausea24.95 (24.27)*c31.75 (26.37)*c<	Loss of appetite	18.90 (22.44) ^a	24.60 (25.55) ^b	28.48 (25.12) ^{ab}	***
Cold limbs41.77 (29.49) ^{ab} 50.35 (30.42) ^a 52.73 (27.72) ^b ***Chills or shivers25.41 (25.50) ^{ab} 37.61 (27.44) ^a 36.21 (24.90) ^b ***Hot/cold for no reason38.11 (28.27) ^{ab} 48.21 (27.86) ^{ac} 53.05 (25.55) ^{cc} ***Feeling like you have high temp.22.82 (24.94) ^{ab} 32.42 (29.28) ^a 33.16 (28.42) ^b ***Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)[Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)[Pain35.22 (18.72)42.18 (17.88) ^{ac} 52.57 (16.81) ^{bc} ***Muscle pain53.77 (28.80) ^{ab} 61.30 (26.55) ^{ac} 79.35 (18.73) ^{bc} ***Joint pain44.23 (33.05) ^a 51.08 (31.74) ^b 69.61 (26.03) ^{ab} ***Eye pain22.99 (25.02) ^a 23.47 (23.81) ^{ac} 31.10 (24.20) ^{bc} ***Bloating38.50 (29.04) ^a 42.07 (27.64) ^b 50.45 (28.81) ^{ab} ***Headaches38.00 (25.64) ^{ab} 50.58 (26.20) ^{ac} 51.32 (24.98) ^{bc} ***Headaches37.15 (33.96) ^{ab} 42.46 (32.78) ^b 51.33 (30.18) ^{bb} ***Bladder problems37.15 (36.95) ^{ab} 29.48 (32.16) ^b 39.90 (31.42) ^{bb} ***Inritable bowel problems27.76 (30.59) ^{ab} 39.50 (27.79) ^{ab} 39.90 (31.42) ^{bb} ***Bladder problems24.95 (24.27) ^{ab} 31.75 (26.37) ^{bb} 39.90 (31.42) ^{bb} ***Nausea24.95 (24.27) ^{ab} 39.50 (27.79) ^{ab} 38.59 (27.10) ^{bb} ***	Sweating Hands	10.01 (21.39)	14.84 (23.95)	14.38 (22.75)	
Chills or shivers25.41 (25.50)ab37.61 (27.44)ab36.21 (24.90)bb****Hot/cold for no reason38.11 (28.27)ab48.21 (27.86)ab53.05 (25.65)abb****Feeling like you have high temp.22.82 (24.94)abb32.42 (29.28)abb33.16 (28.42)abb****Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)****Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)****Muscle pain53.77 (28.80)ab61.30 (26.55)abb69.61 (26.03)abb****Joint pain44.23 (33.05)abb51.08 (31.74)bb69.61 (26.03)abb****Eye pain22.99 (25.02)abb29.47 (28.32)bb36.01 (27.85)abb****Bloating38.50 (29.04)abb23.47 (23.81)abb31.10 (24.20)bc****Headaches38.00 (25.64)abb50.58 (26.20)abb55.12 (24.98)abb****Headaches38.00 (25.64)abbb50.58 (26.20)abbb55.12 (24.98)abbb****Irritable bowel problems37.15 (33.96)abbb42.46 (32.78)abbbb****Bladder problems27.76 (30.59)abbbb29.48 (32.16)abbbb35.53 (30.18)abbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbbb	Night sweats	27.08 (27.08) ^a	33.23 (28.81) ^b	38.91 (29.11) ^{ab}	***
Hot/cold for no reason38.11 (28.27)ab48.21 (27.86)ac53.05 (25.65)bc***Feeling like you have high temp.22.82 (24.94)ab32.42 (29.28)ab33.16 (28.42)bb***Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)***Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)***Muscle pain53.77 (28.80)ab61.30 (26.55)ac79.35 (18.73)bc***Joint pain44.23 (33.05)ab51.08 (31.74)bb69.61 (26.03)abb***Eye pain22.99 (25.02)ab29.47 (28.32)bb36.01 (27.85)abb***Bloating38.50 (29.04)ab42.07 (27.64)bb50.45 (28.81)abb***Stomach pain32.40 (28.12)ab37.29 (28.20)abb51.12 (24.90)bc***Headaches38.00 (25.64)abb50.58 (26.20)acbb51.21 (24.90)bc***Headaches38.00 (25.64)abb50.58 (26.20)acbb51.21 (24.98)bc***Mutonomic28.45 (18.00)abb36.28 (17.88)acbb51.51 (24.98)bc***Bladder problems37.15 (33.96)abb42.46 (32.78)bb53.53 (30.18)abb***Nausea24.95 (24.27)abbb31.75 (26.37)abb35.96 (25.07)abbb***Unsteady on your feet31.07 (26.92)abb31.75 (26.37)abb35.96 (25.07)abbb***Shortness of breath27.36 (25.35)abb39.50 (27.79)abbb38.59 (27.10)abbb***Dizziness or fainting28.26 (26.28)abbb40.01 (26.74abbb42.38 (26.19)bbb***	Cold limbs	41.77 (29.49) ^{ab}	50.35 (30.42) ^a	52.73 (27.72) ^b	***
