

Prevalence and Patterns of Gulf War Illness in Kansas Veterans: Association of Symptoms with Characteristics of Person, Place, and Time of Military Service

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Gulf War veterans have reported health problems that they attribute to their military service, but little is understood about the nature or extent of these conditions. To determine whether Kansas Gulf War veterans are affected by excess health problems, a population-based survey of 1,548 veterans who served in the Persian Gulf War (PGW) and 482 veterans who served elsewhere (non-PGW) was conducted in 1998. Gulf War illness, defined as having chronic symptoms in three of six domains, occurred in 34% of PGW veterans, 12% of non-PGW veterans who reported receiving vaccines during the war, and 4% of non-PGW veterans who did not receive vaccines. The prevalence of Gulf War illness was lowest among PGW veterans who served on board ship (21%) and highest among those who were in Iraq and/or Kuwait (42%). Among PGW veterans who served away from battlefield areas, Gulf War illness was least prevalent among those who departed the region prior to the war (9%) and most prevalent among those who departed in June or July of 1991 (41%). Observed patterns suggest that excess morbidity among Gulf War veterans is associated with characteristics of their wartime service, and that vaccines used during the war may be a contributing factor. *Am J Epidemiol* 2000;152:992–1002.

fatigue syndrome, chronic; Persian Gulf syndrome; risk factors; symptoms and general pathology; veterans

On August 2, 1990, Iraq's Republican Army invaded Kuwait. Within 1 week, US military forces began to arrive in the region as part of Operation Desert Shield. Operation Desert Storm began with the air war on January 17, 1991, and continued with a 4-day ground war that ended February 28, 1991. After the war, the force size was reduced over a period of months, with the majority of troops out of the area by July 1991 (1). Since the war, Gulf War veterans have reported anomalous health problems that include a variety of chronic symptoms such as headache, fatigue, joint pain, rashes, respiratory problems, and neuropsychological difficulties.

Despite a growing body of research on the health problems reported by Gulf War veterans, little is known about their nature or causes. Government review panels (2–4) have generally not found that a single "Gulf War syndrome" is likely to explain all of the health problems reported by veterans. At the same time, research studies have consistently documented similar types of symptoms and illnesses in different groups of Gulf War veterans (5–9) and have invariably found these problems to occur at higher rates in Gulf War veterans than in veterans serving elsewhere (10–15).

Basic epidemiologic questions regarding the prevalence of these conditions and their association with characteristics of Gulf War service have also remained unanswered. The lack of progress in identifying these parameters is due in part to the difficulty of investigating symptom-based health problems that lack corresponding clinical signs and for which no accepted case definition exists (1, 5, 8, 16, 17). By December 1997, about 12 percent of eligible veterans who had served in the Persian Gulf War (PGW) had enrolled in one of two voluntary registries offered by the US Departments of Defense and Veterans Affairs (18). Population-based studies, however, have suggested that a substantially higher proportion of veterans are experiencing health problems (13–15).

The Kansas Persian Gulf War Veterans Health Initiative Program was developed by the state of Kansas in response to veterans' claims that they had health problems resulting from Gulf War service. The present study was designed to determine if Kansas Gulf War veterans experienced a greater burden of health problems than contemporary veterans who did not serve in the Gulf War and, if so, to describe any excess health problems, their prevalence, and patterns of occurrence.

MATERIALS AND METHODS

Study design and population

Veterans were eligible for the study if they 1) were Kansas residents at the time of the study, 2) had served on active military duty for any period between August 1990

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Abbreviations: CI, confidence interval; non-PGW, veterans who did not serve in the Persian Gulf War; OR, odds ratio; PGW, veterans who served in the Persian Gulf War.

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and July 1991, and 3) were separated or retired from the military or currently served in the reserve component. The Defense Manpower Data Center provided names, deployment, and demographic information for individuals who had served on active duty during the target year, whose last address of record was in Kansas. Based on earlier reports that reservists and women were disproportionately affected by post-Gulf War health problems (5, 13, 14), a stratified random sample was drawn to increase representation of those two groups. A sample of 3,138 names, including all activated reservists from the pool of eligible names and a similar number of active component veterans, was selected to be located, screened, and invited to participate. Because the military does not maintain current addresses after veterans have been discharged from service, contact information was identified using state records, telephone directories, Internet listings, and postal service files. Contact attempts were limited to veterans for whom in-state information was identified.

Data collection

Interviews were conducted by telephone between February and August of 1998, using a computer-assisted telephone interviewing system. The survey instrument was designed to provide health information, particularly symptom data, comparable with that from other studies of Gulf War veterans. Questionnaires from previous population-based studies were reviewed. A list of representative health questions was generated and pretested in a group of Missouri Gulf War veterans. Veterans were asked if they had ever been diagnosed or treated by a physician for any of 16 specific medical and psychiatric conditions, or for any medical condition in five general areas, and when each reported condition had developed. Veterans were also asked if 37 individual symptoms had been persistent or recurring problems in the prior year, to rate the severity of each symptom endorsed, and when the problem first began. Only limited questions were asked about veterans' military service. Deployed veterans were asked when they arrived in and departed from the Persian Gulf area, the countries to which they deployed, the units with which they served, and whether they had been notified by the Department of Defense that they had been in the area potentially affected by the Khamisiyah munitions demolition in Iraq. Veterans who did not serve in the Persian Gulf War (non-PGW) were asked if they had received any vaccinations or injections from the military between August 1990 and July 1991.

