

Iraq and Afghanistan Veterans report symptoms consistent with chronic multisymptom illness one year after deployment

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Abstract—Many Veterans returning from service in Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) experience chronic pain. What is not known is whether for some OIF/OEF Veterans this pain is part of a larger condition of diffuse multisystem symptoms consistent with chronic multisymptom illness (CMI). We use data from a prospective longitudinal study of OIF/OEF Veterans to determine the frequency of CMI. We found that 1 yr after deployment, 49.5% of OIF/OEF Veterans met criteria for mild to moderate CMI and 10.8% met criteria for severe CMI. Over 90% of Veterans with chronic pain met criteria for CMI. CMI was not completely accounted for either by posttraumatic stress disorder or by pre-deployment levels of physical symptoms. Veterans with symptoms consistent with CMI reported significantly worse physical health function than Veterans who did not report symptoms consistent with CMI. This study suggests that the presence of CMI should be considered in the evaluation of OIF/OEF Veterans. Further, it suggests that the pain management for these Veterans may need to be tailored to take CMI into consideration.

Key words: chronic multisymptom illness, chronic pain, combat deployment, mental health function, Operation Iraqi Freedom/Operation Enduring Freedom, pain management, Persian Gulf war, physical health function, PTSD, Veterans.

INTRODUCTION

Chronic pain is a significant and complex problem for Veterans who deployed to Iraq (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]). Forty-three percent of OIF/OEF Veterans seeking treatment at a Department of Veterans Affairs (VA) hospital reported pain, with 63 percent of those Veterans reporting clinically significant pain [1]. Further,

Abbreviations: ANCOVA = analysis of covariance, CDC = Centers for Disease Control and Prevention, CMI = chronic multisymptom illness, HEROES = Healthy Resilience after Operational and Environmental Stressors, MCS = mental health composite score, mTBI = mild traumatic brain injury, OEF = Operation Enduring Freedom, OIF = Operation Iraqi Freedom, PCS = physical health composite score, PHQ-15 = Patient Health Questionnaire-15, PTSD = posttraumatic stress disorder, VA = Department of Veterans Affairs, VR-36 = Veterans RAND 36-Item Health Survey.

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OIF/OEF Veterans with chronic pain have worse physical health function than OIF/OEF Veterans without chronic pain [2]. Finally, OIF/OEF Veterans with chronic pain are more likely to present with another postdeployment health condition (i.e., posttraumatic stress disorder [PTSD], mild traumatic brain injury [mTBI], and/or polysubstance abuse) [3] than to present with only chronic pain. What is not known is how often chronic musculoskeletal pain presents with other chronic and comorbid symptoms, such as chronic fatigue, gastrointestinal distress, or cognitive problems such as difficulty finding words. It is possible that for some OIF/OEF Veterans, chronic pain may be only one symptom of a larger multisymptom syndrome. Walker et al. suggested that the most common health concern of OIF/OEF Veterans are diffuse, widespread, and overlapping physical, cognitive, and emotional symptoms [4].

There is good reason to suspect that some OIF/OEF Veterans with chronic pain are also experiencing other chronic symptoms. Multisystem diffuse symptoms have been common in Veterans after every modern war [5–6]. This was particularly clear after the Persian Gulf war (Operation Desert Shield/Operation Desert Storm), when an estimated 30 percent of Veterans experienced multiple chronic symptoms [7–10]. Termed chronic multisymptom illness (CMI) (or Gulf War Illness), the Centers for Disease Control and Prevention (CDC) defines CMI as having one or more chronic symptoms (≥ 6 mo duration) from two or more symptom categories: (1) fatigue, (2) mood and cognition (e.g., concentration problems, depression), or (3) musculoskeletal (e.g., joint pain) [11]. Evidence has found that CMI is distinct from PTSD or depression [12]. CMI causes disability that is as severe as found in other chronic illnesses and continues to affect Persian Gulf war Veterans many years after their deployment [7,13].

There is preliminary evidence to suggest that OIF/OEF Veterans may also be experiencing increases in widespread symptoms. Three cross-sectional studies found heightened physical symptom severity as measured with the Patient Health Questionnaire-15 (PHQ-15). Iverson et al. reported that 41 percent of women and 31 percent of men deployed to OIF/OEF reported medium or higher levels of physical symptom severity [14]. McAndrew et al. reported on the relationship between physical symptoms and environmental exposure concerns among OIF/OEF Veterans seeking care at a VA tertiary clinic [15]. They found, on average, medium levels

of physical symptom severity, and symptom severity was positively associated with environmental exposure concerns [15]. Similarly, Hoge et al. found, on average, medium levels of physical symptom severity among OIF/OEF Veterans and higher symptom severity among OIF/OEF Veterans with PTSD [16]. Medium levels of symptoms are associated with a greater number of physician visits and more disability days [17].

Especially compelling evidence comes from the Millennium Cohort Study. The Millennium Cohort Study is a prospective longitudinal study of 73,078 OIF/OEF military personnel [18], which used a close approximation of the CDC definition of CMI with some modifications (e.g., two instead of three pain symptoms, “unusual fatigue” instead of general fatigue). Comparing military personnel who deployed with those who did not deploy, this study found that combat deployment resulted in a 1.7 times increase in odds of meeting CMI criteria. Further, an estimated 26.5 percent of OIF/OEF Veterans who deployed met criteria for CMI after deployment. These data suggest that CMI is a problem among OIF/OEF Veterans, a view also suggested by the Institute of Medicine [19]. These existing studies are limited by not having used the specific CDC definition; thus, we do not yet know whether OIF/OEF Veterans meet that definition of CMI. Further, no existing study has used a pre-post deployment longitudinal design that provides the ability to assess whether symptoms increase after combat deployment or whether OIF/OEF soldiers could have been experiencing heightened symptoms prior to combat deployment.

