# Post-Traumatic Stress Disorder and Chronic Fatigue Syndrome-like Illness among Gulf War Veterans: A Population-based Survey of 30,000 Veterans

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The authors estimated the prevalence of post-traumatic stress disorder (PTSD) and illness resembling chronic fatigue syndrome (CFS) in the entire population of Gulf War and non-Gulf-War veterans. They also evaluated the relation between the extent of deployment-related stress and the risk of either PTSD or CFS. In 1995–1997, the authors conducted a health survey in which these two symptom-based medical diagnoses in a population-based sample of 15,000 Gulf War veterans representing four military branches and three unit components (active, reserve, and National Guard) were compared with those of 15,000 non-Gulf veteran controls. Gulf War veterans, compared with non-Gulf veteran controls, reported significantly higher rates of PTSD (adjusted odds ratio = 3.1, 95% confidence interval: 2.7, 3.4) and CFS (adjusted odds ratio = 4.8, 95% confidence interval: 3.9, 5.9). The prevalence of PTSD increased monotonically across six levels of deployment-related stress intensity (test for trend: $p < 0.01$), while the prevalence of CFS rose only at the low end of the stress spectrum. While deployment-related stress could account for the higher risks of both PTSD and CFS, additional factor(s) unique to the Gulf environment may have contributed to the risk of CFS among Gulf War veterans.

fatigue syndrome, chronic; Persian Gulf syndrome; stress disorders, post-traumatic; veterans

Abbreviations: CFS, chronic fatigue syndrome; DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised; PTSD, post-traumatic stress disorder.

The health consequences of the 1990–1991 Gulf War on US veterans have been the focus of numerous studies and many committee reports (1–4). Within months of returning from the war, many veterans began to complain of various symptoms and illnesses (5). To date, over 100,000 Gulf War veterans have voluntarily participated in a health registry examination offered by the Department of Defense and the Department of Veterans Affairs (6–8). Several possible etiologic agents for the symptoms reported by Gulf War veterans have been suggested: exposure to multiple vaccines, pyridostigmine bromide, toxic chemicals, chemical and biological warfare agents, or depleted uranium; stress associated with battlefield conditions; and rapid deployment and redeployment (9–14).

The symptoms most commonly reported by Gulf veterans include fatigue, muscle/joint pain, headache, difficulty concentrating, memory loss, sleep disturbance, and skin rash (1–3). Some veterans fulfill the clinical case criteria for illness resembling chronic fatigue syndrome (CFS), an interpretation that has been confirmed in several studies (15, 16). One epidemiologic study of Gulf veterans seeking health care found that 16.8 percent of veterans reported symptoms consistent with CFS (17), while another small population-based study found an estimated minimum prevalence of 2.2 percent (18). All of these rates are significantly higher than the rate seen in nonveterans (19).

The fact that the prevalence of CFS is so much higher among veterans deployed to the Persian Gulf suggests two possible etiologic factors: 1) some environmental factor specific to the Gulf region and 2) the stress of deployment and combat. The availability of data on the Gulf War veteran

population has allowed us to evaluate the role of stress in the development of CFS.

One commonly acknowledged indicator of life-threatening stress is the presence of post-traumatic stress disorder (PTSD). In an evaluation of 76 health-care-seeking Gulf veterans who fulfilled the published case definition for CFS (15) or its less severe variant, idiopathic chronic fatigue, 50 percent were also found to have PTSD (20). Moreover, a population study of Gulf veterans indicated that those with PTSD had significantly more somatic complaints than those without PTSD (21).

In 1995, the Department of Veterans Affairs initiated a health survey entitled "National Health Survey of Gulf War Era Veterans and Their Families," designed to compare the health of a population-based, stratified random sample of 15,000 US troops deployed into the Gulf region with that of 15,000 troops deployed elsewhere (22). We aimed to estimate and compare the prevalence of two symptom-based medical conditions, PTSD and CFS, in these two groups of veterans. Furthermore, we evaluated the etiologic role of deployment-related stress on the development of these conditions.

## MATERIALS AND METHODS

### Study population

The study subjects were 15,000 Gulf veterans and 15,000 non-Gulf veterans who had been randomly selected from populations identified by the Department of Defense as deployed or not deployed to the Gulf. We defined a "veteran" as any individual who had served in the US military on active duty, in the reserves, or in the National Guard, regardless of whether he/she was still in the service or had separated from the military. The Defense Manpower Data Center provided military and demographic information for 1) 693,826 US troops deployed to the Gulf area between September 1990 and May 1991 and 2) 800,680 troops not deployed to the Gulf theater—approximately 50 percent of all military personnel on duty during the same period.