Criteria for "Gulf War illness" symptom complex

The approach used to characterize the health problems reported by Kansas Gulf War veterans relied on two basic premises. First, not all symptoms and conditions experienced by Gulf War veterans were likely to be attributable to their wartime service. Some level of symptomatology and disease would be expected among Gulf War veterans even had they not served in the war (19, 20). Second, the level of morbidity expected in the absence of Gulf War service could

be estimated from an appropriate referent group. Any identified excess or atypical morbidity associated with PGW deployment might then be considered "Gulf War illness." Lacking a gold standard for Gulf War illness, cases were defined by a method similar to that used for another condition defined primarily by symptoms, chronic fatigue syndrome (21). It involved identification of "exclusionary" conditions—that is, medical and psychiatric diagnoses not included under the general category of "Gulf War illness" for current research purposes—and quantifying the symptoms reported by PGW veterans to define "inclusionary" criteria.

Exclusionary conditions. Diagnosed medical and psychiatric conditions were not included under the general rubric of Gulf War illness if they: 1) were not elevated among Kansas PGW veterans but might produce symptoms similar to those previously associated with Gulf War service, or 2) might interfere with respondents' perception or reports of their symptoms (i.e., serious psychiatric conditions). Therefore, veterans who reported being diagnosed or treated by a physician for any of the following conditions were excluded from consideration as Gulf War illness cases: cancer, diabetes, heart disease, chronic infectious disease, problems resulting from postwar injuries, liver disease, lupus, multiple sclerosis, stroke, or any serious psychiatric condition (those associated with psychosis and/or for which the respondent had been hospitalized since 1991).

Symptom groups and criteria. Several approaches to quantifying symptom criteria were considered, including exploratory factor analysis to identify latent constructs that might be used to define symptom groupings or illness subtypes. This approach provided general validation regarding the cooccurrence of symptoms within system-based categories (e.g., respiratory symptoms tended to occur together, as did gastrointestinal symptoms, and so on). The cooccurrence of symptoms in different categories, however, varied in veteran subgroups (e.g., PGW vs. non-PGW veterans, males vs. females, PGW veterans deployed to different areas). This method was therefore not considered a reliable way to define illness subtypes in this population. Instead, a more descriptive approach was taken, defining symptom groups based on measures of correlation and comparisons between PGW and non-PGW veterans. Veterans were asked about symptoms in several general categories (e.g., respiratory, gastrointestinal, neuropsychological, sleep disturbances, pain), as well as symptoms (e.g., fatigue, headache) for which no single category was apparent. Gulf War illness criteria symptoms must have persisted or recurred in the year prior to interview and first have been a problem for respondents in 1990 or later. The correlation of symptom scores was assessed among PGW veterans who did not report exclusionary conditions. The internal reliability of each symptom grouping was determined using Cronbach's alpha (22). Symptom groups were considered reliable constructs if they were associated with an alpha of 0.70 or greater; individual items were retained within symptom groups if they had item-scale correlations of 0.50 or greater. Symptoms not included in a group were iteratively correlated with all symptom groups in order to identify additional

associations according to the above criteria. In this manner, five highly reliable symptom groups were identified: 1) fatigue/sleep problems ($\alpha = 0.81$), 2) pain symptoms ($\alpha = 0.78$), 3) neurologic/cognitive/mood symptoms ($\alpha = 0.89$), 4) gastrointestinal symptoms ($\alpha = 0.77$), and 5) respiratory symptoms ($\alpha = 0.76$). One additional symptom group, skin symptoms, was identified. Veterans were asked specifically about only one skin symptom (rashes), disallowing correlation assessments. This symptom was frequently reported, strongly associated with deployment, and relatively independent of other symptom groups. Veterans also frequently reported other skin problems, about which they had not specifically been asked.

A similar proportion of PGW and non-PGW veterans reported a very low level of symptomatology within most symptom groups (e.g., 9 percent of non-PGW veterans reported a single, mild fatigue/sleep problems symptom, compared with 10 percent of PGW veterans). Greater symptom burdens were significantly associated with PGW deployment in all symptom categories. Therefore, only respondents with at least one moderately severe symptom or two or more symptoms within a group were considered to have an elevated level of symptoms in that group.

Criteria for other symptom-defined outcomes. Cases of multisymptom illness as defined by the Centers for Disease Control and Prevention were required to have one or more chronic symptoms from at least two of the following three groups: 1) fatigue; 2) mood/cognition (feeling down or depressed, memory problems, difficulty concentrating, trouble finding words, problems falling or staying asleep); and 3) musculoskeletal (joint pain, muscle pain) (14). Cases of chronic fatigue syndrome were defined on the basis of self-reported symptoms, fatigue characteristics, and medical diagnoses, according to established criteria (21).

Data analyses

Analyses compared the health of PGW veterans with that of non-PGW veterans using several health indicators, including 1) general health status, 2) medical and psychiatric conditions reported to have been diagnosed or treated by a physician since 1990, 3) symptoms persisting over the prior year, and 4) defined symptom complexes (Gulf War illness, Centers for Disease Control and Prevention-defined multisymptom illness, chronic fatigue syndrome). The incidence of physician-diagnosed conditions and the prevalence of symptoms were assessed among veterans who did not have each problem prior to 1990. All outcomes among non-PGW veterans were stratified by veterans' self-reported receipt of vaccines or injections from the military during the index year.

Among both PGW and non-PGW veterans, health outcomes were frequently associated with veterans' sex, age, income level, and education level. Therefore, all analyses controlled for the effects of these variables. Indicators of general health status were compared using Mantel-Haenszel chi-square tests (23). Odds ratios for the association of deployment and vaccine status with conditions diagnosed or treated by a physician and prevalence odds ratios associated

with chronic symptoms were determined using logistic regression. Prevalence odds ratios for defined symptom complexes were also determined by logistic regression, controlling for military as well as demographic variables.

Statistical analyses were performed using SAS version 6.12 computer software (24).

RESULTS

Study population

Of 3,138 veterans randomly selected for contact and screening, 2,396 (76 percent) were located using in-state contact information. Twenty-four of those located were unable to participate because family members reported them as being deceased, hospitalized, or unreachable by telephone. Of the remaining veterans, 7 percent were ineligible for the study because they did not fulfill residency or military service requirements. The remaining 2,211 veterans were invited to be interviewed for the study; 2,030 (92 percent) agreed and 181 declined. PGW veterans (93 percent vs. 88 percent non-PGW) and women (95 percent vs. 91 percent males) were significantly more likely to agree to participate. Characteristics of the target and study populations are provided in table 1.