To optimally address pain among OIF/OEF Veterans, it is critical that we understand whether CMI is a problem among these Veterans, and if so, its relationship to chronic pain. The presence of chronic pain in the context of CMI likely necessitates modification of pain management treatments. Focusing exclusively on chronic pain without taking into account the patients’ other symptoms may lead to poor adherence to treatment recommendations and low satisfaction with care. Similarly, treatments for CMI need to be tailored when the predominant symptom is pain as compared with when the predominant symptoms are fatigue or gastrointestinal distress.

The goal of the current study was to report the frequency of CMI in soldiers returning from war using data from a longitudinal, prospective study, the Healthy Resilience after Operational and Environmental Stressors (HEROES) Project. The HEROES Project improves upon

limitations of past studies by using the CDC definition of CMI and using a pre-post deployment longitudinal design. The aims of the current study were to—

1. Estimate the frequency of OIF/OEF Veterans who report symptoms consistent with CMI at 1 yr postdeployment.
2. Examine the relationship between CMI at 1 yr postdeployment and chronic pain symptoms at 1 yr postdeployment, PTSD symptoms at 1 yr postdeployment, and physical symptom severity at predeployment.
3. Determine the relationship of CMI assessed at 1 yr postdeployment to physical and mental health function at 1 yr postdeployment, controlling for physical symptom severity and health function at predeployment and PTSD symptoms at 1 yr postdeployment.

METHODS

The HEROES Project is a prospective longitudinal observational cohort design with measures collected at four time points: predeployment, immediately postdeployment, 3 mo postdeployment, and 1 yr postdeployment (for description see McAndrew et al., Yan et al., and Quigley et al. [20–22]).

Participants

Participants were Army National Guard and Army Reserve enlisted soldiers (including noncommissioned officers) deploying to either OIF or OEF who participated in the HEROES Project [20–22]. Exclusion criteria were current self-reported depression, medications with cardiovascular and/or autonomic effects (e.g., beta blockers or other antihypertensive medication), history of schizophrenia or bipolar disorder or current cancer, high blood pressure, or pregnancy. The larger study included a physiological assessment (not reported here) that necessitated excluding patients on medications with cardiovascular and/or autonomic effects and those with high blood pressure.

At the 1 yr postdeployment assessment, 319 soldiers completed the questionnaire on CMI. This was from an initial study sample of 795 soldiers (at predeployment). Out of the initial sample, 32 did not mobilize, were officers, or were severely injured or killed in action. At 1 yr postdeployment, 118 participants declined to participate (14.8%). The remainder of the participants whose data were missing at 1 yr postdeployment were lost to follow-up. Most of these were lost to follow-up because we did

not receive information on when they returned from deployment ($n = 289$); for the others we do not have information on the reasons they were lost to follow-up ($n = 37$). Physical symptom severity at baseline was not related to the likelihood of being lost to follow-up at 1 yr postdeployment ($X^2 = 0.80, p = 0.85$).

Procedure

Study personnel approached soldiers who had just finished their medical processing or were waiting to complete their medical processing. We emphasized the voluntary nature of their participation and that research staff were civilian VA personnel. We examined differences between those who volunteered and those who declined to participate. There was no significant difference in the proportion of males and females in the participant and nonparticipant groups ($X^2 = 2.30, p = 0.13$). However, using a dichotomized variable for general health (excellent/very good vs good/fair/poor), there was a small but statistically significant difference between the participant sample and the nonparticipant sample. There were fewer individuals reporting excellent/very good health in the participant sample (72.1% of participant sample vs 78.8% of nonresponse sample; $X^2 = 8.25, p < 0.01$). We choose to ask about general health because it was only one item and has previously been shown to prospectively predict health.

Following recruitment, soldiers were given information about the study and screened for eligibility, and those who were eligible and interested gave informed consent. Soldiers completed predeployment self-report questionnaires and physiological measures (not included here) while at the Army installation. Immediately postdeployment, soldiers again completed self-report questionnaires at the Army installation. Soldiers who did not return to their installation were sent the immediate postdeployment questionnaires via mail. Data at 3 mo and 1 yr postdeployment were collected through mailed questionnaires. This report focuses on self-report of CMI measured at 1 yr postdeployment controlling for predeployment factors. The protocol was approved by Institutional Review Boards of the VA (VA New Jersey Healthcare System and the G.V. [Sonny] Montgomery VA Medical Center) and by the Walter Reed Department of Clinical Investigation.

Measures

Chronic Multisymptom Illness

CMI was assessed at 1 yr after deployment using the CDC definition. The Institute of Medicine recently released a report that reviewed the evidence for a case definition of CMI. They recommended using either the CDC definition or the Kansas definition [23–24] because both encompassed most of the symptoms of CMI. We chose to use the CDC definition because it provided a broader definition of CMI and can more easily be assessed through self-report because the Kansas definition requires assessment of possible medical exclusions. To meet the CDC criteria for CMI, participants are asked about the severity (mild, moderate, or severe) and duration (≥ 6 mo duration) of 10 common symptoms. CMI is defined as having one or more chronic symptoms (≥ 6 mo duration) from two or more symptom categories. The three symptom categories are (1) fatigue, (2) mood and cognition (symptoms of feeling depressed, difficulty remembering or concentration, feeling moody, feeling anxious, trouble finding words, or difficulty sleeping), and (3) musculoskeletal (symptoms of joint pain, joint stiffness, or muscle pain). We classified participants as having severe CMI if at least one symptom in two or more categories was rated as severe. We also asked about 25 additional symptoms that do not contribute to the definition of CMI. The prevalence of both CMI and these other symptoms is presented in **Table 1**.

