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GRANT NO: DAMD17-95-1-5047

TITLE: Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans

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REPORT DATE: October 1996

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188



| 1. AGENCY USE ONLY (Leave blank) | 2. REPORT DATE | 3. REPORT TYPE AND DATES COVERED |
|---|---|---|
| | October 1996 | Annual (11 Sep 95 - 10 Sep 96) |

**4. TITLE AND SUBTITLE**
Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans

**5. FUNDING NUMBERS**
DAMD17-95-1-5047

**6. AUTHOR(S)**
Jessica Wolfe, Ph.D.

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
Tufts University
Boston, Massachusetts 02111

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Medical Research and Materiel Command
Fort Detrick
Frederick, Maryland 21702-5012

**10. SPONSORING / MONITORING AGENCY REPORT NUMBER**

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for public release; distribution unlimited

**12b. DISTRIBUTION CODE**

**13. ABSTRACT** (Maximum 200 words)

Since deployment from the Persian Gulf War, large numbers of veterans have expressed concerns about their physical health. These concerns raise important questions about combat-zone experiences, particularly the possibility of exposure to hazardous or potentially noxious environmental agents during deployment. Exceedingly little is known about how these possible exposures influence health symptomotology nor how other war-time experiences (e.g., psychological stress) may influence their outcome.

This study expands the third observation phase of an ongoing longitudinal project (the *Ft. Devens ODS Reunion Survey*) aimed at characterizing components of physical and psychological post-deployment readjustment in a cohort of New England area Persian Gulf War veterans. The goals of the investigation are: (a) to identify and examine the role of potential predictors on two critical outcomes - current health status and individual health perceptions, and (b) to evaluate predictors' relevance for veterans' functional health status or disability. A *primary* emphasis will be on investigating whether *female* gender is a significant factor in predicting either functional health status or health perceptions. A secondary objective of the project is to ascertain the prevalence of multiple chemical sensitivity (MCS)-like symptoms reported among this population, and to explore risk factors for the development of this syndrome.

| 14. SUBJECT TERMS | 15. NUMBER OF PAGES |
|---|---|
| functional health status, quality of life, psychological, post-traumatic stress disorder, environmental health, self-reported health. Defense Women's Health Research Program | 22 |
| | 16. PRICE CODE |

| 17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT | 20. LIMITATION OF ABSTRACT |
|---|---|---|---|
| Unclassified | Unclassified | Unclassified | Unlimited |

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# Introduction

## Background and Significance.

With women's increasing proportional representation in the U.S. Armed Forces (Dienstfrey, 1988; Government Accounting Office, 1992; Wolfe, Mori, & Krygeris, 1994; Wolfe, Schnurr, Brown, & Furey, 1994; Wolfe, Brown, & Kelley, 1993), there is rapidly growing interest in factors directly related to female soldiers' total physical and psychological well-being. Of particular interest are variables that potentially influence positive readjustment during and immediately following war-time deployment. To gather unique data on this topic, this study expands the third observation phase of an ongoing longitudinal project involving New England-area Persian Gulf War Army veterans where the overall aim is the characterization of components of positive readjustment following war-time service. Correspondingly, the goal of this *new* proposed phase is to examine the role of potential predictors of functional health status, using current self-reported health status and health perceptions as health status indicators. Carefully defined measures of well-being (e.g., functional well-being/quality of life, physical health status, perceptions of health) will serve as the primary outcome variables of interest. A particular emphasis will be on the role of *female* gender as a possible predictor of functional health status and post-deployment health perceptions (Verbrugge, 1985). Other potential predictors of interest, derived from prior research emphasizing their importance (e.g., Wolfe et al., 1994), include symptoms of post-traumatic stress disorder (PTSD) and self-reported exposure to potentially hazardous environmental agents.

