Scientific Journal of
Neurology & Neurosurgery

Research Article

Post-Exertional Malaise in Patients with ME and CFS with Comorbid Fibromyalgia -

Stephanie L. McManimen[#] and Leonard A. Jason[#*]

[1]*Center for Community Research, DePaul University, 990 W Fullerton Ave, Suite 3100, Chicago, IL, USA*
[#]*Authors contributed equally to this article*

***Address for Correspondence:** Leonard A. Jason, Center for Community Research, DePaul University, 990 W Fullerton Avenue, Suite 3100, Chicago, IL USA, Tel: 773-325-2018; Fax: 773-325-4923; E-mail: ljason@depaul.edu

Submitted: 19 February 2017; Approved: 08 March 2017; Published: 10 March 2017

Citation this article: McManimen SL, Jason LA. Post-Exertional Malaise in Patients with ME and CFS with Comorbid Fibromyalgia. Scientific Journal of Neurology & Neurosurgery. 2017;3(1): 022-027.

ABSTRACT

Background: Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) share some similar symptoms with Fibromyalgia (FM). Prior research has found increased illness severity when patients have FM that is comorbid with ME and CFS. For example, Post-Exertional Malaise (PEM) has been shown to be more severe in those with comorbid FM. However, PEM can be separated into two factors, Muscle and General PEM. It is unknown if the more severe PEM findings in comorbid FM are due to the Muscle or General PEM factor.

Purpose: The purpose of this study was to determine if the PEM differences seen between patients with and without comorbid FM exist for the Muscle or General PEM factors.

Method: An international convenience sample was collected via an online questionnaire. The questionnaire assessed the frequency and severity of several PEM-related symptoms. Additionally, participants provided information regarding the course and characteristics of their illness.

Results: Participants that indicated a comorbid diagnosis of FM displayed significantly more frequent and severe PEM symptoms in the Muscle and General PEM factors. The FM group also indicated significantly worse physical functioning compared to the group without comorbid FM.

Discussion: The secondary diagnosis of FM in addition to ME and CFS appears to amplify the PEM symptomatology and worsen patients' physical functioning. The findings of this study have notable implications on the inclusion of patients with comorbid FM in ME and CFS research studies.

Keywords: Chronic fatigue syndrome; Myalgic encephalomyelitis; Fibromyalgia; Comorbidity; Post-exertional malaise

INTRODUCTION

Myalgic Encephalomyelitis (ME) [1] and Chronic Fatigue Syndrome (CFS) [2] result in profound fatigue for six or more months, post-exertional malaise, neurocognitive deficits, and dysfunctional sleep. Although it is not one of the cardinal symptoms, [3] found that 84% of patients report joint pain and 94% report muscle aches and pain. Similarly, a systematic review by Meeus, Nijs, and De Meirleir, [4] found chronic musculoskeletal pain to be a widespread occurrence in this patient population.

Pain is also a major characteristic of Fibromyalgia (FM) [5] a similar fatiguing illness. There is considerable overlap in the diagnosis of ME and CFS with FM. Studies have shown 20-70% of patients with FM also meet the diagnostic criteria for ME and CFS, while 35-75% of those with ME and CFS also have FM [6-8]. However, at the community-level, Jason, Taylor, and Kennedy, [9] found 22.7% of patients with FM met the CFS criteria and 15.6% of those with CFS met the FM criteria. Although the prior studies have found widely disparate comorbidity rates, the illnesses do co-occur in a substantial amount of patients with ME and CFS.

Due to the diagnostic and symptom overlap, some researchers believe FM is the same illness or in the same functional somatic syndrome category as ME and CFS [8,10,11]. Several studies have demonstrated the many etiological similarities between FM and ME or CFS. They have been found to follow viral infections [12,13] and the hepatitis B vaccine [14]. They have shown dysregulation of the Hypothalamic-Pituitary-Adrenal (HPA) axis [15,16]. They also share antibodies to serotonin, phospholipids, and gangliosides [17-19]. Additionally, FM displays similar symptomatology as ME and CFS with patients in these populations reporting sleep dysfunction, concentration difficulties, headaches, bowel issues, and generalized pain sensitivity [20].