Patient Health Questionnaire-15

Physical symptom severity was assessed at predeployment with the PHQ-15 [17]. Participants were asked to indicate, “During the past 7 days, how much have you been bothered by any of the following problems.” Each item is scored as 0 (not bothered at all), 1 (bothered a little), or 2 (bothered a lot). Generally, cut offs of 0–4 (minimal), 5 (low), 10 (medium), and 15 (high) are used to create physical symptoms severity categories [17]. Items include stomach pain; back pain; pain in arms, legs, or joints; menstrual cramps or other problems with periods; headaches; chest pain; dizziness; fainting spells; feeling the heart pound or race; shortness of breath; pain or problems during sexual intercourse; constipation; loose bowels or diarrhea; nausea; gas or indigestion; feeling tired or having low energy; and trouble sleeping.

Health Function—Veterans RAND 36-Item Health Survey

The Veterans RAND 36-Item Health Survey (VR-36) is a measure of mental and physical health function [25–27] and was assessed at predeployment and 1 yr postdeployment. The VR-36 was developed from the 36-Item Short Form Health Survey. The VR-36 provides two composite scores, physical function (physical health composite score [PCS]) and mental function (mental health composite score [MCS]). These composite scores are composed of eight subscale scores: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Composite and subscale scores are normed to a mean of 50 and a standard deviation of 10.

Posttraumatic Stress Disorder Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition

PTSD symptoms were assessed at 1 yr postdeployment with the Posttraumatic Stress Disorder Checklist-Civilian, which assesses for 17 symptoms of PTSD [28–29]. Participants were asked to indicate “in the past month, how much were you bothered by” each of 17 symptoms. Items are scored on a scale of 1 to 5. A score of 50 or greater is commonly used to denote significant PTSD symptoms [30].

Analysis

We first provide the frequency of CMI and specific physical symptoms at 1 yr postdeployment. A Pearson correlation was used to examine the relationship between CMI and age. Chi-square analyses were used to examine the relationship of CMI to sex and whether or not a participant had previously deployed, which prior research found to be related to increases in physical symptoms [31].

We next report the percentage of Veterans with musculoskeletal chronic pain who met criteria for CMI. To measure chronic pain, we used the musculoskeletal category of the CMI measure (≥ 1 symptoms of joint pain, joint stiffness, and muscle pain). We considered not including joint stiffness, but only eight Veterans reported joint stiffness without joint or muscle pain. Chi-square analyses were conducted to understand the relationship of chronic pain to CMI. Chi-square analyses were also used to examine the relationship of CMI to PTSD symptoms at 1 yr postdeployment and CMI to predeployment physical symptoms.

Table 1.

Operation Iraqi Freedom/Operation Enduring Freedom soldiers reporting symptoms with duration of greater than 6 mo at 1 yr after return from deployment, *n* (%). Bolded items are symptoms of chronic multisymptom illness from Centers for Disease Control and Prevention definition.

Symptom	Mild	Moderate	Severe	Total
Sinus Congestion	43 (13.5)	38 (12.0)	15 (4.7)	96 (30.0)
Headache	46 (14.4)	35 (11.0)	34 (10.7)	115 (36.1)
Fatigue	55 (17.2)	50 (15.7)	21 (6.6)	126 (39.5)
Joint Pain	51 (16.0)	69 (22)	28 (8.8)	148 (46.0)
Difficulty Remembering or Concentrating	60 (18.8)	42 (13.2)	25 (7.8)	127 (39.8)
Joint Stiffness	40 (12.5)	50 (15.7)	18 (5.6)	108 (33.9)
Difficulty Sleeping	44 (13.8)	68 (21.3)	52 (16.3)	164 (51.4)
Gas, Bloating, Cramps, or Abdominal Pain	20 (6.3)	25 (7.8)	10 (3.1)	55 (17.2)
Trouble Finding Words	34 (10.7)	24 (7.5)	15 (4.7)	73 (22.9)
Moody or Irritable	65 (20.4)	61 (19.1)	36 (11.3)	162 (50.8)
Rash or Sores	11 (3.4)	11 (3.4)	5 (1.6)	27 (8.5)
Numbness or Tingling	31 (9.7)	24 (7.5)	6 (1.9)	61 (19.1)
Muscle Pain	31 (9.7)	33 (10.3)	7 (2.2)	71 (22.2)
Hay Fever or Allergies	27 (8.5)	21 (6.6)	15 (4.7)	63 (19.7)
Feeling Depressed	48 (15.0)	27 (8.5)	16 (5.0)	91 (28.5)
Diarrhea (>3 loose stool samples per 24 h)	15 (4.7)	14 (4.4)	6 (1.9)	35 (11.0)
Sore Throat	9 (2.8)	3 (0.9)	0 (0)	12 (3.8)
Cough	25 (7.8)	8 (2.5)	4 (1.3)	37 (11.6)
Feeling Anxious	44 (13.8)	43 (13.5)	19 (6.0)	106 (33.2)
Unintentional Weight Gain ≥10 lb	24 (7.5)	36 (11.3)	15 (4.7)	75 (23.5)
Shortness of Breath	22 (6.9)	17 (5.3)	6 (1.9)	45 (14.1)
Chest Pain	15 (4.7)	9 (2.8)	3 (0.9)	27 (8.5)
Decreased Interest in Sex	21 (6.6)	15 (4.7)	14 (4.3)	50 (15.7)
Dizziness or Trouble Maintaining Balance	21 (6.6)	9 (2.8)	4 (1.3)	34 (10.7)
Night Sweats that Soak Bed Sheets	13 (4.1)	14 (4.4)	10 (3.1)	37 (11.6)
Fatigue Lasting 24 h After Exertion	18 (5.6)	11 (3.4)	9 (2.8)	38 (11.9)
Nasal Sores	4 (1.3)	5 (1.6)	0 (0)	9 (2.8)
Swollen Lymph Nodes	4 (1.3)	2 (0.6)	3 (0.9)	9 (2.8)
Milk Intolerance	7 (2.2)	8 (2.5)	7 (2.2)	22 (6.9)
Episodes of Disorientation	14 (4.4)	5 (1.6)	2 (0.6)	21 (6.6)
Nausea and Vomiting	8 (2.5)	5 (1.6)	3 (0.9)	16 (5.0)
Wheezing	6 (1.9)	9 (2.8)	1 (0.3)	16 (5.0)
Chemical Sensitivity	5 (1.6)	6 (1.9)	3 (0.9)	14 (4.4)
Fever	5 (1.6)	3 (0.9)	1 (0.3)	9 (2.8)
Unintentional Weight Loss >10 lb	5 (1.6)	1 (0.3)	3 (0.9)	9 (2.8)