Feeling like you have high temp.22.82 (24.94) ^{ab} 32.42 (29.28) ^a 33.16 (28.42) ^b ***Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)1Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)1Pain35.22 (18.72)42.18 (17.88) ^{ac} 52.57 (16.81) ^{bc} ***Muscle pain53.77 (28.80) ^{ab} 61.30 (26.55) ^{ac} 79.35 (18.73) ^{bc} ***Joint pain44.23 (33.05) ^a 51.08 (31.74) ^b 69.61 (26.03) ^{ab} ***Eye pain22.99 (25.02) ^a 29.47 (28.32) ^b 36.01 (27.85) ^{ab} ***Bloating38.50 (29.04) ^a 42.07 (27.64) ^b 50.45 (28.81) ^{ab} ***Stomach pain32.40 (28.12) ^a 37.29 (28.29) ^b 46.21 (26.00) ^{ab} ***Headaches38.00 (25.64) ^{ab} 50.58 (26.20) ^{ac} 55.12 (24.98) ^{bc} ***Muscle pain27.76 (30.59) ^a 42.46 (32.78) ^b 53.53 (30.18) ^{ab} ***Meadaches27.76 (30.59) ^a 29.48 (32.16) ^b 39.90 (31.42) ^{ab} ***Irritable bowel problems37.15 (33.96) ^a 42.46 (32.78) ^b 39.90 (31.42) ^{ab} ***Nausea24.95 (24.27)31.75 (26.37) ^b 35.96 (25.07) ^{ab} ***Unsteady on your feet31.07 (26.92) ^{ab} 40.57 (27.45) ^{ac} 48.46 (27.25) ^{bc} ***Shortness of breath27.36 (25.35) ^{ab} 39.50 (27.79) ^a 38.59 (27.10) ^b ***Dizziness or fainting28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} *** </td <td>Chills or shivers</td> <td>25.41 (25.50)^{ab}</td> <td>37.61 (27.44)^a</td> <td>36.21 (24.90)^b</td> <td>***</td>	Chills or shivers	25.41 (25.50) ^{ab}	37.61 (27.44) ^a	36.21 (24.90) ^b	***
Feeling like you have low temp.23.07 (26.82)25.74 (28.34)26.60 (26.78)Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)Pain35.22 (18.72)42.18 (17.88)°52.57 (16.81)°***Muscle pain53.77 (28.80)°61.30 (26.55)°79.35 (18.73)°***Joint pain44.23 (33.05)°51.08 (31.74)°69.61 (26.03)°***Eye pain22.99 (25.02)°29.47 (28.32)°36.01 (27.85)°***Bloating38.50 (29.04)°42.07 (27.64)°50.45 (28.81)°***Stomach pain32.40 (28.12°37.29 (28.29)°46.21 (26.60)°***Headaches38.00 (25.64)°50.58 (26.20)°55.12 (24.98)°***Irritable bowel problems37.15 (33.96)°42.46 (32.78)°53.53 (30.18)°***Bladder problems27.76 (30.59)°29.48 (32.16)°35.96 (25.07)°***Nausea24.95 (24.27)°31.75 (26.37)°35.96 (25.07)°***Shortness of breath27.36 (25.35)°39.50 (27.79)°38.59 (27.10)°***Dizziness or fainting28.26 (26.28)°40.01 (26.74)°42.38 (26.10)°***	Hot/cold for no reason	38.11 (28.27) ^{ab}	48.21 (27.86) ^{ac}	53.05 (25.65) ^{bc}	***
Alcohol intolerance30.13 (33.65)37.43 (35.87)35.51 (36.03)Pain35.22 (18.72)42.18 (17.88)ac52.57 (16.81)bc***Muscle pain53.77 (28.80)ab61.30 (26.55)ac79.35 (18.73)bc***Joint pain44.23 (33.05)a51.08 (31.74)b69.61 (26.03)ab***Eye pain22.99 (25.02)a29.47 (28.32)b36.01 (27.85)ab***Bloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab***Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab***Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***Juritable bowel problems37.15 (33.96)a42.46 (32.78)b35.33 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Feeling like you have high temp.	22.82 (24.94) ^{ab}	32.42 (29.28) ^a	33.16 (28.42) ^b	***