For 143 (7 percent) of the 2,030 study participants, self-reported deployment status differed from that in military personnel records. This was a particular problem among the 482 veterans whose records indicated they had not served in the war, 70 (15 percent) of whom reported they had. Additional study data (e.g., veteran-reported time period and location of service) were used to clarify deployment status, where possible. Veterans for whom additional study data were insufficient to verify deployment status ($n = 50$) were excluded from subsequent analyses.

Health indicators among PGW and non-PGW veterans

PGW veterans generally reported worse overall health and more symptoms than did non-PGW veterans (table 2). Forty-seven percent of all PGW veterans reported a lower level of health in 1998 than in 1990, compared with 19 percent of non-PGW veterans. Non-PGW veterans who received vaccines during the war were more likely to report a worsened health status since 1990 than were non-PGW veterans who did not receive vaccines, and the former endorsed a greater number of symptoms.

A significantly higher proportion of PGW than non-PGW veterans reported being diagnosed or treated by a physician for 10 of 21 types of medical conditions since 1990 (table 3). One condition, hypertension, was significantly higher among non-PGW veterans who had received vaccines than among those who had not (not shown; 11 percent vs. 5 percent, odds ratio (OR) = 2.99, 95 percent confidence interval (CI): 1.19, 7.54).

Table 4 shows the proportion of veterans who reported each of 37 symptoms as persistent problems in the year prior to interview, in the absence of exclusionary conditions. Prevalence odds ratios for the association of symptoms with PGW deployment ranged from 1.95 to 6.63. Among non-

TABLE 1. Distribution of January 1991 characteristics of Kansas Gulf War-era veterans and interviewed sample

	All Kansas PGW*-era veterans			Interviewed veterans		
	% of PGW (n = 6,235)	% of non-PGW* (n = 10,331)	% of total (n = 16,566)	% of PGW (n = 1,548)	% of non-PGW (n = 482)	% of total (n = 2,030)
Demographic characteristics						
Sex						
Male	92	86†	88	86	87	87
Female	8	14	12	14	13	13
Age (years)						
17–21	26	26†	26	19	16†	19
22–25	26	23	24	22	18	21
26–33	26	25	26	27	23	26
≥34	22	26	24	32	42	34
Race/ethnicity						
White	79	83†	82	87	91	88
Black	15	12	13	8	5	8
Hispanic	3	2	2	3	3	3
Other	3	3	3	2	1	2
Military characteristics						
Component						
Active	78	89†	85	47	42	45
Reserve/Guard	22	11	15	53	58	55
Branch						
Army	68	50†	56	66	43†	61
Air Force	11	29	22	16	39	22
Navy	13	14	13	11	9	11
Marines	8	7	7	6	8	7
Coast Guard	0	1	1	0	1	<1
Rank						
Enlisted	89	84†	86	85	80†	84
Officer	11	16	14	15	20	16

* PGW, Persian Gulf War veterans; non-PGW, Persian Gulf War-era veterans who did not serve in the Persian Gulf War.

† Distribution among non-PGW veterans differs significantly from that of PGW veterans ($p < 0.01$).

PGW veterans, six symptoms, all in the pain and neurologic/cognitive/mood symptom categories, were endorsed by significantly more veterans who received vaccines during the war.

Prevalence of symptom-defined health outcomes

A certain level of morbidity was common to all veterans, independent of deployment status. The proportion of veterans reporting any exclusionary condition was similar among PGW and non-PGW veterans (7 percent vs. 6 percent, $p = 0.41$), as was the proportion reporting moderate or multiple symptoms in only one or two defined symptom groups (30 percent vs. 29 percent, $p = 0.78$). For symptomatology in three or more symptom groups, however, a significant difference by deployment status emerged. This pattern of morbidity—moderate or multiple symptoms in at least three of the six defined groups, in the absence of diagnosed exclusionary conditions—was associated with deployment to the Gulf War and defined “Gulf War illness” for purposes of the present study.

Table 5 provides estimates of prevalence and prevalence odds ratios for the association of Gulf War illness with deployment and vaccine status. A similar pattern of association between PGW deployment, vaccine status, and illness was observed for Gulf War illness, Centers for Disease Control and Prevention-defined multisymptom illness, and chronic fatigue syndrome.

Distribution of Gulf War illness in PGW veterans

The prevalence of Gulf War illness among PGW demographic, military, and deployment subgroups is shown in table 6, with unadjusted and adjusted prevalence odds ratios. After adjustment, the prevalence of Gulf War illness was significantly elevated among women, veterans with lower household incomes and less education, Army veterans, and enlisted personnel.

Fewer than 10 percent of Kansas veterans served primarily on board ship during the war. Nearly all remaining veterans were stationed for some period of time in Saudi Arabia and/or the island nation of Bahrain off the coast of Saudi

TABLE 2. General health status of Kansas Gulf War-era veterans, 1990–1998

	PGW* vs. all non-PGW*		Non-PGW only, by vaccine status†	
	% PGW (n = 1,545)	% non-PGW (n = 435)	% receiving vaccines (n = 208)	% receiving no vaccines (n = 187)
Health status in August 1990				
Excellent	61	59	62	53
Good	37	38	37	43
Fair/poor	2	3	1	4
Health status in 1998				
Excellent	25‡	45	47	43
Good	51	47	47	48
Fair/poor	24	8	7	10
Difference in health status category, 1990–1998				
Same or better	53‡	81	78‡	86
Worse	47	19	22	14
No. of chronic symptoms in 1998				
0–3 symptoms	42‡	74	72‡	77
4–6 symptoms	14	13	11	14
≥7 symptoms	44	13	17	9
Hospitalized for any reason, 1991–1998	34	31	29	34
Applied for VA* disability benefits, 1991–1998§	22	19	13‡	25
Believes she/he has had health problems related to 1990–1991 military service	46‡	11	10	11

* PGW, Persian Gulf War veterans; non-PGW, Persian Gulf War-era veterans who did not serve in the Persian Gulf War; VA, US Department of Veterans Affairs.