Finally, we were interested in the relationship of CMI to health function. We first graphically depicted health function scores for each subscale of the VR-36 at three levels of CMI (no CMI, mild to moderate CMI, and severe CMI). We then used two analyses of covariance (ANCOVAs) to examine the relationship of CMI (no CMI, mild to moderate CMI, and severe CMI) to a composite score of mental health function (MCS) and a composite score of physical health function (PCS). Generally, a 2 to 3 point difference on these scores is considered clinically significant. In both models, we respectively

controlled for the MCS or PCS at predeployment and the physical symptom severity from the PHQ-15 at predeployment. Examining postdeployment health function while controlling for predeployment levels of health function allows us to understand the relationship of CMI to postdeployment health function independent of predeployment levels. Similarly, controlling for predeployment physical symptoms allows us to understand the effect of symptoms that emerge after deployment (controlling for pre-existing symptom severity) on health function. We also controlled for PTSD symptoms at 1 yr

postdeployment, age, and sex because these also are related to health function.

RESULTS

Prevalence of Chronic Multisymptom Illness

At 1 yr after return from deployment, physical symptoms were assessed using the CDC measure of CMI; 46.7 percent reported physical symptoms consistent with CMI, and 10.8 percent reported symptoms consistent with severe CMI. Reporting physical symptoms consistent with CMI at 1 yr after return from deployment was not related to sex ($X^2 = 1.49$, $p = 0.47$) or to having deployed previously ($X^2 = 2.89$, $p = 0.24$). Meeting CMI criteria was related to greater age ($r = 0.19$, $p < 0.01$).

Physical Symptoms in Those with Chronic Multisymptom Illness

The prevalence of the 10 chronic (duration ≥ 6 mo) physical symptoms that define CMI at 1 yr postdeployment are listed in **Table 1** (in bold). The severity and duration of an additional 25 physical symptoms are listed in **Table 1**. The most common symptoms were difficulty sleeping (51.4%), being moody or irritable (50.8%), joint pain (46.0%), fatigue (39.5%), difficulty remembering or concentrating (39.8%), headaches (36.1%), and sinus congestion (30.0%).

Relationship of Chronic Multisymptom Illness to Pain Symptoms

We compared the number of Veterans who reported chronic musculoskeletal pain symptoms (defined as reporting either joint pain, joint stiffness, or muscle pain lasting 6 mo or longer) with the number of Veterans who reported symptoms consistent with CMI. We found a total of 166 (52%) Veterans reported chronic musculoskeletal pain, and 150 of these Veterans or 90 percent of those with musculoskeletal pain also met criteria for CMI. Thus, the vast majority of those reporting chronic musculoskeletal pain met criteria for CMI. Further, 82 percent of those who met criteria for CMI reported chronic pain ($X^2 = 291.83$, $p < 0.01$).

Relationship of Chronic Multisymptom Illness to Posttraumatic Stress Disorder

At 1 yr postdeployment, almost all Veterans who reported symptoms consistent with PTSD also reported

symptoms consistent with CMI or severe CMI ($X^2 = 47.27$, $p < 0.01$). Only seven (2.2%) Veterans reported symptoms consistent with PTSD but did not meet criteria for CMI. However, 140 (43.9%) Veterans met criteria for CMI (5% severe CMI) but did not report symptoms consistent with PTSD (**Figure 1**).

Relationship of Chronic Multisymptom Illness to Predeployment Symptoms

Of the Veterans who provided responses at 1 yr postdeployment, at predeployment 162 (50.9%) reported minimal physical symptom severity, 112 (35%) reported low physical symptom severity, 38 (11%) reported medium physical symptom severity, and 6 (1%) reported high physical symptom severity.

Chi-square analyses showed that soldiers who reported greater symptom severity at predeployment were more likely to report physical symptoms consistent with CMI 1 yr postdeployment ($X^2 = 17.84$, $p = 0.01$; **Table 2**). All of the soldiers who reported high symptom severity at baseline also met criteria for CMI at 1 yr postdeployment. Importantly, 150 (47%) soldiers who reported minimal symptom severity (i.e., the lowest category) at baseline also reported physical symptoms consistent with CMI at 1 yr postdeployment.

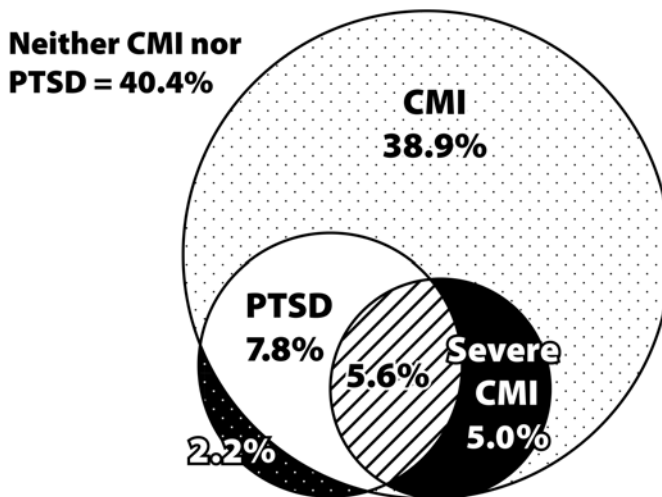


Figure 1. Frequency of chronic multisymptom illness (CMI) and posttraumatic stress disorder (PTSD) among Operation Iraqi Freedom/Operation Enduring Freedom soldiers 1 yr after deployment.