A stratified random sampling method was adopted to ensure that each subgroup was adequately represented among the 15,000 Gulf veterans and 15,000 non-Gulf veterans. The entire population of troops deployed to the Gulf area was stratified by gender (male and female), unit component (active, reserve, and National Guard), and branch of service (Army, Navy, Air Force, and Marine Corps). Women and those who served in reserve or National Guard units were oversampled so that one fifth of the sample would be female ($n = 3,000$), one fourth would be National Guard members ($n = 4,000$), and one third would be reservists ($n = 5,000$). The proportions of these subgroups in the entire population of deployed troops were 7 percent, 7 percent, and 10 percent, respectively. Similarly, the population of 800,680 nondeployed troops was stratified by gender, unit component, and branch of service, and from each stratum a requisite number of troops was randomly sampled to mirror the number in the same stratum in the Gulf-deployed troops. Table 1 gives the final distribution of Gulf and non-Gulf veterans according to the selection criteria.

**TABLE 1. Distribution of Gulf War veterans and non-Gulf-War veterans selected for a survey on post-traumatic stress disorder and chronic fatigue syndrome-like illness, by gender and unit component, 1990–1991**

| Unit component | Gender | | |
| --- | --- | --- | --- |
| | Male | Female | Total |
| Active | 4,800 | 1,200 | 6,000 |
| Reserve | 4,000 | 1,000 | 5,000 |
| National Guard | 3,200 | 800 | 4,000 |
| Total | 12,000 | 3,000 | 15,000 |

### Data collection methods

In phase I, starting in November 1995, a 16-page structured health questionnaire was sent to each of the 30,000 veterans with a preaddressed stamped return envelope. The questionnaire was accompanied by an introductory letter which explained the purpose and nature of the study and informed the veteran that his/her participation was voluntary and confidential. Two weeks after the initial mailing, a postcard was sent to everyone, to thank the respondents and to remind nonrespondents to complete the questionnaire. Ten weeks after the mailing, a letter and replacement questionnaire were sent to the nonrespondents. Six months after the initial mailing, a letter with a replacement questionnaire was again sent to each nonrespondent to emphasize its importance.

In phase II, telephone calls were made to the remaining nonrespondents; computer-assisted telephone interviewing software was used to obtain responses to the questionnaire mailed in phase I. During phase II, a random sample of 4,200 respondents from phases I and II was selected and asked to provide written authorization to allow retrieval of their medical records; we used those records to substantiate information on selected self-reported health conditions obtained from the respondents.

### Questionnaire instruments

A self-administered questionnaire was used to obtain information from study subjects concerning exposure to possible risk factors, potentially confounding variables, presence of various symptoms, measures of functional impairment and limitation of activity, and medical history. To increase the anticipated low response rates typically associated with postal questionnaires, we kept the instrument relatively short; questions were simple and straightforward. We asked a minimum number of questions on demographic and military variables to avoid making the questionnaire any longer than necessary. Basic data on demographic and military variables were available from Defense Manpower Data Center and Veterans Affairs records.

A self-report symptom inventory comprising 48 items representative of the symptoms commonly reported by outpatients was used to assess the prevalence of somatic and psychological symptoms (23). The symptom checklist

collected information on the time of onset and severity of symptoms; eight symptoms for diagnosing CFS/idiopathic chronic fatigue were included (15). Questionnaire items from the National Health Interview Survey were selected to evaluate limitation of activity, prevalence of chronic conditions, self-assessed health status, and use of medical services, including physician contacts and hospitalization (24).

We used the PTSD Checklist, a brief screening instrument for PTSD, to estimate current prevalence of PTSD (25). The PTSD Checklist consists of 17 items that correspond to the PTSD symptoms given in the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised (DSM-III-R). We considered persons with scores of 50 or higher on the PTSD Checklist to have met the criteria for PTSD. A cutoff of 50 points on the PTSD Checklist was a good predictor of PTSD diagnosis based on the Structured Clinical Interview for DSM-III-R among Vietnam veterans (sensitivity = 0.82; specificity = 0.83) (26).