Although there are many similarities between the patient populations, it is important to determine if having a secondary diagnosis of FM adds to the illness burden for symptom severity and disability, which would suggest the illnesses are distinct conditions. Bombardier and Buchwald [21] found patients with FM can be differentiated from those with CFS in terms of functional disability level. Additionally, they found that the patients with both diagnoses, CFS and FM, were significantly more disabled than the patients with only one of the diagnoses. In a survey of the general population of London, Ontario, [22] found individuals meeting diagnostic criteria for FM and CFS reported worse overall health, more dissatisfaction with their health, worse illness course, and a greater disease impact than those with either FM or CFS. Similarly, [23] found patients with ME and CFS that also had an FM diagnosis demonstrated worse physical functioning, more bodily pain, more joint and muscle pain, more severe fatigue after exertion, and a greater impairment on employment compared to patients without comorbid FM. These finding indicate that FM is a distinct clinical illness and possibly indicates underlying etiological differences. McManimen, Sunnquist, and Jason [24] found Post-Exertional Malaise (PEM), a cardinal symptom of ME and CFS, can be divided into two factors: a generalized fatigue factor and a musculoskeletal factor. As musculoskeletal complaints are prominent in FM, it is important to determine if the similarities with ME and CFS occur only in the musculoskeletal factor of PEM or if they extend to the generalized fatigue factor, as well. The purpose of the current study was to determine if there are functional differences in patients with ME and CFS that have a comorbid FM diagnosis compared to those that do not have the comorbid diagnosis. Severity of post-exertional malaise symptoms were also compared as FM is independently known to result in decreases in functioning [23]. It was predicted that an additional diagnosis would add to the illness burden, resulting in worse overall functioning and more severe and frequent post-exertional malaise. Such findings would indicate a need to clarify the diagnostic inclusion and exclusion criteria for future research to assure that findings are specific to ME and CFS and not impacted by the co-occurrence of FM.

METHOD

Participants

An international convenience sample of adult patients self-identifying as having ME or CFS was collected. Participants were recruited from several sources including social media, internet

forums, and newsletters of patient organizations. The questionnaire was completed online using Research Electronic Data Capture (REDCap), an online survey tool [25].

A total of 701 patients participated in this study. The sample was mostly female (89.7%), Caucasian (96.4%), and non-Hispanic (98%). For marital status, the majority were married or living with a partner (56.4%); 2.6% were separated; 1.1% were widowed; 13.4% were divorced; 26.5% were never married. Regarding education, 10.6% completed a high school or less; 22.8% completed at least one year of college; 33.7% held a college degree; 32.9% had a graduate or professional degree. For work status, 42.2% were on disability; 16.8% were unemployed; 10.5% were retired; 15.8% worked part-time; 6.8% worked full-time; 3.0% were students; the remaining 4.9% were homemakers. The majority of participants (54.8%) reported currently living outside of the United States.

Measures

Participants completed a series of questions to assess the frequency and severity of the PEM-related ME and CFS symptoms. In total, 17 questions that measured PEM were selected from Ramsay's clinical description of ME [1], the ME-ICC [26], the [27] CFS screening study, the Depaul Symptom Questionnaire (DSQ) [28], the Chalder Fatigue Scale [29], and the Medical Questionnaire [30]. Items were phrased to assess the frequency and severity of PEM over the past 6 months, a timeframe found to be the most reliable for CFS symptoms [31]. Each PEM symptom's frequency was rated 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. Similarly, each PEM symptom's severity was rated on a 5 - point Likert scale: 0 = symptom not present, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe. Each symptom's frequency and severity was then multiplied by 25 and averaged to create a composite score on a 100-point scale. The six items from the DSQ have been tested on this scale and have evidenced good test-retest reliability [32], but the remaining 11 items have not been previously tested on the same scale.

Participants also completed two additional scales to assess their physical functioning level: the Bell Ability Scale [33] and the SF-36 Physical Functioning subscale [34]. For the Bell Ability Scale, participants were given a list of functional status examples (e.g. unable to care for self) and selected the number that best described their current functioning level. This measure was converted from a 10-point scale to a 100-point scale to allow for more variability in scores should a participant's functioning fall between two examples. Similarly, the SF-36 is a self-report disability measure where participants answer questions on a 3-point Likert scale. These scores are also converted to a 100-point scale. The SF-36 has shown good internal consistency and discriminant validity [35].