Table 2.
Predeployment physical symptom severity and chronic multisymptom illness (CMI) status 1 yr after deployment, *n* (%).

Baseline Physical Symptom Severity	No CMI	Mild to Moderate CMI	Severe CMI
Minimal	85 (52.5)	64 (39.5)	13 (8.0)
Low	40 (35.4)	59 (52.2)	13 (12.4)
Medium	11 (28.9)	22 (57.9)	5 (13.2)
High	0 (0)	4 (66.7)	2 (33.3)

Relationship of Chronic Multisymptom Illness to Physical and Mental Health Function

Figure 2 depicts mental and physical health function at 1 yr postdeployment for Veterans who did not screen positive for CMI, Veterans who screened positive for mild to moderate CMI, and Veterans who screened positive for severe CMI. For reference, a 2 to 3 point difference on one of the subscales of the VR-36 is generally considered clinically significant. For each subscale, Veterans who screened positive for severe CMI reported function-

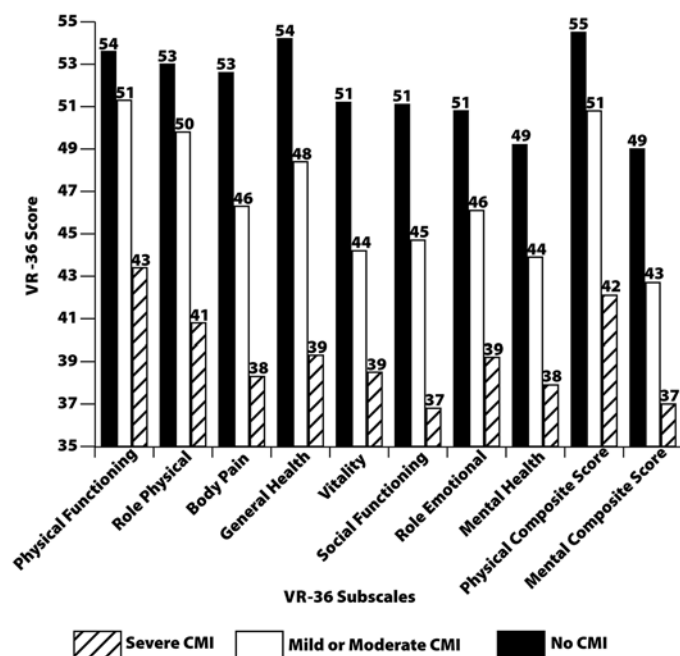


Figure 2.
Physical and mental health function subscales of Veterans RAND 36-Item Health Survey (VR-36) at 1 yr postdeployment for soldiers with no chronic multisymptom illness (CMI), mild to moderate CMI, and severe CMI. Higher scores (*y*-axis) indicate better functioning.

ing 10 points or more lower than that in soldiers who did not screen positive for CMI.

Two ANCOVAs were used to determine the relationship of CMI (no CMI, mild to moderate CMI, and severe CMI) to composite scores of mental (Table 3) and physical health function (Table 4). CMI was strongly related to physical health function 1 yr after deployment after controlling for predeployment levels of physical health function and physical symptoms, and for PTSD symptoms at 1 yr after deployment. CMI and mental health function were not significantly associated after controlling for predeployment levels of mental health function and physical symptoms, and PTSD symptoms at 1 yr postdeployment.

DISCUSSION

Chronic pain is a significant problem for OIF/OEF Veterans. For some OIF/OEF Veterans, this chronic pain may be part of a larger multisystem condition, termed CMI. Using a prospective longitudinal study of OIF/OEF soldiers, we found that 49.5 percent of OIF/OEF Veterans met criteria for mild to moderate CMI at 1 yr after deployment, and 10.8 percent met criteria for severe CMI. Almost all Veterans with chronic musculoskeletal pain also met criteria for CMI (90%). In this study, neither mild to moderate nor severe CMI were completely accounted for by PTSD or by predeployment levels of physical symptom severity. Further, Veterans who met criteria for either mild to moderate or severe CMI also reported clinically and statistically significantly worse physical health function than soldiers without CMI, even after controlling for predeployment physical health function and physical symptoms and PTSD symptoms at 1 yr postdeployment. To put this in perspective, on average, soldiers with severe CMI had physical health function almost as low as civilians with chronic illness [32].

Our results suggest that for some, if not many, OIF/OEF Veterans with chronic musculoskeletal pain, their chronic pain may be part of a larger CMI. This has implications for pain management or treatment. Providers should consider asking about and addressing the other chronic symptoms of OIF/OEF Veterans. Prior research has found that when providers' and patients' views on illnesses are nonconcordant, the patient is less adherent to treatment recommendations and less satisfied with the care [33]. For Veterans with chronic pain, treatments focused

Table 3.Analysis of covariance predicting physical health function 1 yr after deployment (adjusted $R^2 = 0.25$).

	Mean Square	F	p-Value
Sex	0.44	0.01	0.93
Age	431.50	7.55	0.01
Predeployment Physical Functioning	1,113.12	19.47	0.00
Predeployment Physical Symptoms	0.57	0.01	0.92
PTSD symptoms 1 yr After Deployment	654.40	11.45	<0.001
CMI 1 yr After Deployment	587.65	10.28	<0.001

CMI = chronic multisymptom illness, PTSD = posttraumatic stress disorder.

Table 4.Analysis of covariance predicting mental health function 1 yr after deployment (adjusted $R^2 = 0.48$).

