

Caring for ODS/S Veterans at the WRIISC: Focus on Symptoms: Chronic Pain, Chronic fatigue, Irritable Bowel Syndrome, etc.

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PDHS-WRIISC, California Site

June 25, 2018



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PDHS-WRIISC HISTORY

- WRIISC is a National VA Post-Deployment Health Program, established by **Public Law 105-368, 105th Congress, 1998**)
- There are three WRIISC sites: Washington, DC (VISN 5), East Orange, NJ (VISN 2); Palo Alto, CA (VISN 21, since July, 2007)
- The WRIISC, now part of **Post-Deployment Health Services (PDHS)**, develops and provides post-deployment health expertise to Veterans and their health care providers through clinical programs, education and risk communication, and research
- Recently the PDHS-WRIISC was designated as a “**VA-delivered Foundational Service**”



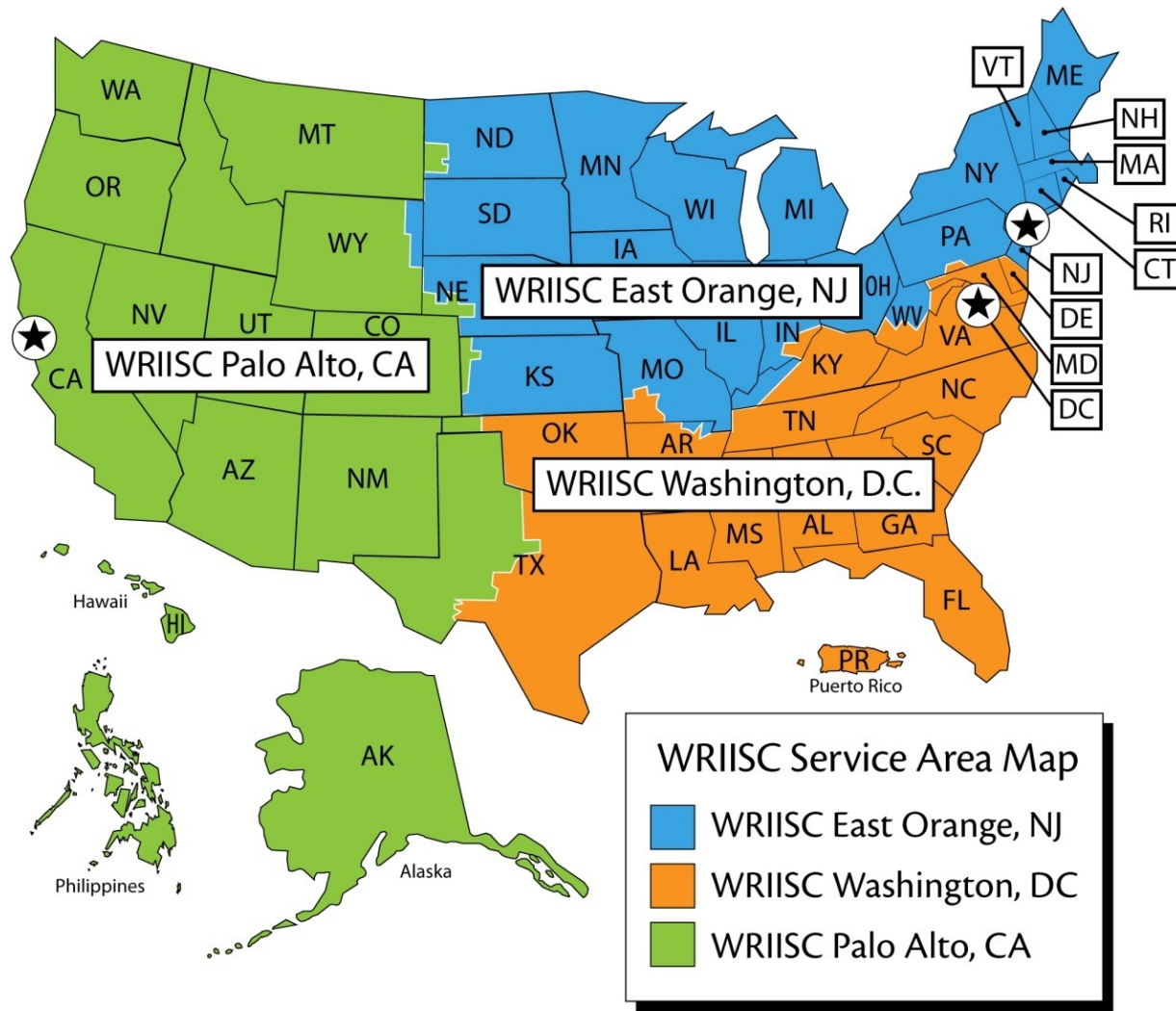
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LOCATIONS & SERVICE AREAS