† Excludes 40 non-PGW veterans who could not recall if they had received vaccines or injections during the war.

‡ Distributions differ significantly ($p < 0.05$), adjusted for sex, age, income level, and education level.

§ Compensation for service-connected disabilities from the US Department of Veterans Affairs.

Arabia. About 40 percent also entered Iraq and/or Kuwait, countries in which the ground war and coalition air strikes occurred. Overall, veterans who served primarily on board ship were least affected by Gulf War illness. The prevalence of Gulf War illness was somewhat higher among those serving in only Saudi Arabia or Bahrain and highest among those who entered Iraq and/or Kuwait.

Most PGW veterans were present in the Gulf region during the ground and air wars in January and February of 1991. Only 56 (4 percent) left the Gulf area prior to January 1991, and 29 (2 percent) arrived in the area in March 1991 or later. The prevalence of Gulf War illness was lowest among veterans who departed the region prior to the war, higher for those present during the war who left the region by March, and highest for those departing in June or July of 1991.

The association of Gulf War illness with time period differed by location in theater (not shown in table). The prevalence of Gulf War illness was highest among veterans who served in Iraq or Kuwait (42 percent), regardless of when they left the region. For veterans not in Iraq or Kuwait, Gulf War illness occurred in 9 percent of those departing prior to the war (referent), 21 percent of those departing in March

(OR = 2.86, 95 percent CI: 1.05, 7.78), 32 percent of those departing in April or May (OR = 3.55, 95 percent CI: 1.28, 9.84), and 41 percent of those departing in June or July (OR = 10.31, 95 percent CI: 2.61, 40.78). This pattern was maintained after adjusting for the number of months veterans spent in the region, with odds ratios ranging from 2.54 for veterans leaving the region in March to 6.04 for those departing in June or July of 1991.

Finally, among non-PGW veterans, Gulf War illness was significantly associated only with self-reported receipt of vaccines (table 5) and being female (OR = 3.19, 95 percent CI: 1.23, 8.29). In multivariable modeling, there was no significant association of Gulf War illness with age, income level, education level, rank, component, or branch of service.

DISCUSSION

The results of this study indicate that, 7 years after serving in the Persian Gulf War, Kansas veterans experienced substantially more health problems than did era veterans who did not serve in the war. Increased morbidity was reflected in worse overall health status, higher rates of med-

TABLE 3. Number and proportion of Kansas Gulf War-era veterans reporting medical conditions diagnosed or treated by a physician, with new onset, 1990–1998

Condition(s)	PGW* (n = 1,545)		Non-PGW* (n = 435)		OR*,†	95% CI*
	No.	%‡	No.	%‡		
Skin condition(s) (other than skin cancer)	299	21	26	6	3.83	2.50, 5.87
Stomach or intestinal condition(s)	219	15	32	8	2.13	1.43, 3.17
Depression	179	12	30	7	1.85	1.22, 2.81
Arthritis	161	11	24	6	1.99	1.27, 3.14
Migraine headaches	160	11	21	5	2.25	1.39, 3.64
High cholesterol	155	11	36	9	1.24	0.84, 1.84
Chronic fatigue syndrome	142	9	5	1	8.70	3.53, 21.46
Bronchitis	138	10	19	5	2.61	1.53, 4.47
High blood pressure	134	9	33	8	1.24	0.82, 1.89
Allergies	119	10	23	7	1.41	0.88, 2.26
Posttraumatic stress disorder	98	6	6	1	4.74	2.05, 10.94
Asthma	63	4	9	2	2.08	1.02, 4.26
Alcohol or drug dependence	43	3	8	2	1.47	0.65, 3.31
Heart disease	37	2	7	2	1.56	0.69, 3.56
Lung disease	37	2	2	<0.5	4.77	1.14, 20.04
Thyroid condition	30	2	4	1	2.32	0.81, 6.67
Fibromyalgia	24	2	2	<0.5	3.69	0.86, 15.84
Skin cancer	23	2	7	2	1.17	0.47, 2.90
Diabetes	21	1	5	1	1.22	0.45, 3.30
Cancer (other than skin cancer)	18	1	4	1	1.21	0.40, 3.69
Seizures	15	1	1	<0.5	4.17	0.51, 31.90

* PGW, Persian Gulf War veterans; non-PGW, Persian Gulf War-era veterans who did not serve in the Persian Gulf War; OR, odds ratio; CI, confidence interval.

† Odds ratio adjusted for sex, age, income, and education level.

‡ Among veterans who did not have condition prior to 1990.

ical and psychiatric diagnoses, and more frequent and severe chronic symptoms.

Among Gulf War veterans, the prevalence of Gulf War illness was most strongly associated with the time period and location in which they served. Earlier reports have hinted at similar associations. US PGW veterans were least likely to participate in government registries if they were in the Gulf region before the war and most likely to participate if they served during Desert Storm (25). A report on veterans participating in the US Department of Veterans Affairs' registry suggested that veterans exhibit different illness profiles in connection with their location of service during the war (26). Iowa PGW veterans were found to have more health problems if they served in Iraq, Kuwait, or Saudi Arabia than if they served elsewhere in the region (13). In addition, Kansas Army veterans, enlisted personnel, and women were disproportionately affected by Gulf War illness, supporting previous indications that ground troops, enlisted personnel, and women may have more health problems than other PGW veterans (7, 10, 14, 27).