Numerous factors have been associated with the report of adverse changes in functional health status in veterans and civilians (Grey, 1993). These include personal

(e.g., age, educational level), psychosocial (e.g., marital status, social network), and exogenous (e.g., lifestyle, work setting) factors (Hibbard & Pope, 1992; Villaneuve, 1992). Extant research on health outcome suggests that these factors can be additionally classified as structural (e.g., demographic, economic status), modifying (health access), or process (family environment) variables (Albrecht & Nelson, 1993), emphasizing the dynamic and interactive nature of elements in the health domain. Certain variables have been increasingly recognized as potent predictors or modifiers of self-reported health outcomes, often in an adverse direction; for example, high levels of psychological distress typically exert pronounced negative effects on health perceptions (Decoufle, Holmgreen, Boyle, & Stroup, 1992). *Female gender* also has been widely associated with higher rates of functional health impairment across a variety of domains including health complaints, actual morbidity, and increased health service utilization (Nathanson, 1977; Verbrugge & Wingard, 1985). Finally, reports of exposure to hazardous domestic and industrial chemical agents have been associated with markedly increased physical symptom reports and concerns, among both veteran and civilian populations (Baum, 1990; Morrow, Kamis, & Hodgson, 1993). Despite these associations, however, the relationship among these experiences and related background characteristics remains complex and poorly understood. In addition, explanatory models have been limited by a common failure to evaluate *functional* implications of health concerns, apart from symptom descriptions (Lees-Haley & Brown, 1992). Hence, the immediate and long-range implications of increased health symptoms often are unclear for the soldier and his/her family, as well as for military and civilian employers and health service providers.

The role of gender in health, while complex, appears critical (Wolinsky & Johnson, 1992). Increasing numbers of studies have shown that *women*, compared to men, consistently report higher rates of physical health complaints, suffer from more chronic, non-fatal illnesses, and utilize more health-related services overall (Rodin & Ickovics, 1990; Verbrugge, 1985). Extant literature on gender, stress, and health status suggest that the relationship between gender and health is multifactorial and likely to reflect the effects of numerous modifiers, for example, adequacy of family background, job satisfaction, mental health history, and social support networks (Shisana & Celetano, 1987). Frequently, however, contributions by these variables are not systematically assessed. When detailed assessments of modifying variables are conducted, results indicate that the association between *female* gender and health is diminished but *not* eliminated (Carmel, Anson, Levinson, Bonned, & Maoz, 1991), emphasizing that the effect of some experiences differs substantially between men and women. Thus, further study is required to elucidate these relationships (Shumaker & Hill, 1991).

Multiple studies show that psychological distress negatively impacts both the perception *and* status of physical well-being (see Cohen & Williamson, 1991, for review; Manning & Wells, 1992). Psychological stress appears to influence health outcome through a range of potential mechanisms: (a) stress may directly decrease immunocompetence, increasing the exposure risk or resulting physiological capability to combat infectious disease (Mishra, Aldwin, Colby, & Oseas, 1991); (b) health-promoting behaviors often are seriously compromised in individuals with significant depression, anxiety, or PTSD (Kiecolt-Glaser & Glaser, 1987); and (c) interpretation of somatic cues

may be disrupted or intensified under conditions of acute psychological distress (Wise & Rieck, 1993). Of most major psychiatric disorders, PTSD in particular has been found to have particularly strong association with increased health concerns and symptoms in a wide variety of populations, including both males and females and veterans and civilians (e.g., Litz, Keane, Fisher, Marx, & Monaco, 1992; Long, Chamberlain, & Vincent, 1992; Shalev, Bleich, & Ursano, 1990; Wolfe et al., in press).

Existing research suggests that some chemical agents purportedly present in the Gulf War theater are capable of affecting diverse organ systems. Lewisite and mustard gas, for example, produce damage to the skin, cause adverse respiratory effects, and serve as potent carcinogens (Chevillard, Lainee, Robineau, & Puchelle, 1992; Pechura & Rall, 1993). Polycyclic aromatic hydrocarbone (PAHs) derived from oil smoke generates *in vitro* genotoxicity, negatively impacting immune and respiratory performance (e.g., Klaassen, Amdur, & Doull, 1986; Kelsey et al., 1994). Other purported environmental exposures also appear capable of producing both acute and chronic neurotoxic effects in animals and humans (e.g., depleted uranium; kerosene and diesel fuel, Andrews & Snyder, 1986; metals and volatile organics found in smoke, Klaassen et al., 1986; pyridostigmine, Almog et al., 1991; Keeler, Hurst, & Dunn, 1991; sarin, Burchfield & Duffy, 1982; Husain, Vijayaraghavan, Pant, Raza, & Pandey, 1993). Thus, there is growing evidence for the negative effects of a spectrum of environmental agents.