For assessment of CFS, we adopted the 1994 Centers for Disease Control and Prevention revised case definition (15). The diagnosis of CFS is made only after excluding alternative medical causes of chronic fatiguing illness. Therefore, we excluded veterans with the following self-reported clinical conditions from the list of veterans who otherwise met the criteria: arthritis, diseases of the tendons, skin cancer, any other cancer, cirrhosis of the liver, hepatitis, any other liver diseases, colitis, diabetes, any other endocrine disorders, repeated seizures, neuralgia or neuritis, any disease of the genital organs, coronary heart diseases, stroke or cerebral vascular accident, tachycardia, asthma, other lung diseases, and frequent bladder infections. To be considered to have CFS, a veteran also had to report having at least four of the following symptoms: sore throat, tender lymph nodes, headache, arthralgia, myalgia, unrefreshing sleep, and substantial problems with cognitive function, and to report that even minimal effort exacerbated the entire symptom complex. The Centers for Disease Control and Prevention case definition distinguishes "prolonged fatigue" (fatigue lasting 1 month or longer) from "chronic fatigue" (persistent or recurring fatigue during 6 or more consecutive months of illness). On the questionnaire instrument, we queried about whether the fatigue had been present during the past year and, if so, whether it had been present during the past month. This is a modification of the published 1994 clinical case definition that we made to assure the presence of current symptoms at the time of the survey. Since respondents were not directly evaluated by a clinician, our diagnosis of CFS should be considered to represent CFS-like illness.

### Stressor severity

We derived an ordinal variable for stressor severity. We defined nondeployed veterans who had been members of a reserve or National Guard unit as veterans with minimal stress. We defined reservists or National Guard members who had been deployed to a location other than the Gulf as veterans with moderate stress. We defined reservists or National Guard members who had been deployed to the Persian Gulf as veterans with high stress. We further strati-

fied the high-stress group on the basis of combat exposure. To do this, we identified those Gulf veterans who 1) reported being "involved in direct combat duty," 2) had "witnessed any deaths," or 3) "wore chemical protective gear (other than for training) or heard chemical alarms sounding." In the analyses, we produced groups with monotonically increasing exposure to stress according to the number(s) of these exposures experienced—that is, no exposure or one, two, or three exposures (high-combat$^0$, high-combat$^1$, high-combat$^2$, and high-combat$^3$).

### Statistical analysis

This was a probability sample in which the population of 693,826 Gulf veterans was stratified by unit, gender, and branch and a probability sample was selected from each stratum. The selection probabilities varied across strata because of oversampling of women, reservists, and National Guard members. Such a design complicated the statistical analysis, since the observations were not independent and identically distributed. Failure to account for the design in the statistical analysis would have resulted in underestimation of standard errors. Consideration of the survey sampling plan and design variables (stratum and weighting variables) permitted inference to the population.

The survey objective was to estimate the prevalence of certain disease entities for the population. The prevalences of PTSD and CFS-like illness for the entire Gulf War veteran population ($N_1$ = 693,826) and the nondeployed population ($N_2$ = 800,860) were obtained from weighted estimates of individual military strata values. To estimate the confidence intervals of the prevalence rates and odds ratios, we used SUDAAN software, which provides consistent variance estimators for statistics derived from complex sample designs (27). Other analyses included contingency table analysis to examine differences with respect to demographic and military factors for the Gulf veterans and the non-Gulf veterans (28). We used the stratified analysis of Cochran-Mantel-Haenszel (29) to compute odds ratios and 95 percent confidence intervals for the relation between Gulf service status and PTSD, with adjustment for gender, age in 1991 (<30 years vs. ≥30 years), marital status (single vs. ever married), rank (enlisted vs. officer or warrant), and unit component (active duty, National Guard, or reserve). Similarly, we computed adjusted odds ratios and 95 percent confidence intervals for Gulf service status and CFS-like illness, adjusted for age, marital status, rank, and unit component. Computations were carried out using standard SAS software (28).

We developed a 6 × 2 table where the row variable, deployment-related stress, was ordinally scaled at six levels, ranging from minimal stress (not activated) to highest stress (deployed to the Gulf with three possible types of combat exposure); the column or response variable, CFS-like illness (or PTSD), was dichotomous and can be considered ordinal. The strategy for assessing association when both row and column variables are ordinal involves assigning scores to the levels of both variables and evaluating their correlation. We adopted two correlation statistics. First, the Cochran-Armitage trend test looks for trends in binomial proportions

