

Symptom Patterns Among Gulf War Registry Veterans

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Nearly 697 000 US service personnel served in Operations Desert Shield and Desert Storm in 1990 and 1991. During the war, casualties among these troops were extraordinarily low. Yet, after the war, many returning veterans complained about persistent, unexplained health problems.^{1–3} Significant controversy erupted concerning the existence, extent, and etiology of what has come to be called “Gulf War syndrome,” or more broadly, “Gulf War–related illnesses.”

In response to the controversy, Congress required that the Department of Veterans Affairs (VA) hospitals offer all Gulf War veterans, who volunteered to be examined, complete physical examinations including appropriate diagnostic tests and referrals. Portions of the resulting information were stored in a database, commonly called the Gulf War Health Registry. More than 70 000 veterans have entered the registry since its inception in 1992. Not all the veterans in the registry believe themselves to be currently ill as the result of Gulf War service. However, the registry represents the largest group of veterans who believe they may have Gulf War–related illnesses; the registry therefore is an excellent resource to further investigate the phenomenon of Gulf War–related illnesses.

In contrast to prior studies that included veterans both in and not in the registry, this investigation of registry veterans identifies patterns of symptoms specifically among veterans who believe they have been made ill as the result of service in the Gulf War. It also takes the logical next step of attempting to characterize cases by identifying specific groups of individuals who share similar patterns of symptoms, and identifying associated demographic, medical history, and other risk factors for membership in those groups.

Some previous attempts at characterizing Gulf War–related illnesses have examined symptom patterns endorsed by small numbers of presumed cases within a single unit⁴

Objectives. We identify symptom patterns among veterans who believe they suffer from Gulf War–related illnesses and characterize groups of individuals with similar patterns.

Methods. A mail survey was completed by 1161 veterans drawn from the Gulf War Health Registry.

Results. An exploratory factor analysis revealed 4 symptom factors. A K-means cluster analysis revealed 2 groups: (1) veterans reporting good health and few moderate/severe symptoms, and (2) veterans reporting fair/poor health and endorsing an average of 37 symptoms, 75% as moderate/severe. Those in Cluster 2 were more likely to report having 1 or more of 24 medical conditions.

Conclusions. These findings are consistent with previous investigations of symptom patterns in Gulf War veterans. This multisymptom illness may be more fully characterized by the extent, breadth, and severity of symptoms reported. (*Am J Public Health.* 2003;93:624–630)

or single branch of service.⁵ One of these studies, supported by the US Centers for Disease Control and Prevention (CDC), studied 3723 deployed and nondeployed Air Force troops from 4 units.⁶ The respondents indicated the presence, duration, and severity of symptoms. Classification of cases using both clinical epidemiological and factor analysis approaches, defined by the Centers for Disease Control and Prevention, were consistent with an illness definition of 1 or more chronic symptoms from at least 2 of 3 symptom categories related to fatigue, mood/cognition, and musculoskeletal symptoms. Deployment to the Gulf War was found to be the most important risk factor for this multisymptom illness. As part of our investigation, we examine the applicability of the CDC’s definition of multisymptom illness in classifying ill veterans in our sample from the registry.

Other studies have attempted to compare the distribution and patterns of symptoms within large groups of deployed and nondeployed groups of veterans.^{1,5,7–10} In each of these comparative studies, Gulf War veterans reported a greater prevalence of symptoms across body systems, but several of the studies concluded that the patterns of symptoms reported by Gulf War veterans did not suggest illnesses distinct from those in the general population.^{5,7–10}

Yet, there is good reason to validate this conclusion in a cohort including a large number of presumed cases. If unique Gulf War–related illnesses do exist, it is unclear how many cases might be captured within any random sample of deployed veterans. If the number of cases is relatively small, any distinct patterns of symptoms characteristic of those cases might be obscured by the larger distribution of symptoms reported by veterans experiencing the normal range of health problems expected in any large population. By examining a sample presumably containing a large number of cases, any underlying pattern of symptoms common to Gulf War–related illnesses would more likely emerge.

METHODS

Participants

A total of 2011 veterans residing in 1 of 7 states—Delaware, Illinois, New Jersey, New York, North Carolina, Ohio, and Pennsylvania—were drawn from the registry. These states were chosen for proximity to the East Orange hospital to facilitate the recruitment of participants for a second phase of the study that included follow-up medical examinations completed at the VA Medical Center in East Orange, NJ. The potential respondents

were selected by the VA's Environmental Epidemiology Service medical center in each state using a simple random sampling procedure, excluding individuals targeted for other major concurrent studies.

