# Surveillance of Health Outcomes of Gulf War Veterans

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# Key Dates During Operations Desert Shield/Desert Storm

#### <u>1990</u>

August 2	Iraq invaded Kuwait
August 8	U.S. Air Force planes arrived in Saudi Arabia
August 9	U.S. ground forces arrived in Saudi Arabia
November 8	President Bush orders an additional 150-200,000 (400,000 total)
November 29	UN resolution authorizing use of "all necessary means"
<u>1991</u>	
January 17	First irretrievable hostile fire
January 20	First oil well fires started in Kuwait
February 19	Majority of oil well fires ignited
February 24	Ground war began
February 28	Offensive operations ceased
March 4,10	Khamisiyah, Iraq chemical munitions destruction
June 13	Last U.S. service members who participated in the ground war returned to the United States

## Number of U.S. Troops in the Persian Gulf Theater of Operations by Month



(SOURCE: Information provided by the Defense Manpower Data Center (DMDC))

# Demographic and Military Characteristics of 695,516 Gulf War Veterans



(SOURCE: Kang and Bullman, NEJM 1996;335:498-504)





# Percent Distribution of Potential Exposures of Concern Reported by Gulf War Veterans

Exposure of Concern	National Survey (N=11,441)	VA Registry (N=15,891)
Petrochemical fumes (including tent heater,		
vehicle exhaust)	80.4	90.3
Ate local food	74.9	70.7
Wore chemical protective gear (other than		
training or heard chemical alarms sound)	65.5	66.6
Smoke from oil well fires	65.1	72.8
Burning trash/feces	60.0	74.7
Skin exposure to diesel, other petrochemical	56.6	73.9
Personal pesticides (creams, sprays, other)	48.4	67.2
SCUD missile explosion	43.2	-
Contact with prisoners of war	32.8	-
Dead animals	32.2	-
Ate food contaminated with smoke, oil, other		
chemicals	30.2	33.9
Other paint and/or solvent and/or petrochemicals	29.7	53.3

(SOURCE: Kang, et al. JOEM 2000; 42:491-501)

# Percent Distribution of Potential Exposures of Concern Reported by Gulf War Veterans, Con't

Exposure of Concern	National Survey (N=11.441)	VA Registry (N=15.891)
Bathed in or drank water contaminated with	28.1	29.3
smoke, oil, other chemicals		
Involved in direct combat duty	27.2	29.9
Witnessed any deaths	26.4	21.7
Microwaves	23.7	34.2
Bathed or swam in a local pond, river, or		
Persian Gulf water	23.3	29.3
Chemical Agent Resistant Compound paint	21.7	35.0
Nerve gas	9.6	15.8
Depleted uranium	9.5	15.1
Experienced sexual harassment	5.1	-
Mustard gas or other blistering agents	4.8	7.2
Suffered forced sexual relations or sexual assault	0.8	-



#### **Gulf War Veterans Mortality**

#### **Publications**

Bullman TA, Mahan CM, Kang HK, Page WF (2005). Mortality in US Army Gulf War veterans exposed to 1991 Khamisiyah chemical munitions destruction. Am J Public Health, <u>95:</u>1382-1388.

Kang HK, Bullman TA, Macfarlane GJ, Gray GC (2002). Mortality among US and UK veterans of the Persian Gulf War: a review. Occup Environ Med, <u>59</u>:794-799.

Kang HK, Bullman, TA (2001). Mortality among U.S. veterans of the Gulf War: seven year follow up. American Journal of Epidemiology, <u>154</u>, 399-405.

Kang HK and Bullman TA (1998). Counterpoint: Negligible "healthy-warrior effect" on Gulf War veterans' mortality. American Journal of Epidemiology, <u>148</u>, 324-325.