**TABLE 2. Characteristics of all Gulf War and non-Gulf-War veterans who participated in a survey on post-traumatic stress disorder and chronic fatigue syndrome-like illness and those deployed in the Gulf who met the criteria for illness, 1990–1991**

| Characteristic | Non-Gulf veterans ($n = 9,476$) | All Gulf veterans ($n = 11,441$) | Gulf post-traumatic stress disorder ($n = 1,381$) | Gulf chronic fatigue syndrome ($n = 640$) |
|---|---|---|---|---|
| Male gender (%) | 78.1 | 81.4 | 75.7 | 83.3 |
| Mean age (years) in 1991 | 31.7 | 30.4 | 31.1 | 28.5 |
| Interquartile range (years) | 24–38 | 23–36 | 24–37 | 22–33 |
| White race (%) | 75.1 | 73.7 | 58.1 | 77.3 |
| Marital status (%) | | | | |
| Married | 55.8 | 52.5 | 53.0 | 46.4 |
| Single | 38.9 | 42.2 | 39.1 | 48.4 |
| Other | 5.3 | 5.3 | 7.9 | 5.2 |
| Enlisted rank (%) | 81.0 | 86.3 | 93.9 | 91.1 |
| Branch (%) | | | | |
| Army | 63.4 | 63.3 | 79.0 | 67.7 |
| Marine Corps | 10.8 | 11.2 | 7.6 | 13.9 |
| Air Force | 13.4 | 12.5 | 5.1 | 9.2 |
| Navy | 12.4 | 13.1 | 8.3 | 9.2 |
| Unit component (%) | | | | |
| Active duty | 40.2 | 37.3 | 30.8 | 31.4 |
| National Guard | 26.5 | 28.3 | 33.4 | 30.5 |
| Reserve | 33.2 | 34.4 | 35.8 | 38.1 |

across the levels of an ordinal covariate (30, 31). Second, the Mantel-Haenszel correlation statistic is developed by assigning scores to the columns and rows of the table and measuring the association between stress and CFS-like illness (or PTSD). We specified modified ridit scores (29). Further details on statistical methods are given in the Appendix.

## RESULTS

### Survey response rates and characteristics of respondents

After three sequential questionnaire mailings, 15,817 veterans responded to the phase I survey. An additional 5,100 veterans completed the phase II telephone survey, which resulted in an overall response rate of 70 percent. A total of 11,441 Gulf veterans (76.3 percent) and 9,476 non-Gulf veterans (63.2 percent) of those randomly selected for the study participated. The veterans who did not respond to all interview efforts from among the 30,000 who had been identified as potential study participants numbered 9,083. They are characterized as younger, non-White, unmarried individuals who had served in enlisted ranks rather than as officers at the time of the Gulf War. Gender and other military characteristics did not predict the likelihood of veterans' participation in the survey. The most important factor associated with participation was our ability to contact the veterans. Of the veterans who were successfully located and

contacted by telephone, over 90 percent completed the survey.

We attempted to assess whether characteristics of respondents were significantly different from those of nonrespondents with respect to self-perceived exposure in the Gulf theater or postwar health status. During phase I, 30,000 questionnaires were mailed initially, and two separate follow-up recruitment packets were sent to nonrespondents. The phase II telephone survey was targeted for nonrespondents after completion of the phase I survey. Therefore, each successive group of respondents could be considered a group of nonrespondents in comparison with the preceding group of veterans, because they would have remained nonrespondents without the follow-up recruitment efforts. We kept a record of the date on which each survey questionnaire was received and classified each respondent as completing his/her survey form during phase I, wave 1, 2, or 3, or phase II.

For three selected exposures during the Gulf War—1) contact with prisoners of war, 2) exposure to nerve gas, and 3) other exposures considered harmful—there were no significant differences in the proportions of individuals reporting positively for each of three exposure questions by survey respondent group (phase I, wave 1, 2, or 3, and phase II). Likewise, in both the Gulf and non-Gulf veteran groups, five categories of self-reported general health status (i.e., excellent, very good, good, fair, and poor) did not differ significantly among the four survey respondent groups. In other words, veterans who chose to participate in the survey earlier did not perceive themselves to be more or less healthy than others. It did not appear that self-perceived exposure to

**TABLE 3. Prevalence of post-traumatic stress disorder and chronic fatigue syndrome-like illness and associated odds ratios among veterans, by Gulf War service status, 1995–1997**

| Condition | Gulf veterans (%) ($n$ = 11,441) | Non-Gulf veterans (%) ($n$ = 9,476) | Crude odds ratio | 95% confidence interval | Adjusted* odds ratio | 95% confidence interval |
|---|---|---|---|---|---|---|
| PTSD† | | | | | | |
| Cohort | 12.1 | 4.3 | 3.1 | 2.8, 3.5 | 3.1 | 2.7, 3.4 |
| Population‡ | 10.1 | 4.2 | 2.6 | 2.2, 3.0 | | |
| CFS†-like illness | | | | | | |
| Cohort | 5.6 | 1.2 | 5.0 | 4.1, 6.2 | 4.8 | 3.9, 5.9 |
| Population‡ | 4.9 | 1.2 | 4.2 | 3.3, 5.5 | | |