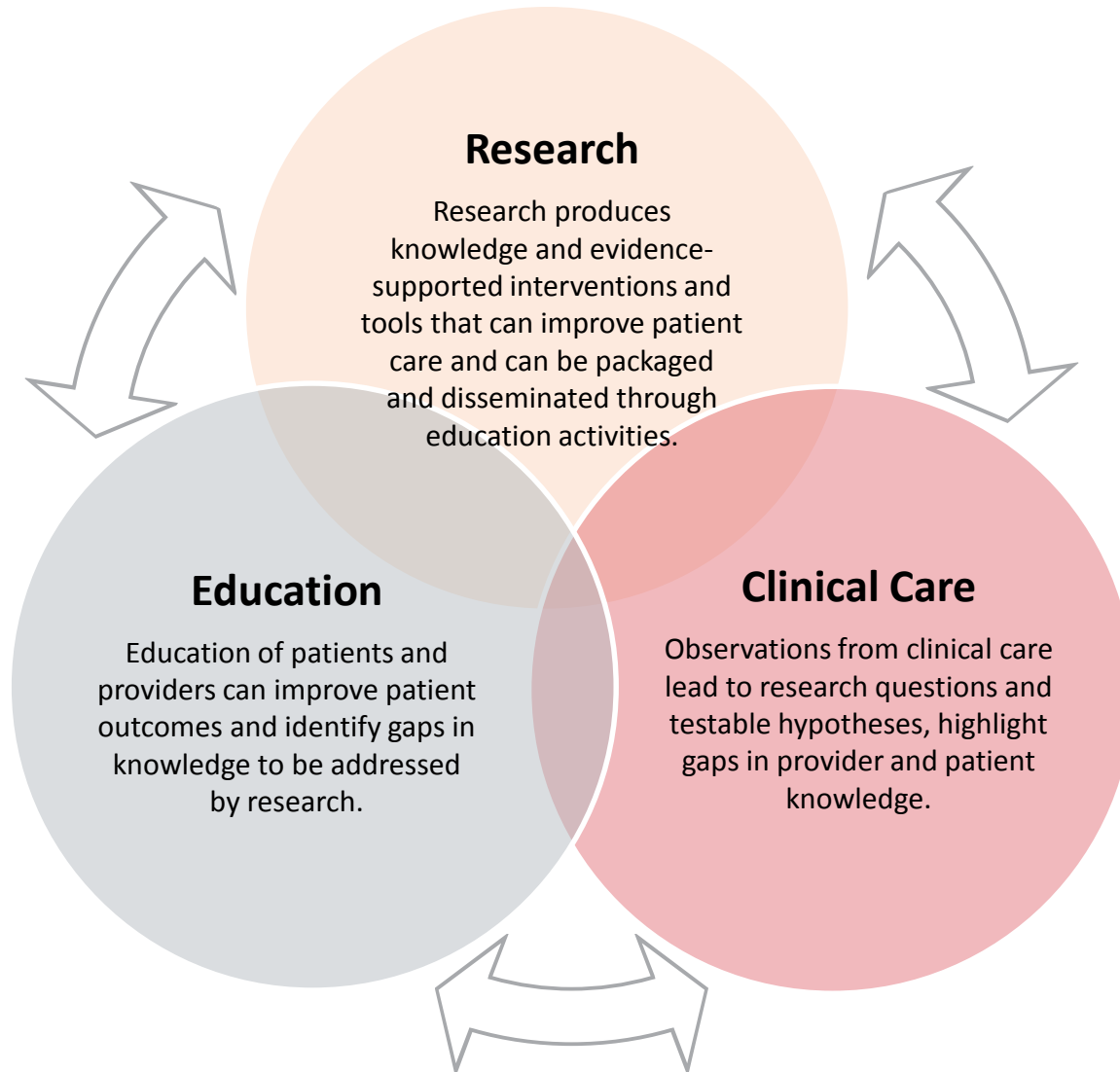
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PDHS-WRIISC MODEL



Operation Desert Storm/Desert Shield (ODS/S) Timeline

1990

- August 2: About 100,000 Iraqi troops invade Kuwait, initiating the Gulf War.
- August 7: U.S. launches Operation Desert Shield. First U.S. troops arrive in Saudi Arabia. US Naval forces were strengthened and 2100 Marines sent to area on aircraft carrier
- November 29: U.N. Security Council Resolution 678: Iraq to withdraw from Kuwait by Jan. 15, 1991

1991

- January 12 : U.S. Congress passes a joint resolution authorizing the use of military against Iraq
- January 16: Operation Desert Storm announced; January 17: air war commences (2:38 am local time)
- January 18: Iraq launches SCUD missiles on Israel. U.S. deploys Patriot missiles
- January 22:: Iraqi troops begin blowing up oil wells in Kuwait, oil well fire smoke becomes a problem
- February 24: Ground war begins, U.S./Coalition forces invaded Iraq and Kuwait at 4 am Baghdad time
- February 25: Iraqi SCUD missile strikes U.S. barracks, Dhahran, Saudi Arabia, killing 28 U.S. troop
- February 26: Saddam Hussein orders the Iraqi withdrawal from Kuwait. About 10,000 retreating Iraqi troops were killed when Coalition aircraft bombs their vehicles (Highway of Death)
- February 27: U.S. Marines and Saudi Arabian troops entered Kuwait City. U.S. Army then engaged the Iraqi Republican Guard in several tank battles in Iraq, also known as the Battle of Medina Ridge
- February 28: Saddam Hussein surrenders, U.S. President George H. W. Bush announces ceasefire
- March 10: Explosive charges at Kamisiyah weapons depot detonated, producing large cloud, ? sarin
- March 17 to June 13: U.S. troops participating in ground war returned home
- April 1991-Present: Operations Northern/Southern Watch, Operations Vigilant Warrior, Vigilant Sentinel, Desert Strike, Operation Iraqi Freedom, Operation New Dawn, etc.