	Mean Square	F	p-Value
Sex	170.41	2.14	0.14
Age	114.73	1.44	0.23
Predeployment Mental Health Functioning	1,392.74	17.50	0.00
Predeployment Physical Symptoms	129.89	1.63	0.20
PTSD Symptoms 1 yr After Deployment	13,464.31	169.16	<0.001
CMI 1 yr After Deployment	155.75	1.96	0.14

CMI = chronic multisymptom illness, PTSD = posttraumatic stress disorder.

on chronic pain that ignore the Veterans' fatigue or cognitive dysfunction may lead to poorer adherence and satisfaction. Management for Veterans with CMI may require going beyond traditional pain management approaches. For example, cognitive behavioral therapy is a recommended treatment for chronic pain. However, there likely needs to be greater tailoring of cognitive behavioral therapy to the specific needs of Veterans with CMI [34]. This may include treatment to improve sleep, scheduling of pleasant activities around episodes of fatigue, and cognitive remediation treatment.

After the Persian Gulf war, there was a prominent focus on CMI (called Gulf War Illness), the associated poor functioning [7], and the possible overlap of this condition with PTSD symptoms [16]. In contrast, the clinical focus for OIF/OEF Veterans has been on multiple diagnoses, each of which can be associated with significant physical symptoms, including chronic pain, PTSD, mTBI, depression, and polysubstance abuse [16,35–37]. Our study was limited in that we only assessed PTSD and pain symptoms and did not have measures of these other common postdeployment health conditions. However, it seems unlikely that unmeasured depression, mTBI, and substance abuse can fully account for the physical symptoms observed here. First, depression and substance abuse frequently co-occur with CMI but in prior studies

have not been demonstrated to account for the symptoms of CMI (for a review see Burton [38]). Second, another possible candidate for the cause of CMI symptoms, mTBI, also appears unlikely to fully explain the extent of CMI. mTBI is thought to affect approximately 15 percent of OIF/OEF Veterans and commonly co-occurs with PTSD, yet we found that 43 percent of OIF/OEF Veterans met criteria for CMI and did not meet criteria for PTSD. Thus, even if mTBI had no overlap with PTSD, there would still be an estimated 28 percent of our sample that met criteria for CMI but not for either PTSD or mTBI (i.e., 43% minus 15%). Future studies should measure the full range of possible comorbidities to better understand the relationship of CMI to each of these other postdeployment conditions.

There are several limitations of this study. Although the CDC definition for CMI is recommended by the Institute of Medicine, it is not without limitations. Most critically, there are no exclusion criteria for the CDC definition, and thus conditions such as HIV, multiple sclerosis, and rheumatoid arthritis may explain these symptoms for some of our participants. The relatively short time frame between deployment and demonstration of CMI in this sample, however, suggests that the overlap with chronic conditions like these should not yet be very high. Second, this definition was developed based on

symptom presentations in Persian Gulf war Veterans. The symptoms we found to be most common were not necessarily those most commonly reported after the Persian Gulf war, suggesting that there may be a unique case definition of CMI for OIF/OEF Veterans that takes into account deployment-related factors that differ for these deployments. Other limitations include that we did not have a complete assessment of CMI symptoms predeployment, and thus had to rely on the PHQ-15–based measure of physical symptom severity at predeployment. We also did not have a validated measure of chronic musculoskeletal pain. Finally, by using a self-report measure of CMI we are capturing the number of soldiers in our sample who have symptoms consistent with CMI. An interview with a provider is necessary to determine the best diagnosis.

CONCLUSIONS

To our knowledge, this is one of the first studies of CMI in OIF/OEF soldiers. Our data suggest that many OIF/OEF Veterans are experiencing multiple chronic symptoms that meet criteria for CMI. Further, meeting CMI criteria is associated with lower physical health function to an extent that is likely clinically significant. Finally, the prevalence of CMI in this sample is not fully accounted for by either predeployment physical symptoms or PTSD. Because we did not use a diagnostic interview with a clinician, we do not know the best diagnosis for participants in this sample. However, our results suggest that clinicians should consider CMI when assessing OIF/OEF Veterans with postdeployment health concerns. This includes considering broader treatment strategies that encompass both pain management as well as attention to other bothersome symptoms such as fatigue, trouble sleeping, or cognitive symptoms.

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REFERENCES

- Haskell SG, Brandt CA, Krebs EE, Skanderson M, Kerns RD, Goulet JL. Pain among Veterans of Operations Enduring Freedom and Iraqi Freedom: Do women and men differ? *Pain Med.* 2009;10(7):1167–73. [PMID:19818028] <http://dx.doi.org/10.1111/j.1526-4637.2009.00714.x>
- Helmer DA, Chandler HK, Quigley KS, Blatt M, Teichman R, Lange G. Chronic widespread pain, mental health, and physical role function in OEF/OIF veterans. *Pain Med.* 2009;10(7):1174–82. [PMID:19818029] <http://dx.doi.org/10.1111/j.1526-4637.2009.00723.x>
- Lew HL, Otis JD, Tun C, Kerns RD, Clark ME, Cifu DX. Prevalence of chronic pain, posttraumatic stress disorder, and persistent postconcussive symptoms in OIF/OEF veterans: Polytrauma clinical triad. *J Rehabil Res Dev.* 2009; 46(6):697–702. [PMID:20104399] <http://dx.doi.org/10.1682/JRRD.2009.01.0006>
- Walker RL, Clark ME, Sanders SH. The “postdeployment multi-symptom disorder”: An emerging syndrome in need of a new treatment paradigm. *Psychol Serv.* 2010;7(3): 136–47. <http://dx.doi.org/10.1037/a0019684>
- Hyams KC, Wignall FS, Roswell R. War syndromes and their evaluation: From the U.S. Civil War to the Persian Gulf War. *Ann Intern Med.* 1996;125(5):398–405. [PMID:8702091] <http://dx.doi.org/10.7326/0003-4819-125-5-199609010-00007>
- Jones E, Hodgins-Vermaas R, McCartney H, Everitt B, Beech C, Poynter D, Palmer I, Hyams K, Wessely S. Post-combat syndromes from the Boer war to the Gulf war: A cluster analysis of their nature and attribution. *BMJ.* 2002;