A question of central importance to veterans, government officials, and healthcare providers is, "How many veterans are affected by Gulf War-related health problems?" The answer depends on how such problems are conceptualized and defined, but a surprisingly consistent estimate for the excess burden of symptom-defined illness is emerging from existing population-based studies. Among four Air National Guard units, 45 percent of PGW veterans and 15 percent of non-PGW veterans met criteria for Centers for Disease

Control and Prevention-defined multisymptom illness, an excess of 30 percent associated with PGW deployment (14). Among servicemen from the United Kingdom, 62 percent of PGW and 36 percent of non-PGW veterans met similar criteria, an excess of 26 percent among PGW veterans (15). In the present study, 47 percent of Kansas PGW veterans met criteria for Centers for Disease Control and Prevention-defined multisymptom illness, compared with 20 percent of non-PGW veterans, an excess of 27 percent. In addition, 34 percent of PGW veterans met the more restrictive criteria for Kansas-defined Gulf War illness, compared with 8 percent of non-PGW veterans, an excess of 26 percent among PGW veterans. Thus, using two definitions in three distinct veteran populations, the excess burden of illness associated with deployment to the Gulf War has consistently been between 25 and 30 percent.

Nearly all PGW veterans were likely to have received vaccines prior to or during the war. Inoculations are routinely given in the military prior to overseas duty (28), and about 98 percent of Iowa veterans reported receiving vaccines in association with PGW deployment (13). The results of the present study suggest that non-PGW veterans who received vaccines during the war may experience some of the same health problems as PGW veterans. The observed association of Gulf War illness with vaccines among non-PGW veterans is based on self-reported receipt of vaccines and so must be considered preliminary in nature. It does not appear to be due to a general overreporting of health problems in this group, however, since only

TABLE 4. Prevalence of chronic symptoms with onset since 1990 among Kansas Gulf War-era veterans reporting no exclusionary conditions

	PGW* vs. all non-PGW*				Non-PGW only, by vaccine status†			
	% PGW (n = 1,435)	% non-PGW (n = 409)	OR*,‡	95% CI*	% receiving vaccines (n = 197)	% receiving no vaccines (n = 177)	OR‡	95% CI
Fatigue/sleep problems								
Not feeling rested after sleep	42	21	2.69	2.04, 3.54	24	18	1.43	0.83, 2.46
Fatigue	36	12	4.10	2.94, 5.72	14	9	1.77	0.89, 5.68
Problems falling or staying asleep	33	14	2.98	2.18, 4.08	15	12	1.22	0.65, 2.31
Feeling unwell after exercise or exertion	17	4	4.28	2.57, 7.13	5	3	1.84	0.58, 5.83
Moderate or multiple fatigue symptoms	47	21	3.32	2.52, 4.38	25	17	1.46	0.84, 2.55
Pain symptoms								
Pain in joints	37	15	3.27	2.40, 4.44	17	11	1.94	1.02, 3.70
Pain in muscles	21	6	4.57	2.90, 7.19	7	5	1.89	0.74, 4.81
Body pain-hurt all over	16	5	3.93	2.39, 6.48	6	2	3.78	1.13, 12.66
Moderate or multiple pain symptoms	34	13	3.57	2.57, 4.98	14	10	2.07	1.01, 4.25
Neurologic/cognitive/mood symptoms								
Problems remembering recent information	32	8	4.92	3.35, 7.21	12	5	3.02	1.28, 7.11
Feeling irritable/angry outbursts	31	8	5.18	3.47, 7.73	10	5	2.28	0.94, 5.53
Numbness or tingling in extremities	29	14	2.33	1.70, 3.18	17	12	1.63	0.86, 3.08
Headaches	29	12	2.96	2.11, 4.15	13	11	1.44	0.73, 2.83
Eyes very sensitive to light	25	11	2.62	1.84, 3.74	14	6	2.25	1.02, 4.94
Trouble finding words when speaking	24	6	4.20	2.76, 6.39	10	3	4.48	1.61, 12.48
Feeling down or depressed	23	9	2.99	2.07, 4.31	11	7	1.64	0.78, 3.48
Difficulty concentrating	22	5	4.60	2.92, 7.26	7	4	2.51	0.95, 6.64
Night sweats	20	4	5.33	3.21, 8.84	5	3	1.68	0.53, 5.29
Feeling dizzy, lightheaded, or faint	19	6	3.35	2.18, 5.17	8	4	2.20	0.86, 5.68
Low tolerance for heat or cold	18	6	3.67	2.30, 5.87	6	5	1.35	0.51, 3.58
Symptomatic response to chemicals, odors	17	4	4.62	2.73, 7.81	4	3	1.63	0.52, 5.06
Blurred or double vision	13	5	2.49	1.55, 4.00	6	3	3.53	1.13, 11.03
Tremors or shaking	9	4	1.95	1.17, 3.25	5	3	2.31	0.74, 7.24
Moderate or multiple neurologic symptoms	59	27	3.94	3.05, 5.10	32	20	2.07	1.23, 3.45
Gastrointestinal symptoms								
Diarrhea	19	6	3.38	2.18, 5.23	8	3	2.60	0.96, 7.02
Nausea or upset stomach	17	4	4.25	2.55, 7.08	6	3	1.69	0.59, 4.88
Abdominal pain or cramping	15	4	4.23	2.46, 7.25	5	2	2.59	0.75, 8.94
Moderate or multiple gastrointestinal symptoms	22	7	3.63	2.38, 5.53	9	5	3.13	1.17, 8.32
Respiratory symptoms								
Difficulty breathing or catching breath	18	4	4.09	2.49, 6.71	5	5	0.91	0.34, 2.42
Persistent cough when don't have cold	17	8	2.20	1.49, 3.26	9	8	1.18	0.55, 2.52
Wheezing in chest	13	5	2.51	1.57, 4.01	6	6	0.89	0.35, 2.23
Moderate or multiple respiratory symptoms	21	7	3.37	2.19, 5.18	6	8	0.81	0.35, 1.87
Skin symptoms								
Rashes	20	4	5.73	3.41, 9.62	4	4	1.03	0.33, 3.22
Moderate or multiple skin symptoms	19	6	4.09	2.53, 6.63	7	3	1.70	0.56, 5.15
Other symptoms								
Sinus congestion	33	15	2.64	1.90, 3.68	17	13	1.37	0.70, 2.68
Ringing in ears	23	7	4.06	2.60, 6.34	7	5	1.91	0.72, 5.09
Hearing loss	19	7	3.34	2.13, 5.23	8	4	1.68	0.65, 4.38
Problems with teeth or gums	14	6	2.04	1.33, 3.14	6	7	1.03	0.44, 2.42
Sore or swollen glands in neck	12	4	2.94	1.73, 5.01	4	3	1.25	0.40, 3.87
Sore throat	11	4	2.39	1.42, 4.03	5	3	1.44	0.49, 4.26
Unusual hair loss	10	2	5.79	2.67, 12.52	3	1	1.64	0.30, 8.87
Veteran or partner feels a burning sensation after sex	8	2	3.75	1.88, 7.49	3	2	2.20	0.52, 9.25
Mouth sores	8	1	6.63	2.68, 16.38	1	1	1.25	0.20, 7.86