Procedures

We mailed introductory letters and questionnaires to the 2011 selected veterans. We followed this with reminder postcards, a second (identical) letter and questionnaire, and a maximum of 3 follow-up phone calls at intervals of approximately 2 weeks until a response was received.¹¹

Measures

In the written questionnaire, respondents were asked to rank their current health status using a 5-point scale that ranged from excellent (1) to poor (5).¹² The respondents were then asked to examine a list of 48 symptoms grouped by organ systems. For each symptom, the respondents indicated whether they had experienced "persistent or recurring" problems within the last year, and if so, whether the problems they had experienced were "mild," "moderate," or "severe." The respondents were asked to assess the effect their health symptoms had on their occupational, educational, and personal activity levels using a scale ranging from 0 (none) to 5 (very severe).

Based on the veterans' responses, we classified the respondents according to definitions of chronic fatigue syndrome (CFS) and chronic multisymptom illness, published by the CDC.^{6,13,14} Using the CDC's definition of CFS,^{13,14} respondents were considered cases if they believed they were suffering from a fatiguing illness, and if that illness had caused at least substantial decrease in activity level in the occupational, educational, social, or personal domains. Inclusion as a case also required the endorsement of at least 4 of 8 minor symptoms, including (1) fatigue not due to exercise; (2) throat problems or swollen lymph nodes in neck or armpit; (3) muscle aches or cramps; (4) pain in more than 1 joint without swelling or redness; (5) headaches; (6) unrefreshing sleep (waking up tired); (7) prolonged fatigue or feeling of illness after mild exercise; and (8) cognitive impairment (difficulty concentrating or

remembering things). Cognitive impairment, if indicated, was required to be of at least moderate severity for inclusion, whereas the other minor symptoms were accepted if they were of any severity.

The respondents were also asked if they had ever been told by a doctor that they had 1 or more of 38 medical and psychiatric conditions and whether they had first been informed of such diagnoses before, during, or after their deployment in the Gulf War. Seventeen of these conditions were used as exclusions for a diagnosis of CFS because they are substantial known causes of fatigue symptoms. These conditions included heart disease, heart attack, tuberculosis, stroke, asthma, emphysema/bronchitis, colitis/intestinal inflammation, liver disease, alcohol problems, eating disorders, multiple sclerosis, bipolar disorder, leishmaniasis, malaria, diabetes, lupus, and a form of cancer other than skin cancer. A category of "other" was also screened for significant conditions, such as renal disease, not specified on the checklist.

Using the CDC's definition of chronic multisymptom illness,⁶ respondents were considered cases if they reported 1 or more chronic symptoms from at least 2 of 3 symptom categories related to fatigue not due to exercise, mood/cognition (feeling depressed, feeling anxious, sudden mood changes, difficulty concentrating or remembering, unrefreshing sleep), and musculoskeletal system (pain in more than 1 joint, muscle ache or pain). Cases were considered to be severe if the case-defining symptoms were rated as severe; otherwise, the cases were classified as mild to moderate.

Statistical Analyses

To examine any underlying factor structure among the symptoms reported, the respondents were randomly split into 2 samples. We conducted exploratory factor analyses using the principal axis method of extraction followed by direct oblimin (oblique) rotation within each half of the sample, treating each symptom as a continuous variable. To determine the optimal number of factors to retain, we obtained a range of factor solutions and compared correlations between the split halves to examine consistency. To examine the replicability of the results, we repeated

this procedure 5 times, with new split-half samples drawn each time. We compared the resulting factor solutions pairwise across all 10 samples. We then selected as a final solution that which had the highest average correlation and largest minimum correlation between individual factors. The items within each factor of the resulting solution were subjected to internal consistency analyses using a Cronbach α of .8 as a critical score. After determining that the items within each factor formed a reliable scale, we created summary scores by taking the mean of the raw scores for the symptoms within each factor.