Kang HK and Bullman TA (1996). Mortality among U.S. veterans of the Persian Gulf War. New England Journal of Medicine <u>335</u>, 1498-1504

#### **Mortality Studies Results**

- 1. Overall mortality rate of Gulf War veterans is not higher than non-Gulf veterans.
- 2. Mortality rates from accidents, especially motor vehicle accident were higher and from disease-related causes were lower among Gulf War veterans than non-Gulf veterans.
- 3. These differences in mortality patterns began to dissipate after 5 years since the war.
- 4. Both Gulf and non-Gulf veterans mortality rates remained less than half that expected from their civilian counterparts.
- 5. Both US and UK study results are remarkably similar.
- 6. Gulf War veterans who were potentially exposed to nerve agent had an increased risk of brain cancer death compared to other Gulf War veterans.

#### Suicide Rates among Male Gulf and Non-Gulf Veterans Compared to U.S. Male Suicide Rates, 1991-2004



Source: Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. N Engl J Med 1996; 335:1498–1504 Kang HK, Bullman TA. Mortality among U.S. veterans of the Gulf War: 7-year follow-up. Am J Epidemiol 2001; 154:399–405 U.S. male suicide rate from www.cdc.gov/niosh/LTAS

#### Suicide Rates among Female Gulf and Non-Gulf Veterans Compared to U.S. Female Suicide Rates, 1991-2004



Source: Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. N Engl J Med 1996; 335:1498–1504 Kang HK, Bullman TA. Mortality among U.S. veterans of the Gulf War: 7-year follow-up. Am J Epidemiol 2001; 154:399–405 U.S. female suicide rate from www.cdc.gov/niosh/LTAS

#### VA/USUHS MVA Study Publications

Hooper TI, DeBakey SF, Bellis KS, Kang HK, Cowan DN, Lincoln A, Gackstetter GD. Understanding the effect of deployment on the risk of fatal motor vehicle crashes: a nested case-control study of fatalities in Gulf War era veterans, 1991-1995. Accident Analysis and Prevention 2006;38: 518-25.

Gackstetter GD, Hooper TI, DeBakey SF, Johnson A, Nagaraj BE, Heller JM, Kang HK. Fatal motor vehicle crashes among veterans of the 1991 Gulf War and exposure to munitions demolitions at Khamisiyah: a nested case-control study. Am J Ind Med 2006;49:261-270.

Lincoln AE, Hooper TI, Kang HK. Motor vehicle fatalities among Gulf War era veterans: characteristics, mechanisms and circumstances. Traffic Injury Prevention 2006; 7:31-37.

Hooper TI, DeBakey SF, Lincoln A, Kang HK, Cowan DN, Gackstetter GD. Leveraging existing databases to study vehicle crashes in combat occupational cohort: epidemiologic methods. Am J Ind Med 2005;48:118-127.

## **MVA Study Findings**

- 1. Veterans who died of MVA were disproportionately younger, less educated, not married, enlisted, and deployed to the Gulf War.
- 2. Gulf veterans who died of MVA were disproportionately more involved in a single-vehicle crash, alcohol related crashes, and non- users of seat belt.
- 3. Possible exposure to nerve agents at Khamisiyah was not associated with post war MVC among Gulf veterans.

#### **Gulf War Veterans Health Registry Publications**

Miller R, Costigan, Costigan D, Young H, Kang H, Dalager N, Mathes R, Crawford H, Page W, Thaul S (2006). Patterns of health care seeking of Persian Gulf War Registry members prior to deployment. Mil Med,171:370-375.

Smith TC, Jimenez DL, Smith B, Gray GC, Hooper TI, Gackstetter GD, Heller JM, Dalager NA, Kang HK, Hyams KC, Ryan MAK (2004). The Postwar Hospitalization Experience of Gulf War Veterans Participating in US Health Registries. J Occup Environ Med, 46(4):386-397.

Hallman WK, Kipen HM, Diefenbach M, Boyd K, Kang H, Leventhal H, Wartenberg D (2003). Symptom patterns among Gulf War Registry Veterans. Am J Public Health, 93(4):624-30.