  \* Adjusted odds ratios and 95% confidence intervals were derived through stratified Cochran-Mantel-Haenszel (29) analysis. Adjustment was made for most of the variables that were correlated with both exposure (Gulf service status) and outcome (PTSD/CFS). In the PTSD analysis, these confounding factors included gender, age, marital status, rank, and unit component. In the analysis of CFS-like illness, the confounding factors for which adjustment was made included age, marital status, rank, and unit component. The number of variables for which adjustment could be made was limited to five in the PTSD analysis and four in the CFS analysis, because of the small cell frequencies that resulted from the stratified analysis.
  † PTSD, post-traumatic stress disorder; CFS, chronic fatigue syndrome.
  ‡ Population rates were calculated using SUDAAN software to account for the complex sample survey design.

harmful situations in the Gulf theater or current health status contributed substantially to their decision as to whether or not to participate.

### Characteristics of veterans with PTSD or CFS and prevalence of conditions

The percentage distributions of selected demographic and military characteristics among the Gulf and non-Gulf veterans who participated in the survey are presented in table 2. The subgroups of Gulf veterans who met the criteria for PTSD or CFS-like illness were compared with the total number of Gulf veteran respondents to determine whether these conditions were concentrated in particular demographic or military strata. There were some differences in demographic and military characteristics when those who met the PTSD criteria were compared with all Gulf veterans. The veterans positive for PTSD criteria ($n$ = 1,381) were more likely to be female, older, non-White, in the enlisted ranks, and in the Army and National Guard ($p$ < 0.001 for each characteristic). The veterans positive for CFS-like illness ($n$ = 640) were more likely to be younger ($p$ < 0.001), single ($p$ < 0.001), in the enlisted ranks ($p$ < 0.001), in the Army or Marines ($p$ < 0.001), and in the reserves ($p$ < 0.02).

Table 3 presents the prevalence of PTSD and CFS-like illness for the Gulf veterans and non-Gulf veteran controls. The odds ratios and 95 percent confidence intervals indicated that the risks of both PTSD and CFS-like illness were significantly higher among Gulf veterans than among non-Gulf veterans. Adjustment was made for most of the variables that were correlated with both Gulf service status and the outcome, either PTSD or CFS-like illness. The number of variables for which adjustment could be made was limited to five in the PTSD analysis and four in the CFS analysis, because of the small cell frequencies that resulted from the stratified analysis. The population prevalences are also

presented in table 3 (PTSD: Gulf, 10.1 percent; non-Gulf, 4.2 percent; CFS-like illness: Gulf, 4.9 percent; non-Gulf, 1.2 percent).

### Deployment and stress

We attempted to differentiate veterans who were not activated from those who were activated but not deployed to the Gulf and from those who were deployed to the Gulf. Active-duty units do not have these distinctions. Hence, veterans on "active duty" were deleted from the analysis of stress intensity as related to PTSD/CFS. Table 4 depicts the relation between stress and PTSD and CFS-like illness. The prevalence of PTSD increased with stress intensity, from 3.3 percent to 22.6 percent (test for trend: $p$ < 0.01). In contrast, risk of CFS-like illness did not show a monotonic relation with stressor intensity for the entire stress spectrum. Prevalence increased significantly when nondeployed troops (0.8 percent) were compared with troops deployed outside of the Gulf region (1.7 percent) and when this latter group was compared with troops deployed to the Gulf in noncombat roles (5.4 percent). However, no significant difference in risk of CFS-like illness occurred among four groups of Gulf veterans with different stressor intensities ($p$ > 0.15).