Pain35.22 (18.72)42.18 (17.88)°52.57 (16.81)°****Muscle pain53.77 (28.80)°61.30 (26.55)°79.35 (18.73)°***Joint pain44.23 (33.05)°51.08 (31.74)°69.61 (26.03)°***Eye pain22.99 (25.02)°29.47 (28.32)°36.01 (27.85)°***Chest pain16.06 (20.92)°23.47 (23.81)°31.10 (24.20)°***Bloating38.50 (29.04)°42.07 (27.64)°50.45 (28.81)°***Stomach pain32.40 (28.12)°37.29 (28.29)°46.21 (26.03)°***Headaches38.00 (25.64)°50.58 (26.20)°55.12 (24.98)°***Irritable bowel problems37.15 (33.96)°42.46 (32.78)°53.53 (30.18)°***Bladder problems27.76 (30.59)°29.48 (32.16)°39.90 (31.42)°***Nausea24.95 (24.27)°31.75 (26.37)°35.96 (25.07)°***Shortness of breath27.36 (25.35)°39.50 (27.79)°38.59 (27.10)°***Dizziness or fainting28.26 (26.28)°40.01 (26.74)°42.38 (26.19)°c***	Feeling like you have low temp.	23.07 (26.82)	25.74 (28.34)	26.60 (26.78)	
Muscle pain53.77 (28.80)ab61.30 (26.55)ac79.35 (18.73)bc****Joint pain44.23 (33.05)a51.08 (31.74)b69.61 (26.03)ab****Eye pain22.99 (25.02)a29.47 (28.32)b36.01 (27.85)ab****Chest pain16.06 (20.92)ab23.47 (23.81)ac31.10 (24.20)bc****Bloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab****Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab****Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc****Irritable bowel problems37.15 (33.96)a42.46 (32.78)b33.53 (30.18)ab****Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab****Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab****Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b****Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc****	Alcohol intolerance	30.13 (33.65)	37.43 (35.87)	35.51 (36.03)	
Joint pain44.23 (33.05)a51.08 (31.74)b69.61 (26.03)ab****Eye pain22.99 (25.02)a29.47 (28.32)b36.01 (27.85)ab****Chest pain16.06 (20.92)ab23.47 (23.81)ac31.10 (24.20)bc****Bloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab****Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab****Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc****Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc****Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab****Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab****Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab****Unsteady on your feet31.07 (26.92)ab40.57 (27.45)ac48.46 (27.25)bc****Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b****Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc****	Pain	35.22 (18.72)	42.18 (17.88) ^{ac}	52.57 (16.81) ^{bc}	***
Eye pain22.99 (25.02)a29.47 (28.32)b36.01 (27.85)ab***aChest pain16.06 (20.92)ab23.47 (23.81)ac31.10 (24.20)bc***aBloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab***aStomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab***aHeadaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***aAutonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***aIrritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***aBladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***aNausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***aShortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***aDizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***a	Muscle pain	53.77 (28.80) ^{ab}	61.30 (26.55) ^{ac}	79.35 (18.73) ^{bc}	***
Chest pain16.06 (20.92)ab23.47 (23.81)ac31.10 (24.20)bc***Bloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab***Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab***Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Joint pain	44.23 (33.05)ª	51.08 (31.74) ^b	69.61 (26.03) ^{ab}	***
Bloating38.50 (29.04)a42.07 (27.64)b50.45 (28.81)ab***Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab***Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Eye pain	22.99 (25.02)ª	29.47 (28.32) ^b	36.01 (27.85) ^{ab}	***