Smith TC, Smith B, Ryan MAK, Gray GC, Hooper TI, Heller JM, Dalager NA, Kang HK, Gackstetter CD (2002). Ten Year and 1000,000 participants later: occupational and other factors influencing participation in U.S. Gulf War Health Registries. J Occup Environ Med 44: 758-768.

Murphy FM, Kang HK, Dalager NA, et al. (1999). The health status of Gulf War veterans: lessons learned from the Department of Veterans Affairs health registry. Military Medicine <u>164</u>, 327-331.

Kipen HM, Hallman W, Kang HK, et al. (1999). Prevalence of chronic fatigue and chemical sensitivities in Gulf Registry veterans. Archives of Environmental Health, <u>54</u>, 313-318.

Gray GC, Hawksworth AW, Smith TC, Kang HK, et al. (1998). Gulf War veterans' health registries. Who is most likely to seek evaluation? American Journal of Epidemiology, <u>148</u>, 343-349.

## Registry Studies Major Findings

- Based on hospitalization data, registry participants sicker than non-participants (Smith, 2004)
- Self reported symptoms: fatigue, headache, memory problems, sleep disturbance, skin rash, joint pain, dyspnea, cough (multiple US and UK studies)
- Registry participants reported high prevalence of GW related exposures (multiple US studies)
- High symptom reporting among registrants associated with belief in chemical or biological warfare exposure, war stressors, & negative life events after the war (Boyd, 2003)
- Most frequently reported disease classifications: mental disorders, respiratory disorders, skin conditions, and musculoskeletal diseases (Gray 1998, 2004; VA 2002)

## Registry Studies Value and Limitations

#### Value

- Identified those seeking medical evaluation
- Detailed clinical exams
- Helped define unexplained illnesses as symptom-based
- Source for case/control study subjects
- Value in negative findings
  - Did not implicate a specific etiologic exposure
  - Did not support existence of a unique group of symptoms or "Gulf War Syndrome"

## Limitations

- Limited research value
- Self selected participants
- Not representative of all deployed personnel
- Motivation for participation varied
  - Illness
  - Possibility of compensation
  - Media influence
- No control population for comparison

#### **Health Care Utilization**

#### **Publications**

Gray GC, Kang HK (2006). Healthcare utilization and mortality among veterans of the Gulf War. Phil Trans R Soc B, <u>361</u>:553-569.

Gray GC, Smith TC, Kang HK, et al. (2000). Are Gulf War veterans suffering war-related illnesses? Federal and civilian hospitalizations examined, June 1991 to December 1994. American Journal of Epidemiology <u>151</u>, 63-71.

Gray GC, Coates BD, Anderson CM, Kang HK, et al. (1996). The postwar hospitalization experience of U.S,veterans of the Persian Gulf War. New England Journal of Medicine <u>335</u>, 1498-1504.

#### **Health Care Utilization Findings**

- 1. No excess postwar hospitalization (1991-1994) due to major categories of diseases in VA, DoD and California hospital system
- 2. However, a small but significant excesses in hospitalization due to mental disorders, diseases of respiratory system and the digestive system, diseases of skin, and symptoms, signs and ill-defined conditions are observed among Gulf veterans treated at VA hospitals.

## **Purpose of the National Health Survey**

- To estimate and compare prevalence of various symptoms and other health outcomes among Gulf veterans and those of non-Gulf veterans.
- To estimate and compare prevalence of various reproductive outcomes among spouses and birth defects among children of Gulf veterans and those non-Gulf veterans.
- To evaluate the relationship between selected symptoms and health outcomes and certain environmental exposures in the Gulf area.

## **STUDY SUBJECTS**

Population based sample of 15,000 Gulf veterans (DS/DS participants) and an equal number of Gulf-era veterans.