To the degree that other medical diagnoses are eliminated, the diagnosis of multiple chemical sensitivity (MCS) has been raised as a possible explanation for the adverse health symptoms suffered by many Persian Gulf War veterans (Riegle, 1994).

Although no definitive classification for this syndrome currently exists, MCS generally is characterized by symptoms triggered by an identifiable environmental exposure, with resultant symptoms present in more than one organ system (see Cullen, 1987). These symptoms typically recur and abate in response to predictable stimuli with low level exposure, that is, exposure significantly below that typically required to produce adverse effects in humans. Current classification requires that no standard test of organ system function can explain the patient's symptomatology; thus, MCS remains a diagnosis of *exclusion* at this time.

Evaluations of patients with this disorder frequently reveal high rates of both psychological symptoms and psychiatric diagnoses (Sparks et al., 1994a, b), the most common of which include depression, anxiety, and stress. Although earlier hypotheses presumed that the etiology of MCS was exclusively psychogenic, more recent investigations have proposed correlational (and potentially causal) linkages to exposure to environmental hazards (Simon, Daniel, Stockbridge, Claypoole, & Rosenstock, 1993; Welch & Solas, 1992). Based on these models, MCS and PTSD could readily co-occur in some individuals, either secondary to underlying individual vulnerabilities or via concurrent mediation of exposure in shared neural pathways (Bell, Miller, & Schwartz, 1992). The possibility also remains that the high rates of psychiatric symptoms and complaints in MCS patients reflect their acute distress secondary to the impact of a physically disabling condition (Sparks et al., 1994a). The speculative nature of all of these models firmly indicates that more comprehensive models of health outcome - which specify relevant psychological stressors, environmental exposures, and background

characteristics (including gender) - are warranted to understand and to treat observed and reported decrements in functional health status (Meggs, 1993).

Overall Project Objective.

This study expands the third observation phase of an ongoing longitudinal project (the Ft. Devens ODS Reunion Survey) aimed at characterizing components of physical and psychological post-deployment readjustment in a cohort of New England area Persian Gulf War Veterans. The primary objective of this study is to identify and describe the effects of potential predictors on the functional health status and health perceptions of male and female veterans approximately five years after their deployment to the Persian Gulf; and to examine if and how identified "risk" factors differ between female and male veterans. A secondary objective of the proposed project is to ascertain the prevalence of multiple chemical sensitivity (MCS)-like symptoms reported among this population, and to explore risk factors for the development of this syndrome.

Specific Aims.

The goals of the investigation are: (a) to identify and examine the role of potential predictors on two critical outcomes - current health status and individual health perceptions, and (b) to evaluate predictors' relevance for veterans' functional health status or disability. A primary emphasis will be on investigating the role of gender, specifically, whether female gender is a significant factor in predicting either functional health status or health perceptions.

Preliminary Studies - the Ft. Devens ODS Reunion Survey.

Time 1. Since 1991, we have systematically followed and studied a large cohort of U.S. Army personnel that includes active, Reserve, and National Guard Persian Gulf War veterans. The first contact with this cohort involved conducting an initial survey (the *Ft. Devens ODS Reunion Survey, aka "Reunion Survey"*) within five days of these soldiers' return to this country (Wolfe, Kelly, Bucsela, & Mark, 1992), representing an unusually early window for observation. Over 84 units (2,949 subjects) were assessed *in person* by us upon their return to Ft. Devens, Massachusetts between April and July of 1991 **(Time 1)**, before any debriefing activities occurred.

The Ft. Devens sample is moderately diverse. The majority of Army soldiers in our original cohort were Guard members, followed proportionately by Reservists and active duty troops. These proportions differ somewhat from those of the total U.S. Gulf force as well as from the Army: approximately 17% of U.S. Gulf personnel were activated Reserve or Guard troops, 72% of whom served with the Army. Although 8% of our cohort is female, nearly 13% percent of U.S. Gulf troops overall were women, with a similar discrepancy for ethnicity (72.4% white, total force vs. 87% white, Reunion Survey; Government Accounting Office, 1992; personal communication, Michael Dove, Defense Manpower Data Center). Accordingly, the composition of Reunion Survey units do not *fully* reflect the troop status, ethnic, or gender breakdown for the total U.S.Army (or Joint Services) Gulf theater force.