* PGW, Persian Gulf War veterans; non-PGW, Persian Gulf War-era veterans who did not serve in the Persian Gulf War; OR, prevalence odds ratio; CI, confidence interval.

† Excludes 35 non-PGW veterans who could not recall if they had received vaccines or injections during the war.

‡ Prevalence odds ratio adjusted for sex, age, income, and education level.

one medical condition (hypertension) and two types of symptoms were significantly associated with receiving vaccines. Additionally, non-PGW veterans who received vac-

cines were no more likely to attribute health problems to their wartime service than were non-PGW veterans who did not receive vaccines.

TABLE 5. 1998 prevalence of symptom-defined health outcomes in Kansas Gulf War-era veterans

	Gulf War illness (Kansas defined)				CDC*-defined multisymptom illness				Chronic fatigue syndrome			
	No.	Pre- valence (%)	OR* †	95% CI*	No.	Pre- valence (%)	OR†	95% CI	No.	Pre- valence (%)	OR†	95% CI
Total												
PGW* vs. all non-PGW* veterans	435	8.3	1.0		86	19.8	1.0		3	0.7	1.0	
All non-PGW veterans	1,545	34.2	4.68	3.25, 6.75	729	47.2	3.26	2.48, 4.28	110	7.1	8.21	2.58, 26.10
PGW veterans												
PGW vs. non-PGW veterans, by vaccine status ‡	187	3.7	1.0		28	15.0	1.0		0	0		
Non-PGW veterans/no vaccines	208	11.5	3.78	1.50, 9.54	48	23.1	2.04	1.15, 3.60	3	1.4	Undefined	
Non-PGW veterans/received vaccines	1,545	34.2	10.64	4.91, 23.06	729	47.2	4.77	3.07, 7.41	110	7.1	Undefined	
PGW veterans												

* CDC; Centers for Disease Control and Prevention; OR, prevalence odds ratio; CI, confidence interval; PGW, Persian Gulf War veterans; non-PGW, Persian Gulf War-era veterans who did not serve in the Persian Gulf War.

† Prevalence odds ratio adjusted for sex, age, income, education, rank, and service branch and component.

‡ Excludes 40 veterans who could not recall if they had received vaccines or injections during the war.

A relation between vaccinations and illness has been observed among Gulf War veterans from the United Kingdom and Canada, and a mechanism for an association of illness with multiple vaccinations has been proposed (29). The prevalence of multisymptom illness was associated with reports by veterans from the United Kingdom of receiving vaccines against biologic warfare agents (anthrax, plague, pertussis adjuvant) and with receiving multiple vaccinations during deployment (15, 30). A 1998 study of Canadian Gulf War veterans found a significant association between receiving “nonroutine immunizations” (anthrax, plague) and several symptom-defined outcomes (10).

Patterns associated with where and when a veteran served suggest that multiple factors likely contributed to the excess morbidity experienced by Gulf War-era veterans. Fewer than 4 percent of era veterans with no identified PGW-related exposures experienced symptoms of Gulf War illness. Between 9 and 12 percent of veterans likely to have had the lowest level of Gulf War-related exposures (non-PGW veterans who received vaccines during the war and veterans returning from the Gulf region prior to Desert Storm) had symptoms of Gulf War illness. The highest rate of illness, independent of time period, occurred among veterans who were in Iraq and/or Kuwait, suggesting that the factor or factors contributing to Gulf War illness were most concentrated in battlefield areas. Veterans in those areas might have encountered a greater number or concentration of potentially toxic exposures and experienced more battle-related trauma.

The observation that veterans in support areas who departed the region soon after the war were less likely to be ill than those who departed months later is particularly intriguing. It suggests an association of illness with toxic exposures, since battle-related stressors were reduced in later months. Potential risk factors that would have been more prevalent in support areas in later months might include exposure to contaminants from oil well fires, exposure to toxicants transferred via people or equipment from battlefield areas, and exposures associated with cleanup and refurbishing of equipment.

The results of this study raise methodological issues likely to be important in other Gulf War-related research. Fifteen percent of Gulf War-era veterans whose military records indicated they had not served in the Gulf War reported that they had. If the discrepancies observed here are representative, large studies of Gulf War-era military populations that rely on military personnel databases to compare outcomes between PGW and non-PGW veterans may be seriously affected by inaccurate assessment of deployment status.

Another important methodological issue relates to the use of non-PGW veterans as an “unexposed” referent group in cross-sectional and cohort studies. If vaccines administered to troops are one of the factors contributing to excess morbidity in Gulf War veterans, studies comparing PGW with non-PGW veterans should assess and control for the effects of vaccines received by non-PGW veterans.