With the summary scores resulting from the factor analysis, we used a *K*-means cluster analysis to group the respondents based on severity of symptoms. Because the summary scores represent the mean rating of the symptoms within each factor, the resulting cluster centers can also be interpreted as mean symptom ratings within each factor. To determine the optimal number of groups and to test the replicability of these groupings, we compared the assignments of individuals to groups across the 10 split halves using κ . We then used univariate logistic regression analyses and resulting odds ratios (ORs) to determine predictors of group status.

RESULTS

Responses

Of the 1935 deliverable questionnaires, 1161 were completed and returned by the respondents, yielding a response rate of 60.0%. To test for potential selection biases, we obtained available demographic data from the registry for each veteran who received a questionnaire ($n=1935$) and compared these data with summary data from the entire registry. Chi-square analyses revealed no significant differences in the distribution of branch of service, duty status (active, reserve, guard), or sex between those randomly selected to be in the sample and those in the registry as a whole.

Logistic regression analyses suggested no significant differences in response rates attributable to sex, date of entry into the registry, branch of service, type of unit, or grade (enlisted, officer, warrant officer). We obtained symptom codes 700 through 799 from the

*International Classification of Diseases, Ninth Revision, Clinical Modification*¹⁵ and diagnostic data determined by the VA examining physician from the registry for each veteran who received a questionnaire. Multivariate analysis of variance revealed no significant differences in response rates attributable to either specific symptoms coded to 1 decimal place or specific diagnoses coded to 3 digits.

Perception of Illness Attributable to Gulf War Service

Of the 1161 respondents, 981 (84.5%) reported believing they have had medical problems as the result of their service in the Gulf War (5.3% did not answer the question). Because the goal of this study is to characterize the illnesses of veterans who believe they have been made ill because of service in the Gulf War, only these 981 were included in further analyses.

Current Health Status

In assessing their own health status, 1.3% of respondents reported that their health was “excellent,” 11.7% reported “very good” health, 35.5% reported “good” health, 31.7% reported “fair” health, 11.2% reported “poor” health, and 8.6% did not answer the question. Of the 48 symptoms presented, the respondents endorsed an average of 9.9 mild symptoms, 9.5 moderate symptoms, and 6.1 severe symptoms (an average total of 25.5 symptoms, standard deviation (SD)= 12.3). Poorer self-assessed health status was correlated with the total number of symptoms reported ($r=.62$; $P<.001$). Correlations between self-assessed health and the rating of the severity of each symptom ranged from .26 to .57 and were significant at the .001 level. Correlations between symptoms ranged from .17 to .79 and were also significant at the .001 level.

Factor Analyses

The results of the analyses within each of the 10 samples were consistent. Within each sample, the exploratory principal axis analysis extracted between 8 and 10 factors (with eigenvalues greater than 1) accounting for between 58% and 60% of the variance in the initial 48 symptom variables. In each analysis, the first factor accounted for the majority of the variance, with each of the remaining fac-

tors accounting for less than 5%. In each analysis, scree plots suggested retaining the first 3 to 5 factors.

We then compared the rotated factor scores from 3-, 4-, and 5-factor solutions between the split halves and then across all the samples. The outcome of these multiple comparisons suggested that retaining 4 factors (accounting for an average of 49.3% of the variance) resulted in the most consistent and replicable set of factors. Correlations between the 4 corresponding factors in the matching

split halves ranged from .86 to .96, with an average correlation of .92. A 3-factor solution resulted in correlations between the 3 corresponding factors in the matching split halves ranging from .66 to .96, with an average correlation of .85. A 5-factor solution resulted in correlations between the 5 corresponding factors in the matching split halves ranging from .15 to .95, with an average correlation of .82.

Table 1 summarizes the rotated pattern matrix factor loadings for the 4 factors obtained in the final exploratory factor analysis,