### DISCUSSION

In addition to estimating the prevalence of PTSD and CFS among Gulf War veterans and non-Gulf veterans, we ascertained the relation between the extent of deployment-related stress and the development of PTSD or CFS-like illness. Our data allowed us to stratify across six progressively more intense levels of stress ranging from the minimal stress of serving at a home base to the most severe stress of being deployed to the Gulf and being involved in direct combat,

**TABLE 4. Prevalence of post-traumatic stress disorder and chronic fatigue syndrome-like illness among members of Gulf-War-era reserve and National Guard units, according to deployment status and intensity of stress, 1995–1997**

| Stress level* | Total no. | PTSD†,‡ | | CFS†-like illness‡ | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| Minimal | 2,844 | 95 | 3.3 | 23 | 0.8 |
| Moderate | 2,963 | 180 | 6.1 | 49 | 1.7 |
| High | | | | | |
| Combat$^0$ | 1,383 | 97 | 7.0 | 75 | 5.4 |
| Combat$^1$ | 3,050 | 362 | 11.9 | 197 | 6.5 |
| Combat$^2$ | 1,415 | 260 | 18.4 | 104 | 7.3 |
| Combat$^3$ | 769 | 174 | 22.6 | 50 | 6.5 |

* Non-Gulf reserve or National Guard unit members who were not activated were defined as having "minimal" stress. Non-Gulf reserve or National Guard unit members who were activated and deployed but not in the Persian Gulf were defined as having "moderate" stress. National Guard or reserve unit members with a combat exposure level of 0, 1, 2, or 3 while in the Persian Gulf were defined as having "high" stress. Veterans were asked whether, during their Gulf deployment, they 1) had worn chemical protective gear or heard chemical alarms sounding, 2) had been involved in direct combat duty, or 3) had witnessed any deaths. Combat exposure levels were then defined as follows: "Combat$^0$" was defined as answering "no" to all three questions on combat exposure; "Combat$^1$" was defined as answering "yes" for only one of the three combat exposures; "Combat$^2$" was defined as answering "yes" for exactly two of the three combat exposures; and "Combat$^3$" was defined as answering "yes" for all three of the combat exposures.

† PTSD, post-traumatic stress disorder; CFS, chronic fatigue syndrome.

‡ Cochran-Armitage trend test: for PTSD, $Z = -21.335$; for CFS-like illness, $Z = -14.098$.

being involved in a potential chemical warfare attack, and witnessing deaths.

Earlier research has shown that rates of PTSD are sensitive to stressor intensity (32). However, to our knowledge, no prior study has examined the entire breadth of stressor intensity as was done here. The data reported here make it clear that rates of PTSD track stressor intensity extremely closely. Rates of PTSD increased monotonically across these six stressor intensities, from 3.3 percent in the least stressful situation to 22.6 percent in the most stressful situation. This result is impressive when we realize that the period of stressor exposure during this war, relative to other conflicts, was relatively short. The significant relation between stressor intensity and PTSD leads to two conclusions: 1) that the existing case definition for PTSD adequately captures a stress-related behavioral syndrome and 2) that rates could be substantially higher in conflicts where stressor intensity and/or duration were greater than in the Gulf War.

Rates of CFS-like illness did show a relation to stressor intensity, but the pattern was quite different from that for PTSD. The rate of CFS-like illness was 0.8 percent for the nondeployed, while the rate for veterans deployed elsewhere but not in the Gulf was 1.7 percent. Rates again increased to

5.4 percent for veterans deployed to the Gulf but in noncombat roles. Rates of CFS-like illness did not change significantly for Gulf veterans in the more stressful situations related to combat. It appears that deployment-related stress has a role in the genesis of CFS in a veteran population. However, the data do not rule out the possibility that, in addition to stress, some unmeasured factors specific to serving in the Gulf could be responsible for the high rates of CFS among Gulf War veterans.

This overall pattern indicates some parallels between CFS-like illness and PTSD in that both have a relation to stress. However, the pattern of that relation—linear for PTSD and linear for CFS only at lower stressor intensities—suggests that the two conditions are not merely variants of one another. Except for the data presented here, which were collected from a Gulf-War-era veteran population, no study has clearly shown an existing relation between stress and CFS in civilians. An initial small case-control study did find that CFS patients reported a higher rate of exposure to serious stressors in the year prior to their illness onset (33). Since that study did not randomly recruit control subjects and did not use rigid inclusion and exclusion criteria to identify CFS patients, a follow-up study was conducted in which both of those deficiencies were corrected. That study found no difference in self-reported exposure to stressors between CFS patients and controls (J. G. Dobbins and B. H. Natelson, Veterans Affairs Medical Center (East Orange, New Jersey), personal communication, 2002). Obviously, such studies have the limitation of a small sample size. Although veterans with CFS are demographically very different from nonveteran CFS patients (nonveteran patients are predominantly White females), one might expect to find, with larger sample sizes, that exposure to psychological stress can be a risk factor for developing CFS among nonveterans also.