There are limitations to consider in interpreting the findings reported here. First, all health and most military infor-

TABLE 6. 1998 prevalence of Gulf War illness (GWI) among Kansas Gulf War veterans, stratified by demographic, military, and wartime service characteristics

	Total	% with GWI	Unadjusted		Adjusted	
			OR*	95% CI*	OR†	95% CI
Demographic characteristics						
Sex						
Male	1,358	33	1.0		1.0	
Female	187	41	1.36	1.00, 1.87	1.49	1.06, 2.08
Age (years)‡						
24–29	362	35	1.0		1.0	
30–39	621	36	1.07	0.82, 1.41	1.16	0.86, 1.57
40–49	374	34	0.96	0.71, 1.31	1.23	0.84, 1.80
≥50	188	27	0.68	0.46, 1.00	1.40	0.83, 2.34
Race						
White	1,309	33	1.0		1.0	
Black	112	48	1.93	1.32, 2.83	1.23	0.81, 1.87
Other	118	39	1.32	0.90, 1.95	1.08	0.70, 1.65
Annual income (\$)‡						
≥35,000	931	31	1.0		1.0	
<35,000	577	41	1.56	1.26, 1.93	1.30	1.02, 1.66
Education‡						
≥4-year college degree	436	24	1.0		1.0	
<4-year college degree	1,102	38	1.93	1.51, 2.48	1.60	1.18, 2.15
Military characteristics, 1990–1991						
Branch						
Air Force	284	19	1.0		1.0	
Navy	176	23	1.32	0.84, 2.09	1.18	0.62, 2.21
Marines	94	33	2.14	1.28, 3.60	1.26	0.65, 2.44
Army	991	41	3.00	2.19, 4.11	1.71	1.12, 2.61
Component						
Active	687	36	1.0		1.0	
Reserves	507	38	1.08	0.85, 1.37	1.21	0.93, 1.59
National Guard	348	26	0.62	0.47, 0.83	1.10	0.77, 1.58
Rank						
Officer	224	18	1.0		1.0	
Enlisted	1,318	37	2.61	1.84, 3.69	1.70	1.12, 2.58
Time and location of Gulf War service						
Months in theater (August 1990–July 1991)						
1–3 months	290	26	1.0		1.0	
4–6 months	889	37	1.66	1.24, 2.23	0.91	0.63, 1.32
7–12 months	350	36	1.61	1.15, 2.27	1.01	0.65, 1.60
Notified of proximity to Khamisiyah demolition site						
No	1,156	33	1.0		1.0	
Yes	271	42	1.47	1.12, 1.92	1.28	0.95, 1.73
Location in theater						
On board ship	121	21	1.0		1.0	
Saudi Arabia/Bahrain (not Iraq/Kuwait)	792	31	1.64	1.04, 2.58	1.73	0.99, 3.04
Entered Iraq/Kuwait	606	42	2.62	1.67, 4.11	2.73	1.52, 4.90
Time period in theater						
Left Gulf area prior to January 1991	56	9	1.0		1.0	
Present during war, left March 1991	295	25	3.35	1.35, 8.33	3.27	1.19, 8.96
Present during war, left April–May 1991	779	36	5.85	2.56, 13.40	3.22	1.17, 8.83
Present during war, left June–July 1991	311	43	7.72	3.38, 17.66	11.70	3.16, 43.40

* OR, prevalence odds ratio; CI, confidence interval.

† Prevalence odds ratio adjusted for sex, income, education level, branch of service, rank, location in theater, and time period in theater.

‡ Age, annual household income, and level of education at time of interview.

mation was self-reported. The considerable amount of media attention given to issues surrounding Gulf War-related health problems may have generated an increased awareness of symptoms among PGW veterans and an increased willingness to report them. The possible impact of differential recall or reporting on apparent increases in morbidity among Gulf War veterans is difficult to quantify but has been assessed in previous studies. A large national sur-

vey of Gulf War-era veterans found that veteran-reported information relating to clinical encounters was in good agreement with medical records in 93 percent of cases and in partial agreement in 4–6 percent of cases (31). The Iowa Persian Gulf Study Group, using measures of physical function and veterans' tendency to respond to questions in a socially desirable way, concluded that recall bias may not explain the higher prevalence of health problems observed

among PGW veterans (13). It is also unlikely that increased symptom awareness or reporting among PGW veterans would fully account for the high odds ratios associated with Gulf War illness in the present study. In particular, media influence would not explain the nonrandom distribution of Gulf War illness observed here, since associations of illness with time and place of Gulf War service have not been widely reported.

Limitations generally associated with self-reported exposures in the Gulf War theater were minimized in this study by including only more objective service-related indicators—rank, branch of service, dates of service, and the countries in which veterans served. The accuracy of self-reported receipt of vaccines by non-PGW veterans is open to question, however, and could have biased the associations observed here in either direction.

Further, it is not known whether the health experience of Kansas veterans is representative of Gulf War veterans nationally. Overall, Kansas Gulf War veterans were similar to their national peers with respect to rank, gender, and age distribution but included fewer non-Caucasians and a lower proportion of Navy and Marine Corps veterans (25). Still, the prevalence of Centers for Disease Control and Prevention-defined multisymptom illness observed in Kansas veterans was similar to that found among Air National Guard units (14), and the estimated prevalence of chronic fatigue syndrome in Kansas PGW veterans (7 percent) was similar to that reported from a nationwide survey of PGW veterans (5 percent) (27).