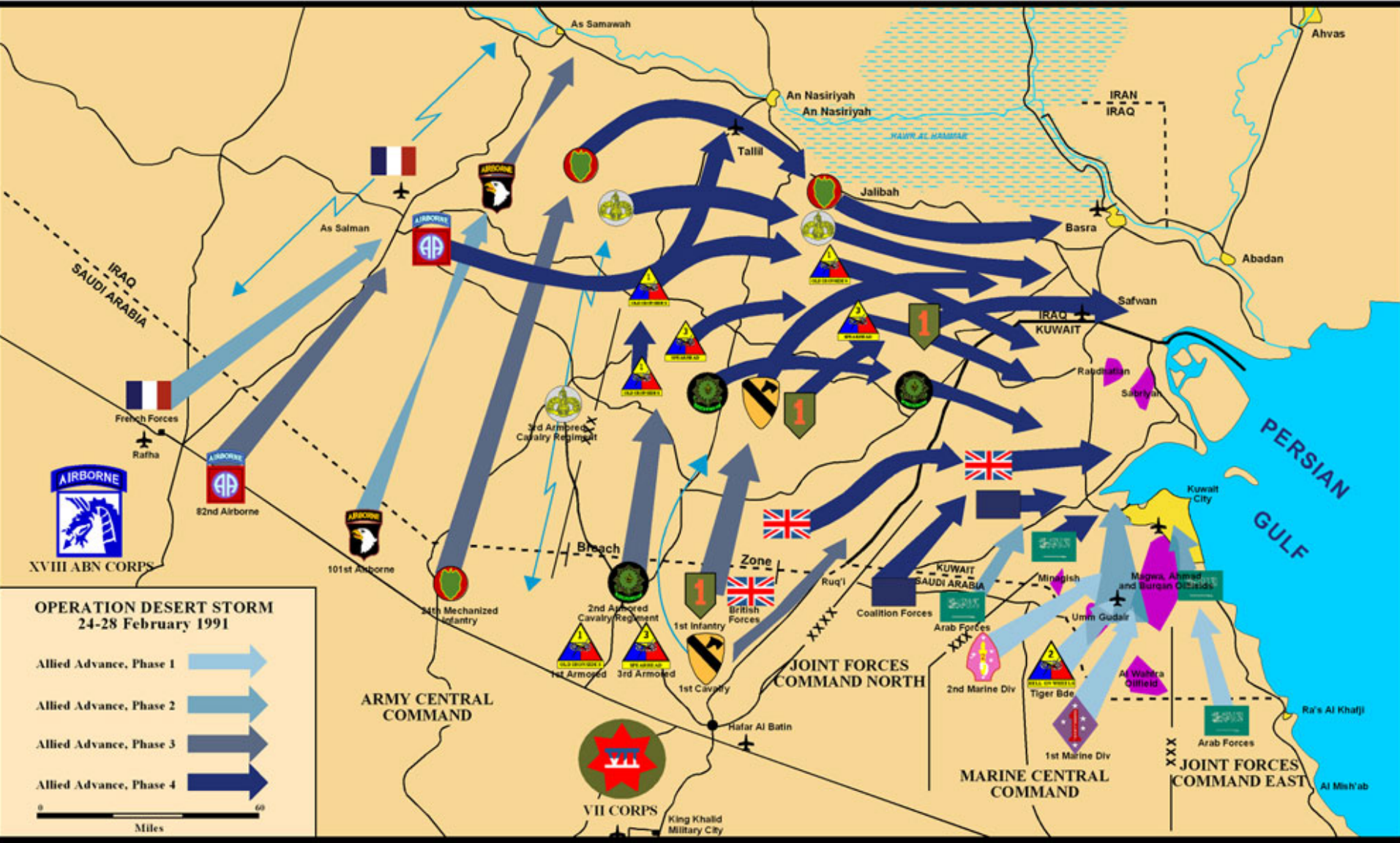
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Summary of the Offensive Ground Campaign, February, 1991



Exposures

- Gulf War Troops were exposed to multiple exposures despite the short time of the ground offensive
- The etiology of what we call either Gulf War illness (GWI) or Chronic Multi-symptom Illness (CMI) is unclear but Service Members did have multiple possible exposures.