TABLE 1—Factor Loadings of Symptoms

Symptom	Factor			
	Mood/Memory/Fatigue	Musculoskeletal	Gastrointestinal	Throat/Breathing
Feeling depressed or blue	-.827	-.060	.076	.048
Sudden mood changes	-.806	.001	.080	.035
Fatigue not due to exercise	-.781	.021	-.123	-.124
Feeling anxious or upset	-.802	.010	.071	.052
Unrefreshing sleep	-.758	.007	-.047	-.044
Difficulty concentrating	-.743	.034	-.021	-.019
Prolonged fatigue after mild exercise	-.668	.012	-.138	.032
Difficulty remembering	-.693	.077	-.010	-.033
Unexplained weakness	-.649	.160	-.094	-.011
Feeling sickly	-.516	-.018	-.311	.085
Sleeping more than usual	-.492	-.036	-.086	.019
Sensitivity to heat or cold	-.463	.068	-.023	.193
Pain in arms or legs	.018	.839	-.069	-.031
Pain in more than 1 joint, or swelling or redness	-.041	.783	-.013	-.031
Pain in arms, hands, or shoulders	.060	.757	-.044	.024
Muscle aches or cramps	-.139	.643	-.094	-.011
Numbness or tingling sensations	-.083	.588	-.006	.136
Back problems	-.128	.453	-.047	.072
Stomach or digestive system problems	-.003	-.004	-.828	-.064
Abdominal pain	-.006	.166	-.741	-.075
Diarrhea	-.051	-.019	-.607	-.015
Abdominal gas	-.055	.110	-.628	-.040
Nausea	-.080	-.010	-.619	.117
Vomiting	.019	-.083	-.560	.192
Throat problems	.045	-.126	-.051	.769
Difficulty swallowing	.032	-.075	-.082	.705
Reduced ability to taste	-.024	.116	.037	.556
Swollen glands	-.010	-.013	-.102	.574
Coughing	-.061	.046	-.096	.497
Nose or sinus problems	-.036	.095	-.033	.399
Difficulty breathing	-.126	.169	-.027	.433

TABLE 2—Final Cluster Centers Obtained Using K-Means Cluster Analysis

	Cluster	
	1	2
Number of respondents	591	387
Percent of sample	60.4	39.6
Mood/memory/fatigue symptoms	.81	2.12
Musculoskeletal symptoms	.73	2.08
Gastrointestinal symptoms	.43	1.47
Throat/breathing symptoms	.42	1.29

Note. Factor values are interpretable as mean symptom scores on a scale of 0 (not present), 1 (mild), 2 (moderate), and 3 (severe).

using all 981 eligible cases. Factor 1 (mood/memory/fatigue problems) incorporates symptoms of depression, anxiety, and sudden mood changes with problems concentrating and remembering, unexplained weakness, sleep problems, and unexplained fatigue. Factor 2 (musculoskeletal problems) combines problems describing pain or numbness in joints or muscles. Factor 3 (gastrointestinal problems) describes complaints of the stomach and digestive system including abdominal pain and gas, diarrhea, nausea, and vomiting. Factor 4 (throat/breathing problems) connects symptoms involving problems with the throat (including difficulty swallowing) and swollen glands with those involving nose or sinus problems, coughing, difficulty breathing, and difficulty tasting. The 4 factors accounted for 50.2% of the variance in the original set of variables. Scores of internal reliability (α) were .94 for the mood/memory/fatigue problems factor, .89 for the musculoskeletal problems factor, .86 for the gastrointestinal problems factor, and .82 for the throat/breathing problems factor.

Cluster Analyses

The results of the cluster analyses within each of the 10 samples were consistent. We could identify 2 stable clusters of respondents in each sample. Assignment of group membership across sample splits was also consistent, with an average κ across samples of .98. Table 2 shows the final cluster centers obtained for the 2 groups after running the K-means procedure on the total sample. The

cluster centers can be interpreted as average severity scores on a scale of 0 (no problem) to 3 (severe problem).

As such, Cluster 1 (60.4% of the respondents) represents a group of veterans who report mild or no problems with symptoms in the 4 factors. In contrast, Cluster 2 (39.6% of the respondents) represents a group of veterans with moderate to severe mood/memory/fatigue and musculoskeletal problems, and mild to moderate gastrointestinal and throat/breathing problems.

Predictors of Group Membership

Symptoms and health status. Those in Cluster 2 reported having twice as many symptoms overall (mean=37.23; SD=6.17) as those in Cluster 1 (mean=17.83; SD=8.76; $t_{(976)}=37.82$; $P<.001$). In addition, those in Cluster 2 consistently reported more severe problems with every symptom compared with those in Cluster 1 (Table 3). Thirty-five percent of the symptoms endorsed by those in Cluster 2 were reported to be “severe” and 40% “moderate.” In contrast, only 11% of the symptoms endorsed by those in Cluster 1 were reported to be “severe” and 33% “moderate.” Consistent with this, those in Cluster 2 reported being in poorer health (mean=4.07; SD=.70) than did those in Cluster 1 (mean=3.02; SD=.79; $t_{(895)}=20.40$; $P<.001$). Those in Cluster 2 also reported a greater reduction in activity (mean=3.56; SD=.99) than did those in Cluster 1 (mean=2.14; SD=1.0; $t_{(954)}=21.55$; $P<.001$).