RESULTS

Demographics

As shown in (Table 1), 12.82% (n = 90) of participants reported having comorbid fibromyalgia, similar to the community-based study by Jason, et al. [9]. There were no significant differences for gender, race, ethnicity, marital status, education level, work status, or household income. There was a significant effect of age [F (1, 686) = 4.28, p < .05] with the FM group being significantly older than the group without FM. As a result, age was controlled for in subsequent analyses.

Table 1: Demographics of participants with and without comorbid fibromyalgia (n = 701).

	Comorbid Fibromyalgia	No Fibromyalgia
	(n = 90)	(n = 611)
	M (SD)	M (SD)
Age	49.82 (11.68)	46.95 (12.34)*
	% (N)	% (N)
Gender		
Female	93.3 (84)	89.2 (543)
Male	6.7 (6)	10.8 (66)
Race		
Black, African-American	0.0 (0)	0.2 (1)
White	96.7 (87)	96.4 (589)
American Indian or Alaskan Native	3.3 (3)	0.7 (4)
Asian or Pacific Islander	0.0 (0)	1.1 (7)
Other	0.0 (0)	1.6 (10)
Ethnicity		
Non-Hispanic or Latino	94.3 (83)	98.5 (593)
Hispanic or Latino	5.7 (5)	1.5 (9)
Marital Status		
Married/Living with Partner	58.4 (52)	56.1 (342)
Separated, Widowed, or Divorced	21.3 (19)	16.6 (101)
Never Married	20.2 (18)	27.4 (167)
Education Level		
High School or Less	7.8 (7)	11.0 (67)
Partial College	23.3 (21)	22.7 (138)
College Degree	33.3 (30)	33.8 (205)
Graduate/Professional Degree	35.6 (32)	32.5 (197)
Current Work Status		
On Disability	42.7 (38)	42.1 (255)
Student	2.2 (2)	3.1 (19)
Homemaker	4.5 (4)	5.0 (30)
Retired	12.4 (11)	10.2 (62)
Unemployed	18.0 (16)	16.7 (101)
Working Part-Time	10.1 (9)	16.7 (101)
Working Full-Time	10.1 (9)	6.3 (38)
Household Income		
Less than $24,999	45.2 (33)	33.3 (166)
$25,000 to $49,999	23.3 (17)	25.7 (128)
$50,000 to $99,999	23.3 (17)	23.1 (115)
$100,000 to $149,999	5.5 (4)	11.6 (58)
$150,000 or more	2.7 (2)	6.2 (31)

* p < .05

Functioning Level

As shown in (Table 2), there were many significant differences in functioning level between the two groups. Those with FM had significantly lower functioning on the SF-36 Physical Functioning subscale [F (1, 587) = 3.81, p < .05]. The PEM symptoms were split into the Muscle and General factors found by McManimen, Sunnquist, and Jason [24]. The participants with FM had significantly higher scores for overall PEM [F (1, 685) = 16.36, p < .001], the Muscle factor [F (1, 648) = 23.34, p < .001], and the General factor [F (1, 638) = 7.90, p < .01]. Scores were significantly higher for the FM group for all but three of the individual PEM items. The higher scores indicate that the FM group is experiencing PEM-related symptoms more frequently and more severely than the group without FM. There were no significant differences for the Bell Ability Scale, p > .05.

Table 2: Mean functioning levels of participants (n = 701).