The reason why CFS is related to only lower intensities of stressor exposure is unclear. In experimental work, we have shown that stressor intensity is an important variable in predicting the medical consequences of stress (34). One possibility might be that stress, although a factor for CFS, plays a relatively minor role compared with other contributing factors unique to the Gulf War environment.

This survey is one of a few population-based studies of Gulf veterans with contemporary veteran controls. The relatively high participation rate of 70 percent and lack of evidence of response bias, either by self-reported general health status or in theater exposure status, indicate that there is little likelihood of selection bias in this self-administered postal survey questionnaire. In this population-based study, 10.1 percent of the entire deployed population of 693,826 Gulf War troops was estimated to have PTSD during the month prior to completing the questionnaire. This prevalence is compared with 4.2 percent of the 800,680 comparable veterans who were not deployed to the Gulf region. An estimated 4.9 percent of Gulf veterans and 1.2 percent of non-Gulf troops met the modified case definition for CFS. The results suggest that PTSD and CFS may account for a substantial portion of Gulf veterans who complain of a medically unexplained constellation of symptoms.

The Department of Defense should include screening for PTSD/CFS as part of postdeployment clinical examinations

for troops returning from future military conflicts, and appropriate follow-up health care should be planned by both the Department of Defense and the Department of Veterans Affairs.

## ACKNOWLEDGMENTS

## REFERENCES

1. National Institutes of Health Technology Assessment Workshop Panel. The Persian Gulf experience and health. JAMA 1994;272:391–5.
2. Institute of Medicine, National Academy of Sciences. Health consequences of service during the Persian Gulf War: recommendations for research and information systems. Washington, DC: National Academy Press, 1996.
3. Presidential Advisory Committee on Gulf War Veterans' Illnesses: final report. Washington, DC: US GPO, December 1996. (ISBN 0-16-048942-3).
4. Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. N Engl J Med 1996;335:1498–504.
5. DeFraites RF, Wanat ER, Norwood AE, et al. Investigation of a suspected outbreak of an unknown disease among veterans of Operation Desert Shield/Storm. 123rd Army reserve Command, Fort Benjamin Harrison, Indiana. Washington, DC: Walter Reed Army Institute of Research, 1992.
6. Murphy FM, Kang HK, Dalager N, et al. The health status of Gulf War veterans: lessons learned from the Department of Veterans Affairs health registry. Mil Med 1999;164:327–31.
7. Joseph SC, Comprehensive Clinical Evaluation Program Team. A comprehensive clinical evaluation of 20,000 Persian Gulf War veterans. Mil Med 1997;162:149–55.
8. Gray GC, Hawkowarth AW, Smith TC, et al. Gulf War veterans' health registries: who is most likely to seek evaluation? Am J Epidemiol 1998;148:343–9.
9. Nicolson GL, Rosenberg-Nicolson NI. Doxycycline treatment and Desert Storm. JAMA 1995;273:618–19.
10. Abou-Donia MB, Wilmarth KR, Jensen KF, et al. Neurotoxicity resulting from coexposure to pyriodostigmine bromide, DEET, and permethrin: implications of Gulf War chemical exposures. J Toxicol Environ Health 1996;48:35–56.
11. Magill AJ, Grogl M, Gasser RA, et al. Visceral infection caused by *Leishmania tropica* in veterans of Operation Desert Storm. N Engl J Med 1993;328:1383–7.
12. Sutker PB, Uddo M, Brailey K, et al. War-zone trauma and stress-related symptoms in Operation Desert Shield/Storm (ODS) returnees. J Soc Issues 1993;49:33–49.
13. 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;125:398–405.
14. Augerson WS. Chemical and biological warfare agents. In: A review of the scientific literature as it pertains to Gulf War illnesses, National Defense Research Institute. Santa Monica, CA: The RAND Corporation, 2000. (http://www.gulf-like.osd.mil/library /randrep/ bw_paper/).
15. Fukuda K, Straus SE, Hickie I, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study.