Demographic characteristics of the clusters. We used logistic regression analyses to examine demographic predictors of cluster membership. The predictors included race/ethnicity, rank, branch of service, duty status (active, reserve, or guard), sex, and marital status at deployment. The univariate results suggested that those in Cluster 2 were more likely to be African American (OR=1.9 [95% confidence interval (CI)=1.4, 2.6]) or other racial/ethnic minority (OR=2.3 [95% CI=1.5, 3.6]), are more likely to be enlisted or noncommissioned officers than officers (OR=1.8 [95% CI=1.1, 2.8]), and are more likely to have served in the Army than in the other branches of the services (OR=1.4 [95% CI=1.1, 1.9]). Those in Cluster 2 are also more likely to have completed high

school or some college or vocational school than to have completed a college or postgraduate degree (OR=2.3 [95% CI=1.6, 3.3]). There were no significant increases in risk associated with age, duty status, sex, or marital status at deployment.

Self-reported medical conditions. The respondents were asked if they had ever been told by a doctor that they had 1 or more of 38 medical and psychiatric conditions and when they had first been informed of such diagnoses. Those in Cluster 2 reported a greater likelihood of having been told they had 1 or more of 24 of these conditions (Table 4), but were less likely to have had a history of mononucleosis. Moreover, those in Cluster 2 reported twice as many medical conditions (mean=3.96; SD=3.57) as those in Cluster 1 (mean=1.83; SD=2.29; $t_{(976)}=11.38$; $P<.001$). Consistent with the apparently acquired nature of Gulf War-related illnesses, the great majority of the respondents reported being first told of their condition after the war, except for those who were diagnosed with mononucleosis, malaria, concussion, hay fever, and tuberculosis.

To test the predictive power of self-reported medical conditions, we used a backwards conditional stepwise logistic regression analysis beginning with all 38 conditions to classify all participants. This final model correctly classified 72% of the participants overall and 92% of those in Cluster 1, but only 42% of those in Cluster 2. In other words, although the model fit the data fairly well overall, it did poorly in predicting those reporting the most symptoms. The final model included heart disease, chronic emphysema/bronchitis, colitis/intestinal inflammation, stomach ulcers, hypertension, mononucleosis, multiple sclerosis, CFS, eczema/psoriasis, bipolar disorder, depression, anxiety/panic disorder, and post-traumatic stress disorder.

Tobacco, alcohol, and drug use. Those in Cluster 2 are more likely to be current smokers (OR=1.8 [95% CI=1.3, 2.3]) and more likely to report that a doctor had told them that they had a problem with drugs or alcohol (OR=2.6 [95% CI=1.6, 4.3]). Indicative of possible alcohol problems, those in Cluster 2 were more likely to answer affirmatively the question “Has there ever been a period of 2 weeks when every day you were drinking 7