	Comorbid Fibromyalgia	No Fibromyalgia
	(n = 90)	(n = 611)
	M (SD)	M (SD)
SF-36 Physical Functioning	19.58 (19.30)	25.12 (20.79) *
Bell Ability Scale	31.32 (14.96)	33.98 (15.37)
All PEM Symptoms	**79.63 (13.57)**	**71.18 (17.17)** **
Muscle Factor	**77.26 (16.82)**	**64.82 (21.48)** **
Muscle weakness after minor exertion	75.35 (22.20)	61.92 (27.68) **
Muscle fatigability after minor exertion	78.64 (20.60)	67.22 (24.96) **
Muscle pain after minor exertion	72.74 (22.92)	56.90 (28.40) **
Next day soreness or fatigue after non-strenuous, everyday activities	78.12 (18.02)	68.69 (22.59) **
Dead, heavy feeling after starting to exercise	81.25 (19.79)	69.36 (28.69) **
General Factor	**80.61 (12.94)**	**73.83 (16.70)** **
Post-exertional malaise	80.73 (13.42)	73.53 (19.60) *
Prolonged generalized fatigue or malaise following previously tolerable levels of exercise	88.02 (13.01)	80.35 (21.60) **
Post-exertional exhaustion that is immediate or delayed	81.60 (16.52)	75.13 (19.02) *
Symptoms worsen with exertion	84.55 (15.20)	77.99 (18.70) *
Substantial reduction in pre-illness activity level due to low threshold physical and mental fatigability	85.59 (18.49)	85.09 (17.88)
Fatigue/extreme tiredness	83.68 (13.21)	75.18 (18.13) **
Marked, rapid physical or cognitive fatigability in response to exertion	75.35 (22.40)	69.88 (22.24)
Exhaustion not relieved by rest	80.38 (18.27)	72.08 (23.08) *
Prolonged worsening of symptoms after physical activity	79.86 (16.05)	70.94 (22.58) **
Minimum exercise makes you physically tired	81.94 (17.03)	73.12 (22.97) **
Physically drained or sick after mild activity	76.04 (19.08)	69.17 (22.38) *
Mentally tired after the slightest effort	69.79 (20.31)	63.36 (24.86)
* p < .05, ** p <.01		

Illness Characteristics

Table 3 shows additional illness characteristics for each group. There was a significant difference for length of illness onset, F (7, 697) = 17.81, $p < .05$. The group without FM had a significantly more acute illness onset compared to the more gradual onset shown for the comorbid FM group. Additionally, there was a significant difference for course of illness, F (4, 701) = 10.00, $p < .05$. This indicated that significantly more participants with comorbid FM are reporting an illness course of "Constantly getting worse" compared to the group without comorbid FM. There was no significant difference for bedbound status or the PEM onset timeframe following activities, $p > .05$.

DISCUSSION

This study investigated the effects of comorbid fibromyalgia in patients with ME and CFS. The purpose of the study was to determine if patients with multiple fatiguing illnesses are experiencing PEM more frequently and severely than patients without an additional fatiguing illness. An international sample of participants self-reporting an ME or CFS diagnosis provided frequency and severity of several PEM-related symptoms and provided information on the course and onset of their illness. Those that also reported a secondary diagnosis of FM were compared to those that did not report a secondary diagnosis of FM.

As shown in table 2, co-morbid FM has a significant impact on PEM-related symptoms and overall functioning level. Participants in the FM group have worse overall physical functioning on the SF-36 measure compared to those without FM. Additionally, the FM group is experiencing PEM-related symptoms more severely and more frequently than those without FM. As shown in table 3, the FM group also has a different illness course and illness onset length compared to those without FM. These results indicate that having an additional diagnosis of FM leads to a greater illness impact and a worse illness course than if the patient did not have an additional fatiguing illness. The differences between the FM and the no FM groups also suggest that, although there are many similarities between illnesses, FM is a separate clinical entity as suggested by prior studies [21-23].

These results have important implications for future research on ME and CFS. The Institute of Medicine (IOM) [36] clinical case definition does not consider a comorbid illness to be an exclusionary condition unless it can explain all of the ME and CFS symptomatology. As a result, using this clinical case definition includes many individuals with comorbid diagnoses, such as FM. Since the broad IOM criteria is for clinical use, there is a need for a research criteria that selects a more homogenous group of patients. Given the differences between patients with and without comorbid FM found in this study and others [37,21,38], it may be useful to develop a research criteria that is cognizant of comorbidities. The comorbidities could be excluded to obtain a more homogenous sample with only ME and CFS. However, findings from studies with this second possible research

Table 3: Illness characteristics of patients with and without comorbid fibromyalgia (n = 701).