Living Conditions During War Prep

- U.S. service members in the 1991 Gulf War region were stationed for months in isolation in a bleak desert environment
- Few amenities and arduous and austere conditions - not conducive to good health
- Weather was initially extremely hot and humid; changed to cold and damp by the time the war began
- Some housed in crowded warehouses



Living Conditions (cont'd)

- Diet of prepackaged meals (local produce and goods were quickly put off-limits for health reasons after many GI problems)
- Military sanitation - latrines and communal washing facilities
- Sand flies and insecticides were pervasive
- Exposed to a wide range of hazardous materials
- Administration of pyridostigmine bromide (PB) tabs variably enforced



Casualties

- 293 U.S. service members killed
 - 148 combat-related (35 due to friendly fire)
 - 145 non-combat deaths
- Estimated 20,000 – 35,000 Iraqi soldiers killed; 75,000 wounded
- Civilian fatalities
 - 1000 Kuwait civilians killed; 600 missing
 - ~3500 Iraqi civilians killed by bombings
 - Estimates of 100,000 more Iraqis from the war's other effects (economic, sanitation, etc.)



Overview of Exposure Concerns

Weapons

Bullets, explosions (IED), shrapnel, chemical warfare agents, biological warfare agents, depleted uranium

Local Environment

Smoke (Oil well fires, burning trash and human waste), poor ambient air quality (dust, smog), local food (bacteria, viruses), bites (insects, spiders, etc.), harsh weather (heat, cold), contaminated water (biological or toxic chemical)

Preventive, therapeutic treatments

Pesticides, PB tablets, vaccinations

Occupational agents

Diesel, kerosene, gasoline, jet fuels, hydraulic fluids, paints, solvents



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Possible ODS/S Chemical Weapon Exposures

Many chemical alarms sounded, troops told to put on MOPP suits as protection – feared life threatening attacks

- Anecdotal reports of isolated chemical weapon exposures to nerve agents however no cases of acute poisoning were documented
- U. S. destroyed ammunition depot in Khamisiyah containing Sarin and Cyclosarin nerve agents
 - DoD notified 100,000 Veterans that that may have been exposed to low levels of chemical agents
- No specific tests available to detect sarin or cyclosarin exposure



Initial Cloud from Khamisiyah Explosion



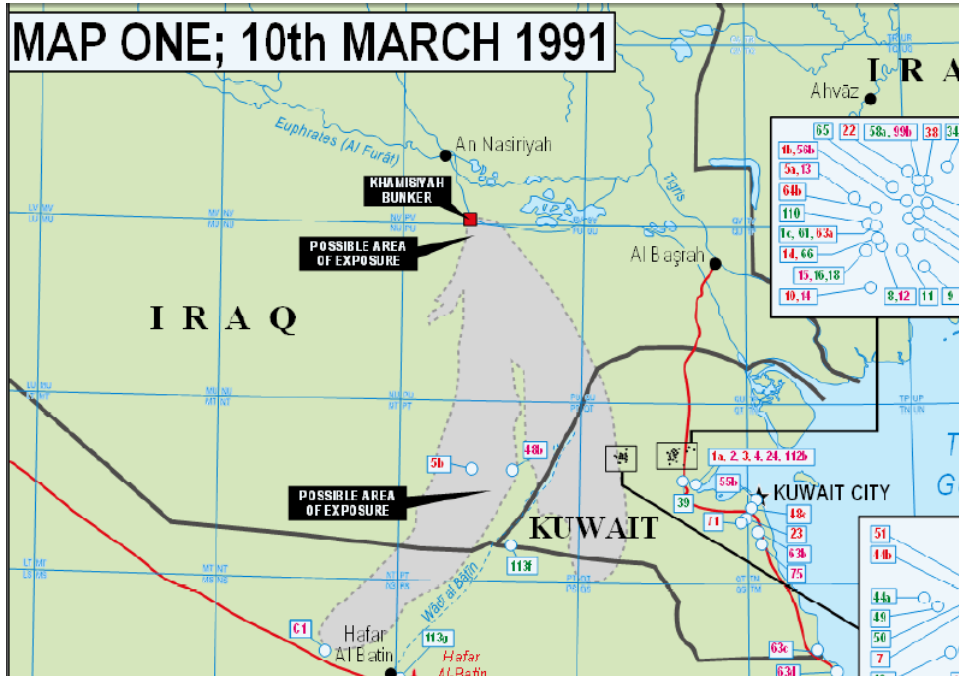
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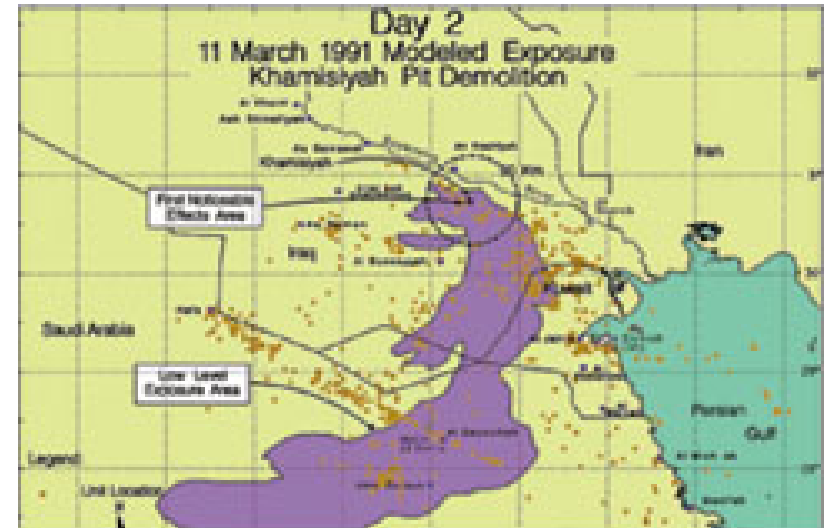


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Model of Sarin Exposure from Khamisiyah



DGIA Ministry of Defense, UK, 2004



Models of chemical exposure were developed using data supplied by NRL from the Coupled Ocean/Atmosphere Mesoscale Prediction System (COAMPS). COAMPS, which generates high resolution numerical models of the atmosphere, is an analysis-nowcast and forecast tool applicable for any given region of the earth.