TABLE 3—Means and Standard Deviations of Symptom Rating by Cluster

Symptom	Cluster (Mean [Standard Deviation])		Mean Difference	T value ^a
	1	2		
Unexplained weakness	.60 (.79)	2.12 (.88)	1.52	28.12
Pain in arms or legs	.73 (.90)	2.23 (.83)	1.50	26.28
Prolonged fatigue after mild exercise	.58 (.84)	2.08 (.94)	1.50	26.14
Pain in more than 1 joint	.88 (.94)	2.29 (.84)	1.42	24.01
Sudden mood changes	.95 (.98)	2.36 (.91)	1.41	22.71
Muscle aches or cramps	.73 (.83)	2.14 (.78)	1.41	26.54
Feeling anxious or upset	.81 (.91)	2.20 (.93)	1.40	23.29
Fatigue not due to exercise	1.13 (.93)	2.48 (.69)	1.34	24.29
Feeling sickly	.47 (.72)	1.80 (.92)	1.33	25.37
Pain in arms, hands, or shoulders	.67 (.89)	1.99 (1.02)	1.32	21.36
Feeling depressed or blue	.80 (.91)	2.10 (.97)	1.30	21.23
Numbness or tingling sensations	.60 (.81)	1.86 (.94)	1.26	22.45
Sensitivity to heat or cold	.49 (.85)	1.74 (1.15)	1.25	19.46
Unrefreshing sleep (waking up tired)	1.32 (1.00)	2.55 (.69)	1.23	21.12
Abdominal pain	.39 (.71)	1.63 (.99)	1.23	22.59
Difficulty concentrating	.87 (.91)	2.09 (.87)	1.22	20.81
Stomach or digestive system problems	.63 (.90)	1.85 (.98)	1.22	19.89
Back problems	.80 (.95)	1.98 (.99)	1.18	18.59
Abdominal gas	.68 (.87)	1.85 (.97)	1.17	19.62
Difficulty remembering	1.08 (.94)	2.25 (.81)	1.17	20.04
Chest discomfort or pain	.56 (.78)	1.72 (.91)	1.17	21.42
Difficulty breathing	.51 (.78)	1.62 (.93)	1.11	20.14
Losing balance or feeling dizzy	.47 (.70)	1.55 (.94)	1.08	20.49
Extra sensitivity to chemicals	.57 (.89)	1.64 (1.11)	1.07	16.66
Headaches	1.06 (1.05)	2.12 (.88)	1.06	16.50
Nausea	.26 (.56)	1.30 (.96)	1.04	21.39
Fever or chills	.22 (.56)	1.25 (1.06)	1.02	19.78
Coughing	.52 (.76)	1.53 (.98)	1.02	18.32
Sleeping more than usual	.65 (.91)	1.64 (1.23)	.99	14.48
Diarrhea	.55 (.84)	1.50 (1.05)	.95	15.68
Sweating (not due to exercise)	.47 (.86)	1.42 (1.12)	.95	14.95
Mouth, teeth, or gum problems	.52 (.83)	1.44 (1.11)	.93	14.85
Nose or sinus problems	1.07 (1.06)	2.00 (1.02)	.93	13.62
Skin problems (including rashes)	.92 (1.03)	1.82 (1.05)	.90	13.21
Ear or hearing problems	.61 (.83)	1.47 (1.01)	.86	14.57
Throat problems	.29 (.63)	1.14 (1.00)	.85	16.22
Eye or vision problems	.66 (.83)	1.48 (.96)	.82	14.22
Swollen glands	.29 (.61)	1.08 (1.05)	.80	14.87
Cuts or sores that heal slowly	.38 (.71)	1.17 (1.12)	.79	13.56
Sexual or genital problems	.34 (.72)	1.09 (1.15)	.76	12.64
Difficulty swallowing	.17 (.49)	.87 (.94)	.70	15.32
Hair problems	.28 (.70)	.95 (1.09)	.67	11.71
Reduced ability to taste	.13 (.41)	.78 (.94)	.65	14.73
Irregular heartbeat	.25 (.60)	.87 (1.04)	.63	11.95
Constipation	.22 (.54)	.83 (1.01)	.61	12.34
Frequent or painful urination	.24 (.59)	.85 (.99)	.61	12.02
Vomiting	.09 (.38)	.69 (.91)	.61	14.39
Fainting spells	.05 (.25)	.42 (.81)	.38	10.68

Note. Factor values are on a scale of 0 (not present), 1 (mild), 2 (moderate), and 3 (severe).

^aAll T values significant at $P < .0001$.

or more beers, 7 or more drinks, or 7 or more glasses of wine?" (OR=1.6 [95% CI=1.1, 2.2]). Similarly, although they were no more likely to report having used drugs than those in Cluster 1, those in Cluster 2 were more likely to report that they had reached a point at which they needed larger amounts of drugs to get high (OR=3.4 [95% CI=1.7, 6.8]) and to have had emotional or psychological problems resulting from using drugs (OR=3.1 [95% CI=1.6, 6.0]).

Cluster Membership and CDC Definitions of Chronic Multisymptom Illness and CFS

Three-quarters (75.1%) of those in Cluster 1 and all but 1 (99.7%) of the respondents in Cluster 2 met the CDC's definition of having a severe case of chronic multisymptom illness.⁶ Nearly all (95.3%) of those in Cluster 1 and all of those in Cluster 2 met the definition of having a mild to moderate case.