Stomach pain32.40 (28.12)a37.29 (28.29)b46.21 (26.60)ab***Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Unsteady on your feet31.07 (26.92)ab40.57 (27.45)ac48.46 (27.25)bc***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Chest pain	16.06 (20.92) ^{ab}	23.47 (23.81) ^{ac}	31.10 (24.20) ^{bc}	***
Headaches38.00 (25.64)ab50.58 (26.20)ac55.12 (24.98)bc***Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Unsteady on your feet31.07 (26.92)ab40.57 (27.45)ac48.46 (27.25)bc***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Bloating	38.50 (29.04) ^a	42.07 (27.64) ^b		***
Autonomic28.45 (18.00)ab36.28 (17.88)ac41.52 (16.94)bc***Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Unsteady on your feet31.07 (26.92)ab40.57 (27.45)ac48.46 (27.25)bc***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Stomach pain	32.40 (28.12) ^a	37.29 (28.29) ^b		***
Irritable bowel problems37.15 (33.96)a42.46 (32.78)b53.53 (30.18)ab***Bladder problems27.76 (30.59)a29.48 (32.16)b39.90 (31.42)ab***Nausea24.95 (24.27)a31.75 (26.37)b35.96 (25.07)ab***Unsteady on your feet31.07 (26.92)ab40.57 (27.45)ac48.46 (27.25)bc***Shortness of breath27.36 (25.35)ab39.50 (27.79)a38.59 (27.10)b***Dizziness or fainting28.26 (26.28)ab40.01 (26.74)ac42.38 (26.19)bc***	Headaches	38.00 (25.64) ^{ab}	50.58 (26.20) ^{ac}	55.12 (24.98) ^{bc}	***
Bladder problems 27.76 (30.59) ^a 29.48 (32.16) ^b 39.90 (31.42) ^{ab} *** Nausea 24.95 (24.27) ^a 31.75 (26.37) ^b 35.96 (25.07) ^{ab} *** Unsteady on your feet 31.07 (26.92) ^{ab} 40.57 (27.45) ^{ac} 48.46 (27.25) ^{bc} *** Shortness of breath 27.36 (25.35) ^{ab} 39.50 (27.79) ^a 38.59 (27.10) ^b *** Dizziness or fainting 28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} ***	Autonomic	28.45 (18.00) ^{ab}	36.28 (17.88) ^{ac}	41.52 (16.94) ^{bc}	***
Nausea 24.95 (24.27) ^a 31.75 (26.37) ^b 35.96 (25.07) ^{ab} *** Unsteady on your feet 31.07 (26.92) ^{ab} 40.57 (27.45) ^{ac} 48.46 (27.25) ^{bc} *** Shortness of breath 27.36 (25.35) ^{ab} 39.50 (27.79) ^a 38.59 (27.10) ^b *** Dizziness or fainting 28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} ***	Irritable bowel problems	37.15 (33.96)ª	42.46 (32.78) ^b	53.53 (30.18) ^{ab}	***
Unsteady on your feet 31.07 (26.92) ^{ab} 40.57 (27.45) ^{ac} 48.46 (27.25) ^{bc} *** Shortness of breath 27.36 (25.35) ^{ab} 39.50 (27.79) ^a 38.59 (27.10) ^b *** Dizziness or fainting 28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} ***	Bladder problems	27.76 (30.59) ^a	29.48 (32.16) ^b	39.90 (31.42) ^{ab}	***
Shortness of breath 27.36 (25.35) ^{ab} 39.50 (27.79) ^a 38.59 (27.10) ^b *** Dizziness or fainting 28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} ***	Nausea	24.95 (24.27) ^a	31.75 (26.37) ^b	35.96 (25.07) ^{ab}	***
Dizziness or fainting 28.26 (26.28) ^{ab} 40.01 (26.74) ^{ac} 42.38 (26.19) ^{bc} ***	Unsteady on your feet	31.07 (26.92) ^{ab}	40.57 (27.45) ^{ac}	48.46 (27.25) ^{bc}	***
	Shortness of breath	27.36 (25.35) ^{ab}	39.50 (27.79) ^a	38.59 (27.10) ^b	***
Irregular heartbeats 22.29 (24.60) ^{ab} 30.12 (27.46) ^a 31.76 (26.22) ^b ***	Dizziness or fainting	28.26 (26.28) ^{ab}	40.01 (26.74) ^{ac}	42.38 (26.19) ^{bc}	***
	Irregular heartbeats	22.29 (24.60) ^{ab}	30.12 (27.46) ^a	31.76 (26.22) ^b	***