	Comorbid Fibromyalgia		No Fibromyalgia	
	(n = 90)		(n = 611)	
	%	(N)	%	(N)
Onset				*
Within 24 hours	16.7	(15)	20.4	(124)
Over 1 week	6.7	(6)	11.8	(72)
Over 1 month	6.7	(6)	12.3	(75)
Over 2-6 months	16.7	(15)	14.6	(89)
Over 7-12 months	11.1	(10)	6.2	(38)
Over 1-2 years	1.1	(1)	7.4	(45)
Longer than 2 years	24.4	(22)	15.0	(91)
Since childhood or adolescence	16.7	(15)	12.2	(74)
Course of illness				*
Constantly getting worse	32.2	(29)	21.5	(132)
Constantly improving	0.0	(0)	1.5	(9)
Persisting	7.8	(7)	13.4	(82)
Relapsing & remitting	3.3	(3)	8.6	(53)
Fluctuating	56.7	(51)	55.0	(338)
Functional status				
Bedridden/Walk around the house	41.6	(37)	37.3	(228)
Can do light housework	38.2	(34)	37.4	(229)
Able to work	20.2	(18)	25.3	(155)
PEM onset after activities				
1 hour or less	26.7	(8)	22.3	(48)
2-3 hours	26.7	(8)	14.0	(30)
4-10 hours	3.3	(1)	15.8	(34)
11-13 hours	10.0	(3)	4.7	(10)
14-23 hours	13.3	(4)	12.1	(26)
More than 24 hours	20.0	(6)	31.2	(67)
* $p < .05$				

criteria may not generalize to patients with comorbid FM as they have shown to have a more severe illness impact than those without FM. Several studies have displayed the inconsistencies in symptom rates, prevalence, functioning, and treatment efficacy found in ME and CFS research [39-42]. These inconsistencies may be explained by the inclusion criteria and the presence of comorbid illnesses, such as FM. Thus, it may be beneficial to use a more homogenous patient population, without such comorbidities, in future research. Such a criteria would allow researchers to identify biomarkers and treatments specific to ME and CFS without a confounding variable like a comorbid illness. Alternatively, the research criteria could include the comorbid FM as a significant amount of patients with ME and CFS also have FM. Similar to the first possible solution, the results of studies utilizing such a criteria many not generalize to patients without comorbid FM since the illness burden is significantly increased with the additional fatiguing illness.

This study has several limitations. Most notably, there was no independent verification of the ME, CFS, or FM diagnoses. Additionally, as a result of the self-reported diagnoses, there was no set case definition for ME and CFS that participants were required to meet in order to be included in this study. Demographically, this population was mostly Caucasian, non-Hispanic females. However, community samples have shown more diversity in ethnic minorities and socioeconomic status than displayed in this study [43]. Finally, an international convenience sample was used in this study. Prior research by Zdunek, Jason, and Evans, et al. [44] has shown significant differences in disability level and symptomology between samples from the United States and samples from the United Kingdom. The present sample was collected from various countries, but this could be advantageous as it may allow the findings to be generalized across multiple settings and geographic locations.

This study found that patients with comorbid FM experience PEM-related symptoms significantly more frequently and severely than patients without FM in both PEM domains. Additionally, the additional fatiguing illness appears to significantly increase the illness burden for patients with ME and CFS. Due to these significant differences within the patient population, it may be beneficial to consider the ramifications of including or excluding comorbid illnesses in the research setting. Future research should determine if comorbid illnesses, such as FM, should be exclusionary conditions in ME and CFS research by considering the possible limitations on generalizability for any potential findings.

FUNDING

Funding was provided by the National Institute of Allergy and Infectious Diseases (Grant number AI105781).