The Time 1 Reunion Survey comprised a broad range of paper and pencil instruments administered *face-to-face* with units at the base. The survey contained

extensive demographic questions along with assessments of combat-zone exposure (Gallops, Laufer, & Yager 1981), theater experiences (Rosenheck, 1992), general deployment events, attitudes and perceptions, and descriptions of war-related PTSD symptomatology (the Mississippi Scale for Combat-related PTSD; Keane, Cadell, & Taylor, 1988) and general psychological status/symptoms using nine previously validated subscales (the Brief Symptom Inventory, BSI; Derogatis, 1992). Wherever possible, measures were specifically chosen for their known, well-established psychometric properties as well as their prior use with military populations (see Wolfe et al., 1992). Besides offering data on rates of positive adjustment and psychological symptomatology in the *immediate*, post-deployment period, this phase also provided some of the first empirical classification of Persian Gulf theater stressors and a comparison of their similarity/dissimilarity among and between men and women to combat exposure domains described in earlier wars (Wolfe et al., 1993; Wolfe, Keane, & Young, 1996).

Time 2. Approximately twenty months after the initial survey, veterans were reevaluated (**Time 2**) to assess longer-term self-reported physical and psychological well-being (Wolfe et al., 1993). A total of 2,315 persons completed the Time 2 survey (2,121 men, 194 women), yielding an overall response rate of 79%. Comparison of Time 2 respondents and non-respondents indicated that a significantly higher percentage of Time 2 non-respondents were on active duty and of Afro-American background; non-respondents also were significantly younger, and these factors have been treated as covariates in subsequent analyses. All Time 1 measures were repeated at Time 2 along with additional queries of other critical functional domains including: alterations in work,

marital, familial, social, or behavioral status (e.g., substance abuse), current family and social adjustment, social networks, occurrence of post-deployment major life stressors (e.g., death of a loved one, stressful separation or divorce, physical or sexual assault or victimization), and self-reported health perceptions, health status, health symptomatology, and health service utilization. Physical symptoms were evaluated using the Health Symptom Checklist (Bartone, Ursano, Wright, & Ingraham, 1989).

Analyses of the Time 2 data to date reveal important findings concerning mental and physical health status of soldiers. Findings show that overall rates of PTSD in our Devens cohort vary considerably, depending in part on the specific unit function and location in the Persian Gulf. Generally, rates of presumptive PTSD at that time average nearly 11% (9.7% male, 20.7% female; Wolfe et al., 1993). Consistent with prior research from the Vietnam War (e.g., Kulka et al., 1990), these results confirm that higher levels of PTSD symptomatology in our cohort are associated with greater reported combat-zone or theater stressor exposure. Importantly, *female* soldiers in our sample at Time 2 also report higher rates of both general (i.e., overall) and specific psychological distress (including depression, anxiety, and PTSD) than men, a finding largely consistent with the study of traumatic stress in civilian samples (e.g., Breslau & Davies, 1992). Finally, data from our sample reveals numerous incidences of deployment-related sexual harassment, including attempted or completed sexual assault (Wolfe, Young, & Brown, 1992). Exposure to these events were *more* strongly predictive of PTSD symptomatology in these women than accompanying exposure to more "traditional" war-zone stressors (e.g., SCUD attacks or alert; contact with severe injury and death). Thus, our work provides additional

support for the differential impact of certain forms of war-zone stress on outcome, at least in women (Wolfe et al., 1993; Wolfe et al., 1994).

Examination of self-reported physical health among our male and female soldier at Time 2 indicate that nearly 17% of the *total* Time 2 sample reported substandard physical health (i.e., "fair" or "poor") following their deployment, with a greater proportion (30%) stating that their health had been adversely affected in some significant way (Wolfe et al., 1992; Wolfe et al., 1993). *Female* veterans in our sample were significantly more likely than males to describe these physical health decrements following Persian Gulf service (41% female versus 29% male; Wolfe et al., 1993). In terms of multifactorial models, Devens' cohort soldiers with war-related PTSD symptoms were significantly more likely than non-distressed counterparts to report post-deployment deterioration in their health status: Over 75% of study subjects with PTSD symptomatology reported serious declines in their physical health, and substantially more women than men described these changes (93% female versus 74% male). Thus, as with mental health, physical health outcome showed an association with gender.