#### Distribution of Gulf War Veterans and Non-Gulf War Veterans in the survey by Gender and Unit Component

		Gender	
Unit Component	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

## **SURVEY DESIGN**

- Questionnaires through the mail
- Supplemental telephone interviews
- Physical examinations on a sample of veterans
- Validation through civilian, military and VA medical records

#### **QUESTIONNARE INSTRUMENTS**

- Limitations of activities
- Use of medical services (hospitalization, clinic visit)
- Chronic medical conditions (31 items)
- Prevalence of symptoms (48 items)
- Exposures in the Gulf theater (24 items)
- Prophylactics, vaccines (9 items)
- Reproductive health and pregnancy outcomes
  - live birth birth defects
  - still birth •infant deaths
  - miscarriage
- Life events (14 items)
- Smoking & drinking histories
- PTSD check list (PCL), 17 items

#### National Health Survey Phase I and II

#### **Publications**

Kang HK, Mahan CM, Lee KY, Magee CA, Murphy FM. Illness among United States veterans of the Gulf War; a population based survey of 30,000 veterans. J Occup Environ Med 2000;42:491-501.

Kang HK, Magee C, Mahan CM, Lee KY, Murphy FM, et al. Pregnancy outcomes among US Gulf War veterans: a population based survey of 30,000 veterans. Ann Epidemiology 2001;11:504-511

Kang HK, Mahan CM, Lee KY, Murphy FM, et al. Evidence for a deployment related Gulf War syndrome by factor analysis. Archives Environmental Health 2002; 57:61-68

Kang HK, Natelson BH, Mahan CM, Lee KY, et al. Post-traumatic stress disorder and chronic fatigue syndrome-like illness among Gulf War veterans: A population based survey of 30,000 veterans. Am J Epidemiol 2003;157:141-148

Kang HK, Dalager NA, Mahan CM, Ishii E. The role of sexual assault on the risk of PTSD among Gulf War veterans, Ann Epidemiol 2005;15:191-95.

Mahan CM, Kang HK, Dalager NA, Heller, JM. Anthrax vaccination and selfreported symptoms, functional status, and medical conditions in the National Health Survey of Gulf War Era Veterans and Their Families. Ann Epidemiol 2004; 14:81-88.

#### National Health Survey Phase I and II Publications

Young HA, Simmens SJ, Kang HK, Mahan CM, Levine PH. Factor analysis of fatiguing syndrome in Gulf War era veterans. J Occup Environ Med 2003; 45: 1268-1273.

Mahan, C.M., Page, W.F., Bullman, T.A., & Kang, H.K. Health effects in Army Gulf War veterans possibly exposed to chemical munitions destruction at Khamisiyah, Iraq, I. Morbidity associated with potential exposure. Mil Med 2005;170:935-944

Page WF, Mahan CM, Kang HK, Bullman TA. Health effects in Army Gulf War veterans possibly exposed to chemical munitions destruction at Khamisiyah, Iraq. II. Morbidity associated with notification of potential exposure. Mil Med 2005;170:945-951.

# National Health Survey Phase 1 and II Findings

I. Physical Health

**Gulf veterans reported higher prevalence of:** 

•Functional impairment

•Health care utilization

•A wide variety of symptoms

•Serious chronic health conditions

•Lower perception of general health

#### II. Psychological Health

- Gulf veterans reported higher prevalence of symptoms endorsing PTSD (PCL-M) and chronic fatigue syndrome (CDC 1994)
- The prevalence of PTSD increased monotonically across 6 levels of deployment-related stress intensity (test of trend, p <0.01)</li>
- Gulf veterans reported higher rate of sexual trauma (harassment/assault) in theater, which in turn was associated with the higher prevalence of PTSD even after adjusting for the combat trauma.