REFERENCES

1. Ramsay AM. Myalgic Encephalomyelitis and Post viral Fatigue States: The Saga of Royal Free Disease. London: Gower Medical Publishing for the Myalgic Encephalomyelitis Association; 1988. https://goo.gl/pHe2NL
2. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Intern Med. 1994; 121: 953-959. https://goo.gl/GXUhui
3. Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor RR, et al. A community-based study of chronic fatigue syndrome. Arch Inter Med. 1999; 159: 2129-37. https://goo.gl/YqTa1E
4. Meeus M, Nijs J, Meirleir KD. Chronic musculoskeletal pain in patients with the chronic fatigue syndrome: a systematic review. Eur J Pain. 2007; 11: 377-386. https://goo.gl/4l5kb9
5. Katz RS, Wolfe F, Michaud K. Fibromyalgia diagnosis: a comparison of clinical, survey, and American College of Rheumatology criteria. Arthritis Rheum. 2006; 54: 169-176. https://goo.gl/Fb2QjA
6. Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia, and chemical sensitivities. Arch Intern Med. 1994; 154: 2049-2053. https://goo.gl/M7H6in
7. Wysenbeek AJ, Shapira Y, Leibovici L. Primary fibromyalgia and the chronic fatigue syndrome. RheumatolInt. 1991; 10: 227-229. https://goo.gl/bkPPzO
8. Hudson JI, Goldenberg DL, Pope HG Jr, Keck PE Jr, Schlesinger L. Comorbidity of fibromyalgia with medical and psychiatric disorders. Am J Med. 1992; 92: 363-367. https://goo.gl/tLafyB
9. Jason LA, Taylor RR, Kennedy CL. Chronic fatigue syndrome, Fibromyalgia, and Multiple Chemical Sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms. Psychosom Med. 2000; 62: 655-663. https://goo.gl/huop5t
10. Deary IJ. A taxonomy of medically unexplained symptoms. J Psychosom Res. 1999; 47: 51-9. https://goo.gl/a3kYyV
11. Barsky AJ, Borus JF. Functional somatic syndromes. Ann Intern Med. 1999; 130: 910-921. https://goo.gl/B2Ih1U
12. Jiao J, Vincent A, Cha SS, Luedtke CA, Kim CH, Oh TH. Physical trauma and infection as precipitating factors in patients with fibromyalgia. Am J Phys Med Rehabil. 2015; 94: 1075-1082. https://goo.gl/nF1pTm
13. Katz BZ, Jason LA. Chronic fatigue syndrome following infections in adolescents. Curr Opin Pediatr. 2013; 25: 95-102. https://goo.gl/9YITtZ
14. Agmon-Levin N, Zafrir Y, Kivity S, Balofsky A, Amital H, Shoenfeld Y. Chronic fatigue syndrome and fibromyalgia following immunization with the hepatitis B vaccine: another angle of the 'autoimmune (auto-inflammatory) syndrome induced by adjuvants'(ASIA). Immunol Res. 2014; 60: 376-383. https://goo.gl/O9Y0qe
15. Genc A, Tur BS, Aytur YK, Oztuna D, Erdogan MF. Does aerobic exercise affect the hypothalamic-pituitary-adrenal hormonal response in patients with fibromyalgia syndrome? J Phys TherSci. 2015; 27: 2225-2231. https://goo.gl/VTcSfZ
16. Tomas C, Newton J, Watson S. A review of hypothalamic-pituitary-adrenal axis function in chronic fatigue syndrome. ISRN Neurosci. 2013. https://goo.gl/ygbGpd
17. Berg D, Berg LH, Couvaras J, Harrison H. Chronic fatigue syndrome and/or fibromyalgia as a variation of antiphospholipid antibody syndrome: an explanatory model and approach to laboratory diagnosis. Blood Coagul Fibrinolysis. 1999; 10: 435-438. https://goo.gl/r6pDib
18. Nishikai M, Tomomatsu S, Hankins RW, Takagi S, Miyachi K, Kosaka S, et al. Autoantibodies to a 68/48 kDa protein in chronic fatigue syndrome and primary fibromyalgia: a possible marker for hypersomnia and cognitive disorders. Rheumatol. 2001; 40: 806-810. https://goo.gl/Fkaee0
19. Klein R, Berg PA. High incidence of antibodies to 5-hydroxytryptamine, gangliosides and phospholipids in patients with chronic fatigue and fibromyalgia syndrome and their relatives: evidence for a clinical entity of both disorders. Eur J Med Res. 1995; 1: 21-26. https://goo.gl/rCZkdy
20. Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. Arch Intern Med. 2000; 160: 221-227. https://goo.gl/SRJw8n
21. Bombardier CH, Buchwald D. Chronic fatigue, chronic fatigue syndrome, and fibromyalgia. Disability and health-care use. Med Care. 1996; 34: 924-930. https://goo.gl/1sIIUn
22. White KP, Speechley M, Harth M, Ostbye T. Co-existence of chronic fatigue syndrome with fibromyalgia syndrome in the general population: a controlled study. Scand J Rheumatol. 2000; 29: 44-51. https://goo.gl/H47gF5
23. Jason LA, Taylor RR, Kennedy CL, Song S, Johnson D, Torres MA. Chronic fatigue syndrome: comorbidity with fibromyalgia and psychiatric illness. Med & Psychia. 2001; 4: 29-34.
24. McManimen SL, Sunnquist ML, Jason LA. Deconstructing post-exertional malaise: An exploratory factor analysis. J Health Psychol. 2016; 1359105316664139. https://goo.gl/DjbuBB
25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research

electronic data capture (REDCap)-a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42: 377-381. https://goo.gl/YrhlSu