****** p<.01, *** p<.001, Similar letters denote significant differences</th>

Illness Characteristics: There are several additional differences between the three groups as shown in Table 4. The FM group had a statistically significant longer illness duration than the IOM of CF groups. The FM group had larger percent reduction in hours spent on activities for family and work activities when compared to the IOM group. The FM group had greater reductions in household, social family and work activities compared to the CF group. The IOM group had significantly more reductions in household, social, and work activities compared to the CF group. In other words, the CF group reductions were not as large as the IOM and FM groups, and largest reductions occurred for the FM group. There was a significant difference for length of illness onset, χ^2 (14) = 39.99, p < 0.001, suggesting that the FM group is more likely to have a sudden illness onset. The course of illness was significantly different, χ^2 (10) = 40.46, p < 0.001, with more individuals in the FM group selecting "Constantly getting worse" to describe their illness. The duration of symptom exacerbation following effort was significantly different, χ^2 (10) = 26.62, p < 0.01, with the FM group being more impacted. Similarly, there was a significant difference in fatigue that is relieved by rest, χ^2 (6) = 62.16, p < 0.001, with a higher percent in the FM group indicating that Fatigue was not improved with rest.

	CF	IOM	FM	
	(n = 304)	(n = 542)	(n = 366)	
	M (SD)	M(SD)	M (SD)	Sig.
Illness duration	11.64 (8.89) ^a	9.24(8.95) ^b	13.32 (9.34) ^{ab}	***
Percent reduction in hours spent on activities				
Household	44.70 (31.42) ^{ab}	54.18(29.25)ª	55.28 (29.78) ^b	**
Social	61.95 (29.76) ^{ab}	72.08 (25.25) ^a	74.91 (26.64) ^b	***
Family	54.90 (34.47) ^a	59.86 (32.90) ^b	66.40 (31.12) ^{ab}	**
Work	77.40 (33.54) ^{ab}	86.74 (25.98) ^a	89.86 (23.22) ^b	***
	% (n)	% (n)	% (n)	
Onset length				***
Within 24 hours	15.4 (46)	17.5 (91)	18.6 (67)	
Over 1 week	13.1 (39)	10.6 (55)	13.3 (48)	
Over 1 month-2 years	35.2 (105)	50.2 (261)	47.1 (170)	
Over 3+ years	35.6 (106)	21.7 (113)	21.1 (76)	
Illness course				***
Constantly getting worse	16.9 (51)	16.3 (87)	23.9 (87)	
Constantly improving	5.3 (16)	1.5 (8)	0.3 (1)	
Persisting	12.6 (38)	19.3 (103)	13.5 (49)	
Relapsing and remitting	10.6 (32)	8.8 (47)	8.2 (30)	
Fluctuating	54.2 (163)	54.2 (290)	54.1 (197)	
Duration of worsened symptoms after effort				**
1 hour or less	1.8 (5)	1.0 (5)	1.4 (5)	
2-3 hours	9.6 (26)	5.6 (29)	1.9 (7)	
4-10 hours	9.6 (26)	6.9 (36)	9.2 (33)	
11-13 hours	2.2 (6)	4.2 (22)	2.2 (8)	
14-23 hours	11.8 (32)	15.0 (78)	12.8 (46)	
More than 24 hours	65.1 (177)	67.3 (350)	72.5 (261)	
Fatigue goes away with rest				***
Entirely	3.4 (10)	0.0 (0)	0.0 (0)	
Partially	53.9 (160)	43.7 (237)	38.0 (139)	
Not improved by rest	41.8 (124)	56.3 (305)	62.0 (227)	