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Other Exposures to Anti-cholinesterase Agents

- Insecticide spray cans, unofficial flea collar use
- Other pesticides applied by trained personnel
- Pyridostigmine Bromide (PB) tablets (peripheral action)
 - Used as pretreatment for exposure to nerve agents
 - ~250000 U.S. troop took PB at least once
 - Some troops experienced acute GI and urinary problems
- Clothing treated with permethrin (not anti-AChE)

Respiratory Exposures in ODS/S

- Burn pits
- 700 Kuwaiti oil wells set on fire by Iraqi army
(beginning 1/22/1991, all out about 11/1991)
 - Many veterans describe black nasal discharge and mucous, skin rashes, shortness of breath
 - Worsening of existing respiratory conditions (asthma, bronchitis) or provoke respiratory tract irritation
 - No specific tests for this type of exposure
- Exposure to particulate matter - sand & dust storms, vehicle exhaust, emissions from local industries, construction sites and farming
- Exacerbated by tobacco/nicotine use



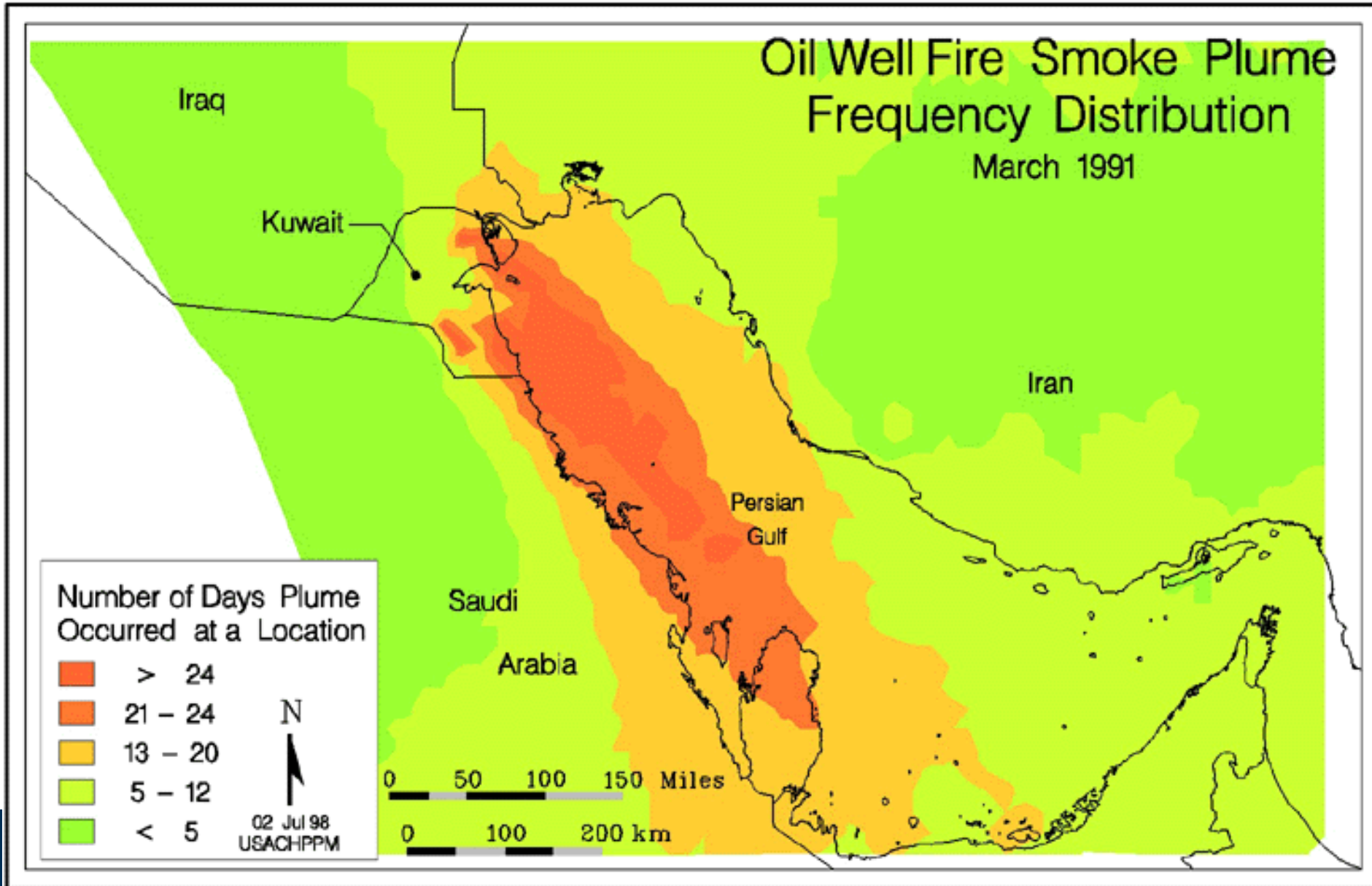
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http://www.gulflink.osd.mil/owf_ii/fig12.htm (this site shows numerous other times)