16. International Chronic Fatigue Syndrome Study Group. Ann Intern Med 1994;121:953–9.
17. Pollet C, Natelson BH, Lange G, et al. Medical evaluation of Persian Gulf veterans with fatigue and/or chemical sensitivity. J Med 1998;29:101–13.
18. Kipen HM, Hallman W, Kang HK, et al. Prevalence of chronic fatigue and chemical sensitivities in Gulf registry veterans. Arch Environ Health 1999;54:313–18.
19. Bourdette DN, McCaulet LA, Barkhuizen A, et al. Symptom factor analysis, clinical findings, and functional status in a population based case control study of Gulf War unexplained illness. J Occup Environ Med 2001;43:1026–40.
20. Jason LA, Richman JA, Rademaker AW, et al. A community-based study of chronic fatigue syndrome. Arch Intern Med 1999;159:1229–37.
21. Natelson BH, Tiersky L, Nelson J. The diagnosis of post-traumatic stress disorder in Gulf veterans with medically unexplained fatiguing illness. J Nerv Ment Dis 2001;189:795–6.
22. Engel CC Jr, Liu X, McCarthy BD, et al. Relationship of physical symptoms to posttraumatic stress disorder among veterans seeking care for Gulf War-related health concerns. Psychosom Med 2000;62:739–45.
23. Kang HK, Mahan CM, Lee KY, et al. Illnesses among United States veterans of the Gulf war: a population-based survey of 30,000 veterans. J Occup Environ Med 2000;42:491–501.
24. Cameron L, Leventhal EA, Leventhal H. Seeking medical care in response to symptoms and life stress. Psychosom Med 1995; 57:37–47.
25. National Center for Health Statistics. Current estimates from the National Health Interview Survey, 1992. Hyattsville, MD: National Center for Health Statistics, 1994. (DHHS publication no. (PHS) 94-1517).
26. Blanchard EB, Jones-Alexander J, Buckley TC, et al. Psychometric properties of the PTSD Checklist (PCL). Behav Res Ther 1996;34:669–73.
27. Weathers FW, Litz BT, Herman DS, et al. The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. Presented at the ninth annual meeting of the International Society for Traumatic Stress Studies, October 24–27, 1993. (Available from the National Center for PTSD, Boston Veterans Affairs Medical Center, 150 South Huntington Avenue, Boston, MA 02130).
28. Shah BV, Barbwell BG, Bieler GS. SUDAAN software for the statistical analysis of correlated data. User's manual, release 7.5. Research Triangle Park, NC: Research Triangle Institute, 1997.
29. SAS Institute, Inc. PROC FREQ. In: SAS/STAT user's guide, version 8. Cary, NC: SAS Institute, Inc, 2001.
30. Stokes ME, Davis CS, Koch GG. Categorical data analysis using the SAS system. 2nd ed. Cary, NC: SAS Institute, Inc, 2000.
31. Cochran WG. Some methods of strengthening the common $\chi^2$ tests. Biometrics 1954;10:417–51.
32. Armitage P. Tests for linear trends in proportions and frequencies. Biometrics 1955;11:375–86.
33. Kulka RA, Schlenger WE, Fairbank JA, et al. Trauma and the Vietnam War generation. New York, NY: Brunner/Mazel, 1990:81–5.
34. Dobbins JG, Natelson BH, Brasslof I, et al. Physical, behavioral and psychological risk factors for chronic fatigue syndrome: a central role for stress? J Chronic Fatigue Syndr 1995;1:43–58.
35. Tapp WN, Natelson BH. Consequences of stress: a multiplicative function of health status. FASEB J 1988;2:2268–71.
36. Lohr SL. Sampling: design and analysis. Pacific Grove, CA: Duxbury Press, Brooks/Cole Publishing Company, 1999:265.

### APPENDIX

The prevalences of post-traumatic stress disorder and chronic fatigue syndrome-like illness for the entire Gulf War veteran and nondeployed populations were obtained from weighted estimates of individual military strata values according to the sampling design. Potential nonresponse bias in this survey was mitigated by calculation of weighting stratum estimators assuming that nonresponses were missing at random, given covariates, also termed "ignorable nonresponse." "Ignorable" means that a model can explain the nonresponse mechanism and that the nonresponse can be ignored after the model accounts for it, not that the nonresponse can be completely ignored and complete-data methods used (35). Nonresponses were handled by weighting responding units by the inverse of the probability of selection and response in the weighting stratum estima-tors. The weighted stratum estimators adjust the distribution in the observed sample so as to compensate for the distortion that might have resulted from the nonresponse. To estimate the confidence interval of the prevalence, we estimated the sampling variance that was a nonlinear estimator in the presence of nonresponse. We used SUDAAN software, which could handle this nonlinear estimator of the variance in accordance with the complex sampling design, to estimate prevalences and confidence intervals (27). This survey was complex in that the sampling design was stratified random sampling with unequal probabilities of selection from the various strata (gender; branch of service; active, reserve, or National Guard unit status; and deployment status). There were 52 strata in all: 20 strata for Gulf veterans, 20 strata for non-Gulf activated veterans, and 12 strata for non-Gulf nonactivated veterans.