- 324(7333):321–24. [PMID:11834557]
<http://dx.doi.org/10.1136/bmj.324.7333.321>
7. Blanchard MS, Eisen SA, Alpern R, Karlinsky J, Toomey R, Reda DJ, Murphy FM, Jackson LW, Kang HK. Chronic multisymptom illness complex in Gulf War I veterans 10 years later. *Am J Epidemiol.* 2006;163(1):66–75. [PMID:16293719]
<http://dx.doi.org/10.1093/aje/kwj008>
 8. Eisen SA, Kang HK, Murphy FM, Blanchard MS, Reda DJ, Henderson WG, Toomey R, Jackson LW, Alpern R, Parks BJ, Klimas N, Hall C, Pak HS, Hunter J, Karlinsky J, Battistone MJ, Lyons MJ; Gulf War Study Participating Investigators. Gulf War veterans' health: Medical evaluation of a U.S. cohort. *Ann Intern Med.* 2005;142(11):881–90. [PMID:15941694]
<http://dx.doi.org/10.7326/0003-4819-142-11-200506070-00005>
 9. Kang HK, Mahan CM, Lee KY, Magee CA, Murphy FM. Illnesses among United States veterans of the Gulf War: A population-based survey of 30,000 veterans. *J Occup Environ Med.* 2000;42(5):491–501. [PMID:10824302]
<http://dx.doi.org/10.1097/00043764-200005000-00006>
 10. Proctor SP, Heeren T, White RF, Wolfe J, Borgos MS, Davis JD, Pepper L, Clapp R, Sutker PB, Vasterling JJ, Ozonoff D. Health status of Persian Gulf War veterans: Self-reported symptoms, environmental exposures and the effect of stress. *Int J Epidemiol.* 1998;27(6):1000–1010. [PMID:10024195]
<http://dx.doi.org/10.1093/ije/27.6.1000>
 11. Fukuda K, Nisenbaum R, Stewart G, Thompson WW, Robin L, Washko RM, Noah DL, Barrett DH, Randall B, Herwaldt BL, Mawle AC, Reeves WC. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA.* 1998;280(11):981–88. [PMID:9749480]
<http://dx.doi.org/10.1001/jama.280.11.981>
 12. Henningsen P, Zimmermann T, Sattel H. Medically unexplained physical symptoms, anxiety, and depression: A meta-analytic review. *Psychosom Med.* 2003;65(4):528–33. [PMID:12883101]
<http://dx.doi.org/10.1097/01.PSY.0000075977.90337.E7>
 13. Ozakinci G, Hallman WK, Kipen HM. Persistence of symptoms in veterans of the First Gulf War: 5-year follow-up. *Environ Health Perspect.* 2006;114(10):1553–57. [PMID:17035142]
<http://dx.doi.org/10.1289/ehp.9251>
 14. Iverson KM, Pogoda TK, Gradus JL, Street AE. Deployment-related traumatic brain injury among Operation Enduring Freedom/Operation Iraqi Freedom veterans: Associations with mental and physical health by gender. *J Womens Health (Larchmt).* 2013;22(3):267–75. [PMID:23421581]
<http://dx.doi.org/10.1089/jwh.2012.3755>
 15. McAndrew LM, Teichman RF, Osinubi OY, Jasien JV, Quigley KS. Environmental exposure and health of Operation Enduring Freedom/Operation Iraqi Freedom veterans. *J Occup Environ Med.* 2012;54(6):665–69. [PMID:22684317]
<http://dx.doi.org/10.1097/JOM.0b013e318255ba1b>
 16. Hoge CW, Terhakopian A, Castro CA, Messer SC, Engel CC. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. *Am J Psychiatry.* 2007;164(1):150–53. [PMID:17202557]
<http://dx.doi.org/10.1176/ajp.2007.164.1.150>
 17. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: Validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med.* 2002;64(2):258–66. [PMID:11914441]
<http://dx.doi.org/10.1097/00006842-200203000-00008>
 18. Smith TC, Powell TM, Jacobson IG, Smith B, Hooper TI, Boyko EJ, Gackstetter GD. Chronic multisymptom illness: A comparison of Iraq and Afghanistan deployers with veterans of the 1991 Gulf War. *Am J Epidemiol.* 2014;180(12):1176–87. [PMID:25466246]
<http://dx.doi.org/10.1093/aje/kwu240>
 19. Institute of Medicine. Gulf war and health. Volume 8: Update of health effects of serving in the gulf war. Washington (DC): National Academy Press; 2010.
 20. McAndrew LM, D'Andrea E, Lu SE, Abbi B, Yan GW, Engel C, Quigley KS. What pre-deployment and early post-deployment factors predict health function after combat deployment?: A prospective longitudinal study of Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) soldiers. *Health Qual Life Outcomes.* 2013;11:73. [PMID:23631419]
<http://dx.doi.org/10.1186/1477-7525-11-73>
 21. Yan GW, McAndrew L, D'Andrea EA, Lange G, Santos SL, Engel CC, Quigley KS. Self-reported stressors of National Guard women veterans before and after deployment: The relevance of interpersonal relationships. *J Gen Intern Med.* 2013;28(Suppl 2):S549–55. [PMID:23807064]
<http://dx.doi.org/10.1007/s11606-012-2247-6>
 22. Quigley KS, McAndrew LM, Almeida L, D'Andrea EA, Engel CC, Hamtil H, Ackerman AJ. Prevalence of environmental and other military exposure concerns in Operation Enduring Freedom and Operation Iraqi Freedom veterans. *J Occup Environ Med.* 2012;54(6):659–64. [PMID:22588478]
<http://dx.doi.org/10.1097/JOM.0b013e3182570506>
 23. Fukuda K, Nisenbaum R, Stewart G, Thompson WW, Robin L, Washko RM, Noah DL, Barrett DH, Randall B, Herwaldt BL, Mawle AC, Reeves W. Chronic multisymptom illness affecting Air Force veterans of the Gulf War.