Possible Exposures to Infectious Agents in ODS/S, OEF, OIF, OND

- Episodes of severe diarrheal illnesses
 - ETEC (enterotoxigenic E. coli) and Shigella
- Continuing episodes of diarrhea
 - Intestinal parasites common in Iraq & Afghanistan
- Amoebic, giardia exposures
- Leishmaniasis
- Q-fever, sand-fly fever, malaria, TB
- Mycolplasma fermentans (Popular Science)



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Results of Iowa Study

3,695 Veterans of ODS/S

Symptoms, % Prevalence

	GW Veterans	Non-GW Veterans
Fibromyalgia	19.2	9.6
Cognitive Dysfunction	18.7	7.6
Alcohol Abuse	17.4	12.6
Depression	17.0	10.9
Asthma	7.2	4.1
PTSD	1.9	0.8
Sexual Discomfort	1.5	1.1
Chronic fatigue	1.5	0.3

Iowa Persian gulf Study Group, 1997



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Most Frequent Symptoms, Affected Systems of Veterans from ODS/S

Frequency of Symptoms of 53,835 Participants in VA Registry (1992–1997)

Symptoms

	Percentage
– Fatigue	20.5
– Skin rash	18.4
– Headache	18.0
– Muscle and joint pain	16.8
– Loss of memory	14.0
– Shortness of breath	7.9
– Sleep disturbances	5.9

Systems

– Musculoskeletal and connective tissue	25.4
– Mental disorders	14.7
– Respiratory system	14.0
– Skin and subcutaneous tissue	13.4
– Digestive system	11.1
– Chest pain	3.5

Symptoms shared with of fibromyalgia

Murphy et al., 1999



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Defining Gulf War Illness

CDC Definition

1. Onset 1990 - 1998
2. ≥ 6 months duration
3. ≥ 1 chronic symptom from ≥ 2 categories
 - a) Fatigue
 - b) Musculoskeletal
 - c) Mood & cognition

Fukuda et al., 1998

Kansas Definition

1. Onset 1990 - 1998
2. Moderate or Multiple Symptoms in 3 of 6 complexes
 - a) Fatigue/Sleep
 - b) Pain
 - c) Neuro/Cognitive/Mood
 - d) Gastrointestinal
 - e) Respiratory
 - f) Skin
3. Absence of Exclusion Criteria

Steele, 2000



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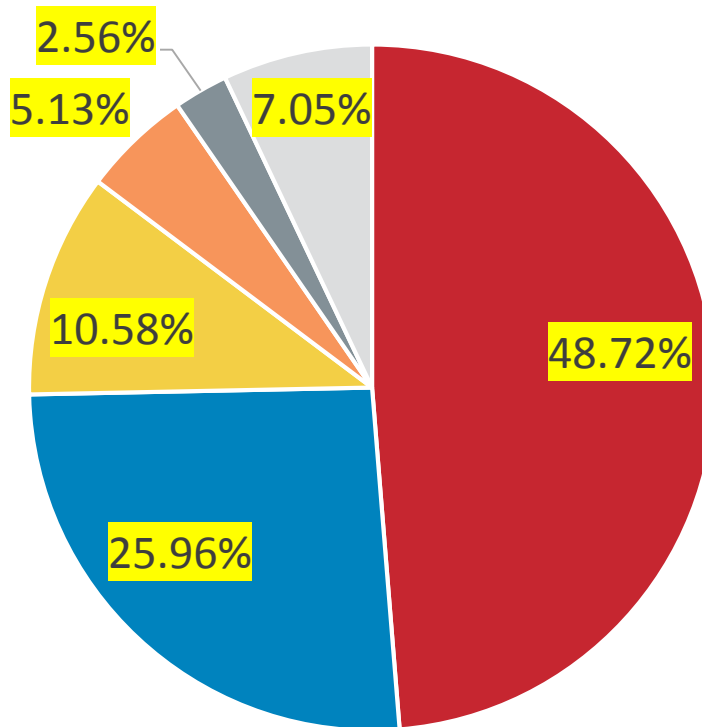


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The Veterans Served by WRIISC CA Site

Most recent deployment for Inter-Facility Consults received, 7/2016 – 6/2018

N = 312; ODS/S = 106 (34%)