More detailed analyses of the number and type of health symptoms two years post-deployment are currently ongoing, using our Time 2 data from the 20-item Health Symptom Checklist (Bartone et al., 1989) and soldiers' reported environmental exposures. Initial analyses indicate that the three most prevalent health complaints in our soldiers include general aches and pains, headaches, and lack of energy. Sixty-one persons (3.4%) reported being exposed to poison gas or germ warfare at least once or twice. After adjusting for the effects of age, race, gender, current alcohol problems, social

support resources, and general psychological well-being in multiple regression analysis, reported exposure to poison gas or germ warfare was significantly associated with an increase in the total number of health symptoms reported for both men and women ($p<0.05$; Wolfe, Proctor, Davis, Sullivan, & Friedman, 1996).

These data in total offer strong, preliminary support for a relationship among gender, psychological well-being, perceived hazardous environmental exposure, and self-reported health status, with further study needed to elucidate the distinctive impact and significance of gender.

Time 3. In the Spring of 1993, a subset of 200 subjects were selected to participate in a more in-depth, face-to-face evaluation of the precise relationship of self-reported health symptoms and environmental hazard exposure to cognitive test performance, as assessed by neuropsychological measures (**Time 3a**). This study phase grew directly out of male and female soldiers' health complaints that were reported to us during field re-evaluation at Time 2, in particular, soldiers' concerns with their attention, concentration, and memory. Time 3a was derived to include specifically individual soldiers who had reported *none or very few* health symptoms at Time 2 and a corresponding group who reported *numerous* health symptoms, based on the Health Symptom Checklist. The Time 3a protocol, which is currently ongoing, includes detailed structured interviews concerning purported Gulf environmental exposure (e.g., unit and individual locations, duties in the Gulf, perceived exposures) as well as the administration of comprehensive medical and symptom questionnaires, state-of-the-art neuropsychological testing, and psychiatric diagnostic interviews (including structured

review of PTSD symptomatology). All testing is conducted by highly skilled professional staff specifically trained in behavioral psychopathology, environmental hygiene and medicine, industrial health, and neuropsychology. To date, 220 subjects from the Devens cohort sample have been tested (137 have come to the Boston VAMC and completed all parts of the protocol; 83 have partially completed the protocol generally because they live geographically too far away). In addition, 47 veteran subjects (part of the larger Devens cohort but not the projected sample), and 50 controls (veterans deployed to Germany but not the Gulf) have completed the protocol.

## Research Design and Methodology

By using cross-sectional and longitudinal data from an existing, carefully followed military cohort and by expanding predefined measures of health and positive adjustment (including functional well-being/quality of life, self-reported health symptoms and health perceptions), this investigation will conduct analyses that focus directly on: (a) defining the set of reported environmental and psychosocial combat-theater exposures and physical health variables associated with female and male soliders recent deployment and (b) describing the relationship of these variables to functional status and self-reported physical health. Since the impact of female gender, PTSD symptomatology, and reported environmental exposures in recently deployed military samples has not been systematically or concurrently evaluated, analyses will include comparisons between men and women as well as among subsets of female soldiers.

The protocol involves administering a mailed survey to the entire U.S. Army Ft. Devens cohort. The main survey components include: (1) assessment of functional status,

review of medical history and current health status, (2) comprehensive assessment of psychological and physical health symptoms, (3) comprehensive assessment of self-reported environmental exposure history, (4) a review of military and nonmilitary high magnitude life stressors, (5) assessment of social support, and (6) assessment of standard demographic information (e.g., work, military, educational histories). Almost all of these measures are well-validated and have sound psychometric properties.

## Status/Results to Date

One of the first steps in ascertaining the prevalence of multiple chemical sensitivity (MCS)- like symptoms among our study population was to develop a survey instrument to identify subjects with such symptoms. To date, there has been only one survey instrument that has been validated to assess MCS symptoms (Kipen, Hallman, Kelly-McNeil, & Fiedler, 1995). However, due to the length of that scale, we have tested the validity of a shortened version on two groups of subjects: patients referred to the Massachusetts Respiratory Hospital, Braintree, Massachusetts and non-ill controls recruited by participating patients. Statistical analyses on this shorter scale are pending. Also, we are in the final stages of completing the larger survey's development and have preliminarily tested the instrument to determine its length and clarity of questions. We expect to begin full-scale survey administration within two months.

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