26. Carruthers BM, van de Sande MI, De Meirleir KL, Klimas NG, Broderick G, Mitchell T, et al. Myalgic encephalomyelitis: International consensus criteria. J Intern Med. 2011; 270: 327-338. https://goo.gl/hLo8hV

27. Jason LA, Ropacki MT, Santoro NB, Richman JA, Heatherly W, Taylor R, et al. A screening instrument for chronic fatigue syndrome: Reliability and validity. J Chron Fatigue Syndr. 1997; 3: 39-59. https://goo.gl/XI5f2T

28. Jason LA, Evans M, Porter N, Brown M, Brown A, Hunnell J, et al. The development of a revised Canadian myalgic encephalomyelitis chronic fatigue syndrome case definition. Am J Biochem Biotechnol. 2010; 6: 120-135. https://goo.gl/jtSX4u

29. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. J Psychosom Res. 1993; 37: 147-153. https://goo.gl/rCP5xA

30. Komaroff AL, Buchwald D. Symptoms and signs of chronic fatigue syndrome. Rev Infec Dis. 1991; 13: S8-S11. https://goo.gl/II2ARR

31. Evans M, Jason LA. Effects of time frame on the recall reliability of CFS symptoms. Eval Health Prof. 2013; 0: 1-15. https://goo.gl/nczOfL

32. Jason LA, So S, Brown AA, Sunnquist M, Evans M. Test–retest reliability of the DePaul Symptom Questionnaire. Fatigue. 2015; 3: 16-32.

33. Bell DS. The doctor's guide to chronic fatigue syndrome: understanding, treating, and living with CFIDS. New York: Da Capo Press; 1994. https://goo.gl/VthWs4

34. Ware JE, Snow KK, Kosinski M. SF-36 Health Survey: Manual and Interpretation Guide. Lincoln RI: Quality Metric, Inc. 2000. https://goo.gl/TKIZrm

35. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-item short-form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care. 1993; 31: 247-263. https://goo.gl/xlUxbG

36. IOM (Institute of Medicine) Beyond myalgic encephalomyelitis/chronic fatigue syndrome: Redefining an illness. Washington, DC: The National Academies; 2015. https://goo.gl/BxUkZ1

37. Schaefer KM. Sleep disturbances and fatigue in woman with fibromyalgia and chronic fatigue syndrome. J ObstetGynecol Neonatal Nurs. 1995; 24: 229-233. https://goo.gl/5OCUyf

38. Brown MM, Jason LA. Functioning in individuals with chronic fatigue syndrome: Increased impairment with co-occurring multiple chemical sensitivity and fibromyalgia. Dyn Med. 2007; 6: 6. https://goo.gl/6cDSmD

39. McManimen SL, Jason LA, Williams YJ. Variability in symptoms complicates utility of case definitions. Fatigue. 2015; 3: 164-172. https://goo.gl/zHqrMy

40. Cockshell SJ, Mathias JL. Cognitive functioning in chronic fatigue syndrome: a meta-analysis. Psychol Med. 2010; 40: 1253-1267. https://goo.gl/PWkCyQ

41. Johnston S, Brenu EW, Staines D, Marshall-Gradisnik S. The prevalence of chronic fatigue syndrome/myalgic encephalomyelitis: a meta-analysis. Clin Epidemiol. 2013; 5: 105-110. https://goo.gl/vLbL4u

42. Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD, Ramírez G. Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. JAMA. 2001; 286: 1360-1368. https://goo.gl/iXS5xt

43. Jason LA, Taylor R, Wagner L, Holden J, Ferrari JR, Plioplys AV, et al. Estimating rates of chronic fatigue syndrome from a community based sample: A pilot study. Am J Comm Psychol. 1995; 23: 557-568. https://goo.gl/MVkCRx

44. Zdunek M, Jason LA, Evans M, Jantke R, Newton JL. A cross cultural comparison of disability and symptomatology associated with CFS. Int J Psychol BehSci. 2015; 5: 98. https://goo.gl/yBJl3i