■ OEF/OIF/OND

■ ODS/S

■ Vietnam

■ Post-ODS

■ Somalia

■ other



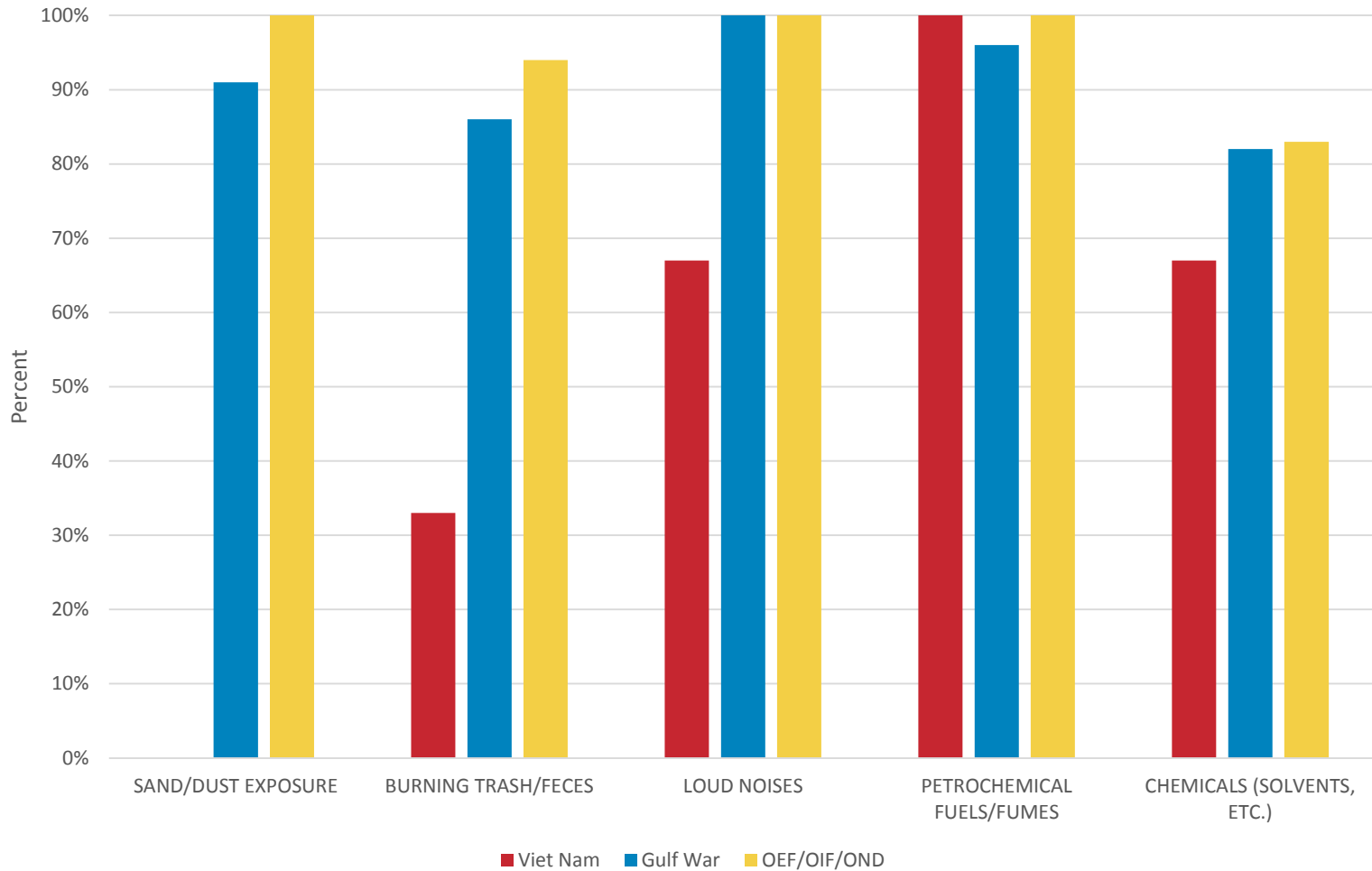
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Veteran's Concerns about Environmental Exposures