- JAMA. 1998;280(11):981–88. [PMID:9749480]
<http://dx.doi.org/10.1001/jama.280.11.981>
24. Steele L. Prevalence and patterns of Gulf War illness in Kansas veterans: Associations of symptoms with characteristics of person, place, and time of military service. *Am J Epidemiol.* 2000;152(10):992–1002. [PMID:11092441]
<http://dx.doi.org/10.1093/aje/152.10.992>
 25. Kazis LE, Miller DR, Clark JA, Skinner KM, Lee A, Ren XS, Spiro A 3rd, Rogers WH, Ware JE Jr. Improving the response choices on the Veterans SF-36 Health Survey role functioning scales: Results from the Veterans Health Study. *J Ambul Care Manage.* 2004;27(3):263–80. [PMID:15287216]
<http://dx.doi.org/10.1097/00004479-200407000-00010>
 26. Kazis LE, Miller DR, Skinner KM, Lee A, Ren XS, Clark JA, Rogers WH, Spiro A 3rd, Selim A, Linzer M, Payne SM, Mansell D, Fincke RG. Patient-reported measures of health: The Veterans Health Study. *J Ambul Care Manage.* 2004;27(1):70–83. [PMID:14717468]
<http://dx.doi.org/10.1097/00004479-200401000-00012>
 27. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473–83. [PMID:1593914]
<http://dx.doi.org/10.1097/00005650-199206000-00002>
 28. McDonald SD, Calhoun PS. The diagnostic accuracy of the PTSD checklist: A critical review. *Clin Psychol Rev.* 2010;30(8):976–87. [PMID:20705376]
<http://dx.doi.org/10.1016/j.cpr.2010.06.012>
 29. Gravely AA, Cutting A, Nugent S, Grill J, Carlson K, Spont M. Validity of PTSD diagnoses in VA administrative data: Comparison of VA administrative PTSD diagnoses to self-reported PTSD Checklist scores. *J Rehabil Res Dev.* 2011;48(1):21–30. [PMID:21328160]
<http://dx.doi.org/10.1682/JRRD.2009.08.0116>
 30. Brady K, Pearlstein T, Asnis GM, Baker D, Rothbaum B, Sikes CR, Farfel GM. Efficacy and safety of sertraline treatment of posttraumatic stress disorder: A randomized controlled trial. *JAMA.* 2000;283(14):1837–44. [PMID:10770145]
<http://dx.doi.org/10.1001/jama.283.14.1837>
 31. Stein PK, Domitrovich PP, Ambrose K, Lyden A, Fine M, Gracely RH, Clauw DJ. Sex effects on heart rate variability in fibromyalgia and Gulf War illness. *Arthritis Rheum.* 2004;51(5):700–708. [PMID:15478168]
<http://dx.doi.org/10.1002/art.20687>
 32. Sprangers MA, de Regt EB, Andries F, van Agt HM, Bijl RV, de Boer JB, Foets M, Hoeymans N, Jacobs AE, Kempen GI, Miedema HS, Tijhuis MA, de Haes HC. Which chronic conditions are associated with better or poorer quality of life? *J Clin Epidemiol.* 2000;53(9):895–907. [PMID:11004416]
[http://dx.doi.org/10.1016/S0895-4356\(00\)00204-3](http://dx.doi.org/10.1016/S0895-4356(00)00204-3)
 33. Christensen AJ, Howren MB, Hillis SL, Kaboli P, Carter BL, Cvetengros JA, Wallston KA, Rosenthal GE. Patient and physician beliefs about control over health: Association of symmetrical beliefs with medication regimen adherence. *J Gen Intern Med.* 2010;25(5):397–402. [PMID:20174972]
<http://dx.doi.org/10.1007/s11606-010-1249-5>
 34. Hotopf M. Treating Gulf War veterans' illnesses—Are more focused studies needed? *JAMA.* 2003;289(11):1436–37. [PMID:12636469]
<http://dx.doi.org/10.1001/jama.289.11.1436>
 35. Falvo MJ, Osinubi OY, Sotolongo AM, Helmer DA. Airborne hazards exposure and respiratory health of Iraq and Afghanistan veterans. *Epidemiol Rev.* 2015;37(1):116–30. [PMID:25589052]
<http://dx.doi.org/10.1093/epirev/mxu009>
 36. Smith-Seemiller L, Fow NR, Kant R, Franzen MD. Presence of post-concussion syndrome symptoms in patients with chronic pain vs mild traumatic brain injury. *Brain Inj.* 2003;17(3):199–206. [PMID:12623496]
<http://dx.doi.org/10.1080/0269905021000030823>
 37. Badura AS, Reiter RC, Altmaier EM, Rhomberg A, Elas D. Dissociation, somatization, substance abuse, and coping in women with chronic pelvic pain. *Obstet Gynecol.* 1997; 90(3):405–10. [PMID:9277653]
[http://dx.doi.org/10.1016/S0029-7844\(97\)00287-1](http://dx.doi.org/10.1016/S0029-7844(97)00287-1)
 38. Burton C. Beyond somatisation: A review of the understanding and treatment of medically unexplained physical symptoms (MUPS). *Br J Gen Pract.* 2003;53(488):231–39. [PMID:14694702]
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