#### **III.** Reproductive Health

Gulf veterans reported higher rates of:

• Miscarriage Male veterans: OR=1.62; 95% CI=1.32-1.99 Female veterans: OR = 1.35; 95% CI =0.97-1.89

• Birth defects among liveborn infants Male veterans: OR = 1.78; 95% CI=1.19-2.66 Female veterans: OR= 2.80; 95% CI=1.26-6.25

#### **IV.** Symptom Cluster

- A cluster of symptoms consistent with neurological impairment were identified by a factor analysis: blurred vision, loss of balance/dizziness, tremors/shaking and speech difficulty
- A clinical evaluation of Gulf veterans with a cluster of neurological symptoms indicated the symptom complex appears to correlate with objective neurological abnormalities including abnormal ENG
- Relatively more symptomatic Gulf veterans were exposed to combat, engaged in military duties in Kuwait and Iraq, and potential nerve gas plume from Khamisiyah incident as determined by the Department of Defense

#### **Clinical Study Publications**

Levine PH, Richardson PK, Zolfaghari L, cleary SD, Geist CE, Potolicchio S, Young HA, Simmens S, Schessel D, Williams K, Mahan CM, Kang HK. A study of Gulf War veterans with a possible deployment-related syndrome. Arch Environ Occp Health 2006;61:271-8.

Toomey R, Kang H, Karlinsky J, Baker D, Vasterling J, Alpern R, Reda D, Henderson W, Murphy F, Eisen S. Mental health of U.S. Gulf War veterans: A psychological evaluation 10 years after the war. British J Psychiatry 2007;190:385-393.

Eisen SA, Karlinsky J, Jackson LW, Blanchard M, Kang HK, Murphy FM, Alpern R, et al. Spouse of Gulf War I veterans: medical evaluation of a U.S. cohort. Mil Med 2006;171:613-618.

Eisen SA, Kang HK, Murphy FM, et al. Gulf War veterans' health: a comprehensive medical evaluation of a population based cohort. Annals Internal Med 2005;142:881-890.

Davis LE, Eisen SA, Murphy FM, Kang HK. Clinical and laboratory assessment of distal peripheral nerves in Gulf War veterans and spouses. Neurology 2004;63:1070-1077.

Karlinsky JB, Blanchard M, Alpern R, Eisen SA, Kang H, Murphy FM, Reda D. Late prevalence of respiratory symptoms and pulmonary function abnormalities in Gulf War 1 veterans. Arch Internal Med 2004;164:2488-2491.

#### **Clinical Study Neurologic Findings**

- No differences in prevalence of distal symmetric polyneuropathy among Gulf veterans and non-Gulf veterans by electrophysiologic assessment of motor and sensory nerves and by history and physical examinations.
- Of the battery of neurologic tests (ENG, VER, BAER and SSEP), only the ENG supported the validity of the neurologic symptoms reported in the 1995 survey

Neurologic and All Cause Mortality, 13 year Follow-up Results

# As of 12/31/2004 among 621,901 Gulf veterans and 746,247 non-Gulf veterans

- 1. All Causes Gulf: 10,869 deaths; non-Gulf: 14,716 deaths
- 2. MVA Gulf:1,776; non-Gulf:1,817
- 3. Suicide Gulf:1,514; non-Gulf:1,722
- 4. MS Gulf:6; non-Gulf:13
- 5. Parkinson's disease Gulf 3:; non-Gulf:8
- 6. ALS Gulf:23; non-Gulf:38
- 7. Brain cancer Gulf:144; non-Gulf:228

#### Summary

The general aims of epidemiologic research are to 1) describe the health status of populations, 2)explain the etiology of diseases, 3) predict and quantify disease occurrence, and 4) control the distributions of diseases in the population.

- Define and characterize population at risk
- Assess potential exposure of concern
- Develop potential health outcomes of interest
- Design a study based on many factors including size of available study group, health outcomes of interest, nature and extent of measurement error

Cohort study vs. Case-control Study Cross-sectional and other types of studies Experimental vs. Observational