****** p<.01, *** p<.001, Similar letters denote significant differences</th>

Discussion

The study found that individuals with FM along with meeting IOM symptoms were identified as having more patients on disability and worse scores on the following SF-36 domains: Physical Functioning, Bodily Pain, General Health, Role Emotional and Mental Health. In addition, the FM group had worse scores on the following symptom domains: Sleep, Neurocognitive, Immune, Neuroendocrine, Pain, and Autonomic. In general, the IOM and FM groups were more impaired on both functional and symptom domains than the CF group. On other measures which involved reductions in activities, the FM group again had the largest impairment, which was followed by the IOM group in comparison to the CF group. In general, these results support differentiating those with FM who also have IOM, from those who only have IOM or CF.

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Examining those Meeting IOM Criteria Versus IOM Plus Fibromyalgia

Those with only CF had better functioning on almost every outcome measure, supporting the differentiation of this group from those with more impairment due to having the core IOM symptoms. If about one out of 20 people seem to have CF [24], it is important to be sure to separate those with CF from studies that involve patients meeting IOM criteria. The differences between IOM clinical and CF criteria might also help us better understand why some non-pharmacologic interventions may have some success with patients who are less impaired [25,26]. Even though those with CF appear to be less impaired than those with IOM, it is of importance to both diagnose and treat those with CF, although it is very likely that the treatment approaches might differ for these different groups of patients.

Not only have there been changes as proposed by the IOM, but even the FM case definition has changed, and Kaseeska, Brown, and Jason [27] found that the newer and more broad FM case definition did not identify those with more physical functioning limitations as the earlier more narrow case definition. It does appear that having FM, at least for those who self-identify with it, does add to the burden of symptoms and disability, when compared to those who just have IOM or CF symptoms. It is still unclear what research case definition to use, as the IOM [2] represents clinical criteria. Some researchers might begin to use the IOM as their research criteria, others may continue to use the Fukuda., *et al.* [1] case definition as a research criteria, and some might use the Canadian Consensus Criteria [6]. For some studies, such as the current one, it might be useful to use a group of patients who have FM as well as IOM symptoms, but no other exclusionary illnesses. Clearly, at the present time, it is unclear what researchers are to use who are more interested in a research approach than an IOM clinical one.

One limitation of the present study is that individuals indicated that they had been diagnosed with FM, but we did not have an independent verification of this diagnosis. It is certainly possible that given the range of practitioners who make this diagnosis, some respondents may have been misdiagnosed with FM. Still, at least for those that self-report having this diagnosis, the findings do suggest that this group does have considerably more pain, which provides some additional supportive data regarding their diagnosis. In addition, there were significant differences between the samples with regards to several demographic variables, but we controlled for them in the analyses. Finally, the samples of patients meeting IOM and CF criteria were gathered from multiple sources, but this could increase the ability to generalize the findings to diverse settings and countries.

The current study does suggest that there is some usefulness in examining those with both IOM criteria as well as FM, as this group does seem to be more impaired. It does appear that increasing the number of symptoms is associated with increasing symptom severity and physical limitations, therefore, when people have substantial pain complaints on top of IOM, they are worse off than those without pain complaints and report more functional disability. It is very possible that other studies will be conducted that find other subgroups, for example those who meet IOM criteria along with Multiple Chemical Sensitivities, or other disorders. Comparing and contrasting such groups will help in better understanding some of the advantages of the IOM criteria as well as some of its limitations. Perhaps the most problematic issue for the field remains in deriving a research case definition, as this will ultimately influence estimating the prevalence, biomarkers, and treatments provided to patients.

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