Over a decade after Iraq invaded Kuwait, the health problems reported by Gulf War veterans remain largely an unsolved mystery. These health problems appear to be complex, and their understanding will likely require an approach that considers “clusters of causes” and “combinations of effects” (32). The basic epidemiologic approach taken here—describing excess health problems reported by veterans and their association with person, place, and time—provides answers to preliminary questions and suggests areas of follow-up that might produce useful insights regarding etiology and illness subtypes. Such investigations should include comparisons between veteran subgroups with higher and lower rates of illness and among those with different types of symptoms. In this way, as the results of this study and of other recent studies suggest, many of the outstanding questions regarding Gulf War-related health problems may be answerable.

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REFERENCES

1. Committee to Review the Health Consequences of Service during the Persian Gulf War. Health consequences of service during the Persian Gulf War: initial findings and recommendations for immediate action. Washington, DC: National Academy Press, 1995.
2. Defense Science Board. Report of the Defense Science Board task force on Persian Gulf War health effects. Washington, DC: Office of the Undersecretary of Defense for Acquisition and Technology, 1994.
3. NIH Technology Assessment Workshop Panel. The Persian Gulf experience and health. *JAMA* 1994;272:391–6.
4. Presidential Advisory Committee on Gulf War Veterans' Illnesses: final report. Washington, DC: US Government Printing Office, 1996.
5. Joseph SC, Comprehensive Clinical Evaluation Program Evaluation Team. A comprehensive clinical evaluation of 20,000 Persian Gulf War veterans. *Mil Med* 1997;162:149–54.
6. Haley RW, Kurt TL, Horn J. Is there a Gulf War syndrome?: searching for syndromes by factor analysis of syndromes. *JAMA* 1997;277:215–22.
7. Wolfe J, Proctor SP, Davis JD, et al. Health symptoms reported by Persian Gulf War veterans two years after return. *Am J Ind Med* 1998;33:104–13.
8. Coker WJ, Bhatt BM, Blatchley NF, et al. Clinical findings for the first 1000 Gulf War veterans in the Ministry of Defence's medical assessment program. *BMJ* 1999;318:290–4.
9. Murphy FM, Kang H, Dalager NA, 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.
10. Goss Gilroy, Inc. Health study of Canadian forces personnel involved in the 1991 conflict in the Persian Gulf. Vol 1. Prepared for Gulf War Illness Advisory Committee, Department of National Defence. Ottawa, Canada: Department of National Defence, 1998. (http://www.dnd.ca/menu/press/Reports/Health/health_study_e_vol1_TOC.htm).
11. Stretch RH, Bliese PD, Marlowe DH, et al. Physical health symptomatology of Gulf War-era service personnel from the states of Pennsylvania and Hawaii. *Mil Med* 1995;160:131–6.
12. Pierce PF. Physical and emotional health of Gulf War veteran women. *Aviat Space Environ Med* 1997;68:317–21.
13. Iowa Persian Gulf Study Group. Self-reported illness and health status among Gulf War veterans—a population-based study. *JAMA* 1997;277:238–45.
14. Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multi-symptom illness affecting Air Force veterans of the Gulf War. *JAMA* 1998;280:981–8.
15. Unwin C, Blatchley N, Coker W, et al. Health of UK service men who served in the Persian Gulf War. *Lancet* 1999;353:169–78.
16. Wegman DH, Woods NF, Bailar JC. How would we know a

- Gulf War syndrome if we saw one? *Am J Epidemiol* 1997;146:704–11.
17. Hyams KC, Roswell RH. Resolving the Gulf War syndrome question. *Am J Epidemiol* 1998;148:339–42.
 18. Department of Veterans Affairs, Veterans Health Administration, Office of Public Health and Environmental Hazards. Consolidation and combined analysis of the databases of the Department of Veterans Affairs' Persian Gulf Health Registry and the Department of Defense's Comprehensive Clinical Evaluation Program, 1997. Cited in US Senate Committee on Veterans' Affairs, report of the Special Investigation Unit on Gulf War Illnesses. Washington, DC: US Government Printing Office, 1998:129.
 19. Kroenke K, Price RK. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. *Arch Intern Med* 1993;153:2474–80.
 20. Verbrugge LM, Ascione FJ. Exploring the iceberg: common symptoms and how people care for them. *Med Care* 1987;25:539–63.
 21. Fukuda K, Straus SE, Hickie I, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study. *Ann Intern Med* 1994;21:953–9.
 22. Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika* 1951;16:297–334.
 23. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;22:719–48.
 24. SAS Institute, Inc. SAS version 6.12. Cary, NC: SAS Institute, Inc, 1997.
 25. Gray GC, Hawksworth AW, Smith TC, et al. Gulf War veterans' health registries: who is most likely to seek evaluation? *Am J Epidemiol* 1998;148:343–9.
 26. Marshall F, Gass A. Gulf War diseases: a critical review of 400 examinations. Presented at the Conference on Federally Sponsored Gulf War Veterans' Illnesses Research, Washington, DC, June 1998.
 27. Kang HK, Mahan CM, Lee KY, et al. Prevalence of chronic fatigue syndrome among U.S. Gulf War veterans. Presented at the Fourth International American Association for Chronic Fatigue Syndrome Research Conference, Cambridge, Massachusetts, October 1998.
 28. Committee to Study the Interactions of Drugs, Biologics, and Chemicals in US Military Forces. Interactions of drugs, biologics, and chemicals in US military forces. Washington, DC: National Academy Press, 1996.
 29. Rook GAW, Zumla A. Gulf War syndrome: is it due to a systemic shift in cytokine balance towards a Th2 profile? *Lancet* 1997;349:1831–3.
 30. Hotopf M, David A, Hull L, et al. Role of vaccinations as risk factors for ill health in veterans of the Gulf War: cross sectional study. *BMJ* 2000;320:1363–7.
 31. Magee CA, Kang HK, Mahan CM, et al. Validation of selected veteran-reported health outcomes in the National Survey of Gulf War-Era Veterans. Presented at the Conference on Federally Sponsored Gulf War Veterans Illnesses Research, Washington, DC, June 1999.
 32. Stallones RA. Community health. (Editorial). *Science* 1972;175:839.