Because fatigue, musculoskeletal problems, and mood/memory impairments are important components in defining the 2 clusters and part of the case definition for CFS,^{13,14} we investigated the prevalence of CFS in this cohort. As reported in a previous article,¹⁴ 15.7% of this sample qualified for CFS according to a questionnaire they filled out that was based on the 1994 CDC clinical definition. Eight percent of those in Cluster 1 and 28% of those in Cluster 2 met the questionnaire definition of CFS (OR=4.4 [95% CI=3.0, 6.4]). Six percent of those in Cluster 1 and 26% of those in Cluster 2 reported that they had been told by a physician that they had CFS (OR=5.4 [95% CI=3.8, 8.1]).

DISCUSSION

The VA's Gulf War Health Registry is the largest identifiable group of Gulf War veterans who believe they may suffer from Gulf War–related illnesses. Yet, it is clear that not everyone in the registry has the same constellation of symptoms. Indeed, about 10% of those in the registry report that they do not believe that they have any current health problems attributable to Gulf War service. In our registry sample, of those who do believe they have Gulf War–related health problems, 85% meet the CDC definition of a severe

TABLE 4—Number Reporting War-Related Medical Conditions by Cluster and Total Diagnosed After the Gulf War

Diagnosis	Probability of Diagnosis OR (95% CI)	Number Reporting Medical Conditions			Told After War, %
		Cluster 1 (n = 591)	Cluster 2 (n = 387)	Total (n = 978)	
Bipolar disorder	11.2 (4.7, 26.7)	6	40	46	97.8
Anxiety or panic disorder	5.7 (3.4, 9.5)	21	67	88	85.2
Other cancer	5.4 (1.1, 26.1)	2	7	9	77.8
Multiple sclerosis	5.4 (1.1, 26.1)	2	7	9	77.8
Chronic fatigue syndrome	5.4 (3.8, 8.1)	36	100	136	95.6
Depression	4.7 (3.4, 6.6)	66	144	210	88.6
Posttraumatic stress disorder	4.7 (3.3, 6.6)	57	129	186	91.9
Heart disease	4.7 (2.4, 9.5)	11	32	43	67.4
Lupus (Erythematosus)	4.7 (1.2, 17.3)	3	9	12	100.0
Circulatory problems	4.1 (2.3, 7.0)	19	46	65	84.6
Multiple chemical sensitivities	3.8 (2.1, 6.0)	23	49	72	88.9
Heart attack	3.8 (1.3, 10.7)	5	12	17	52.9
Colitis/intestinal inflammation	3.6 (2.2, 5.9)	24	51	75	84.0
Eating disorders	3.5 (1.6, 7.5)	10	22	32	84.4
Irritable bowel syndrome	3.1 (2.0, 4.7)	38	68	106	78.3
Sterility/difficulty conceiving	3.1 (1.7, 5.8)	16	31	47	85.1
Fibromyalgia	3.1 (1.1, 9.2)	5	10	15	86.7
Emphysema/bronchitis	2.6 (1.7, 3.9)	43	65	108	62.0
Drug/alcohol problems	2.6 (1.6, 4.3)	28	45	73	65.8
Thyroid condition	2.6 (1.3, 5.1)	14	23	37	67.6
Stomach ulcers	2.4 (1.6, 3.7)	38	55	93	59.1
High blood pressure	2.0 (1.5, 2.7)	99	111	210	69.5
Arthritis	1.9 (1.4, 2.6)	91	100	191	77.0
Asthma	1.7 (1.1, 2.7)	38	40	78	52.6
Mononucleosis	0.4 (0.2, 0.7)	57	16	73	13.7
Lyme disease	3.1 (0.8, 12.4)	3	6	9	77.8
Malaria	2.6 (0.6, 10.8)	3	5	8	25.0
Skin Cancer	2.4 (0.9, 6.4)	7	11	15	73.3
Diabetes	2.2 (0.9, 5.3)	9	13	22	68.2
Liver Disease	1.9 (0.9, 3.6)	16	19	35	74.3
Anemia	1.5 (0.8, 2.7)	24	23	47	59.6
Stroke	1.5 (0.4, 6.2)	4	4	8	87.5
Dermatitis	1.3 (0.8, 2.0)	48	40	88	71.6
Leishmaniasis	1.2 (0.3, 4.6)	5	4	9	77.8
Concussion	1.0 (0.7, 1.6)	59	40	99	11.1
Eczema/psoriasis	1.0 (0.6, 1.6)	48	31	79	74.7
Hay fever	0.8 (0.6, 1.2)	87	49	136	24.3
Tuberculosis	0.8 (0.4, 1.8)	18	10	28	50.0

Note. OR = odds ratio; CI = confidence interval.

musculoskeletal, mood/memory, and fatigue symptoms, and mild to moderate problems with a large number of other symptoms. They also assess their health as fair or poor, and report “substantial” reductions in activity due to symptoms. Members of this cluster are more likely to be African Americans or another minority/ethnicity, to be enlisted or noncommissioned officers, to have served in the Army, and to have completed less than a college degree. As such, membership in Cluster 2 is associated with proxy measures of lower socioeconomic status. This is consistent with findings from the CDC’s investigation of chronic multisymptom illness in Air Force veterans⁶ and with recent data concerning the occurrence of CFS in Chicago.¹⁶ Membership in this cluster was also associated with use of tobacco, alcohol, and drugs.

The results of the factor and cluster analyses are consistent with other recent studies that have found a core group of musculoskeletal, mood, memory, and fatigue problems reported by ill Gulf War veterans, problems that are reported with lower frequency and severity by nondeployed controls from the same era of military service.^{6,9,10} Very similar factors have also been identified in an Australian primary care population¹⁷ and in a sample of the US general population.¹⁸ Although these core complaints do not appear to be unique to ill Gulf War veterans, their association with deployment in Operations Desert Shield and Desert Storm does suggest that service in the Gulf War is a risk factor for such complaints.

The ill Gulf War veterans in this study also reported a large number of health complaints. For these veterans, it “hurts all over,” not just in specific places. In fact, those in Cluster 2 reported having persistent or recurring problems with an average of 37 of 48 symptoms, three-quarters of which they endorsed as moderate or severe. In addition, those in this group reported more severe problems with every symptom, compared with those in Cluster 1. Similar findings have also been reported in studies comparing the distribution and patterns of symptoms within large groups of deployed and nondeployed groups of veterans.^{1,7–10} In each of these comparative studies, Gulf War veterans reported a greater prevalence of symptoms across body systems.

case of chronic multisymptom illness, and 97% meet the definition of a mild to moderate case. Yet, about 60% (Cluster 1) report very few moderate or severe health symp-

toms, assess their health status as relatively good, and report only moderate reductions in activity due to symptoms. About 40% (Cluster 2) have moderate to severe problems with

The severity and extent of symptoms reported by these veterans may be important in helping to determine the etiology of illnesses. The severity and extent of symptoms suggests either a very powerful physiological or psychological explanation yet to be identified, or perhaps a comorbid set of overlapping illnesses. Although there is significant overlap between Gulf War–related illnesses and standard medical and psychiatric diagnoses, these latter diagnoses are inadequate to describe or explain the breadth of symptoms reported by veterans.

Those in Cluster 2 reported having been told by a physician that they had an average of 4 medical conditions and, in comparison to those in Cluster 1, were more likely to report having 1 or more of 24 different conditions. However, this group of self-reported medical conditions does not adequately discriminate those in Cluster 2 from the healthier group. Moreover, many of the more common diagnoses reported, including CFS, depression, posttraumatic stress disorder, arthritis, irritable bowel syndrome, and others, are often used to label groups of otherwise medically unexplainable symptoms. As such, they do not suggest a specific known organic cause of this multisymptom illness.

This study has several limitations. Of necessity, it relies on self-reported measures, and so the data are subject to recall errors and reporting biases. The sample studied is also drawn from a population that is, in part, self-selected on the basis of perceived health problems attributable to service in the Gulf War. As such, it is clearly not representative of the entire population of Gulf War veterans, and may not be truly representative of all ill Gulf War veterans. Studies designed to replicate these findings in random samples of deployed and nondeployed Gulf War–era veterans are already under way. ■

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Contributors

W.K. Hallman and H.M. Kipen planned the study, analyzed the data and wrote the paper. M. Diefenbach assisted with questionnaire construction, data collection and analysis. K. Boyd, H. Leventhal, and D. Wartenberg assisted with data analysis and writing. H. Kang assisted in sample selection, recruitment and data analysis.

Human Participant Protection

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