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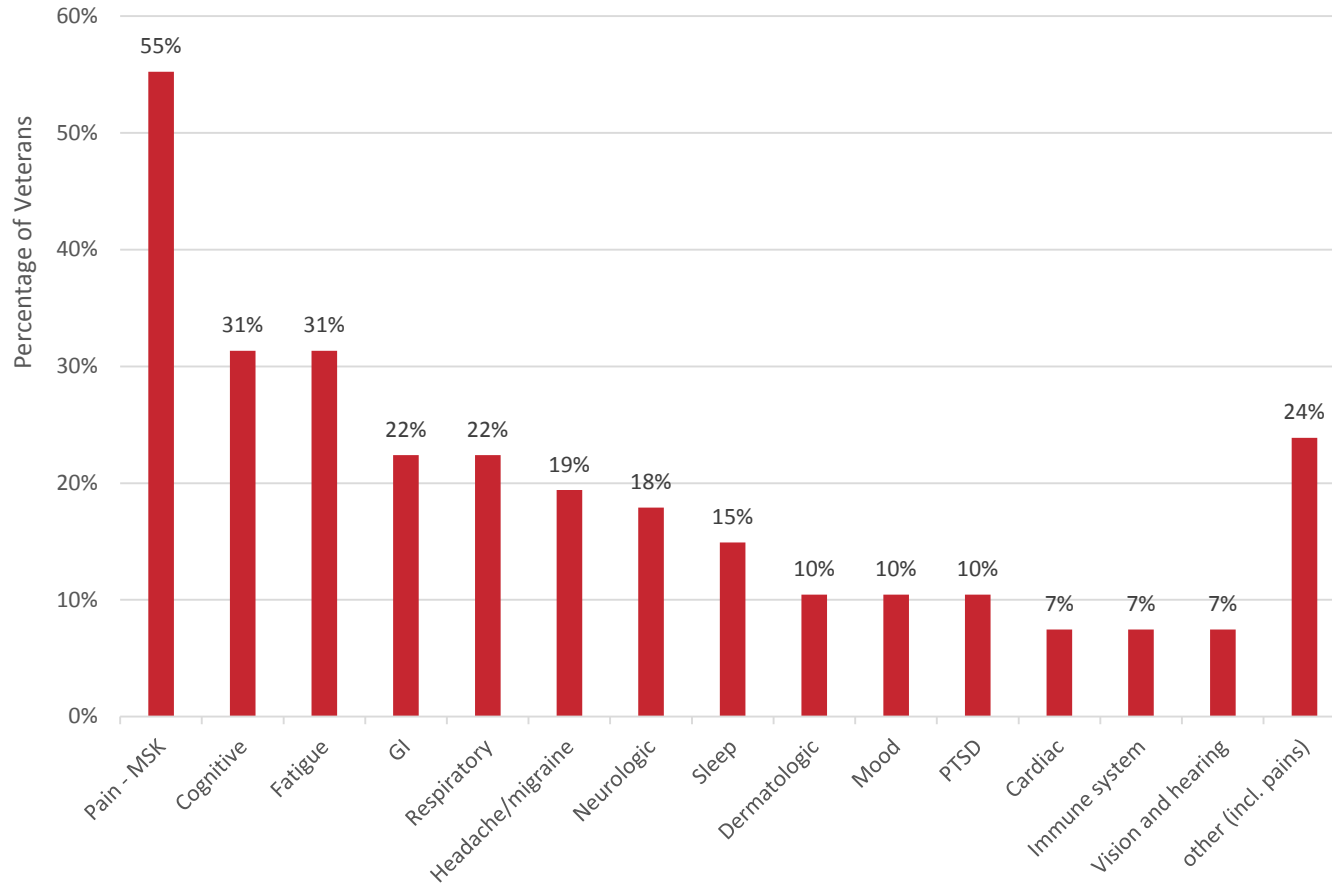
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Veterans' Top 3 Reported Symptoms

ODS/S Veterans seen at CA-WRIISC 7/2016 – 6/2018;
N=67 (20 were later in Somalia, OEF/OIF/OND)



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MEASUREMENT OF PAIN

Digital Pain Matrix

(to be completed by a trained clinician)

ID: DATE: TIME (24hr):

INSTRUCTIONS: Please rate your pain by checking the one number that best describes your pain at its worst in the past month, for each region in which you have had pain:

Regions affected by pain:	None		mild			moderate			severe		extreme	
	0	1	2	3	4	5	6	7	8	9	10	
1. LEFT - Shoulder	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
2. LEFT - Upper arm/elbow	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3. LEFT - Lower arm/wrist/hand	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
4. RIGHT - Shoulder	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
5. RIGHT - Upper arm/elbow	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
6. RIGHT - Lower arm/wrist/hand	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
7. LEFT - Hip	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
8. LEFT - Upper leg/knee	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
9. LEFT - Lower leg/ankle/foot	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
10. RIGHT - Hip	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
11. RIGHT - Upper leg/knee	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
12. RIGHT - Lower leg/ankle/foot	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
13. Neck/cervical spine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
14. Upper back/thoracic spine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
15. Lower back/lumbo-sacral spine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
16. Head /headache	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
17. LEFT - Jaw	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
18. RIGHT - Jaw	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
19. Chest	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
20. Stomach ache / Abdominal pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

Overall pain:	None		mild			moderate			severe		extreme	
	0	1	2	3	4	5	6	7	8	9	10	
General Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Pain at Rest	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Pain with Movement/Activities	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

Digital Pain Matrix designed by: J. Wesson Ashford, Mark Perlow, Quai Wentt



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CASE PRESENTATION - 1

- 48 Year American Indian Male Veteran
- PCP referred Vet for "Pt with ongoing chronic pain issues (muscles and joints) as well as chronic fatigue without clear answers. He has been seen by rheum. He is requesting to be seen at your center in person."
- Marine Corps: 9/7/1988 to 9/8/1992
 - Operation Desert Storm/Desert Shield: 8/10/1990 to 4/1991
 - 7th Engineers, in general vicinity of 2nd Marine Division
- On return from Persian Gulf, 1991, was doing a lot of drinking EtOH, he believes because of the pain he was experiencing. He believes that these pains have gotten slowly and progressively worse since 1991.
- VETERAN's TOP Four HEALTH CONCERNS:
 - 1. Pain
 - 2. Fatigue
 - 3. Sleep
 - 4. GI
- Weight: 170 lbs; BMI: 25.1



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PAIN LEVELS - WORST IN PRIOR MONTH

Specific location and Pain Levels ≥ 4 :

1. LEFT - Shoulder: - moderate - 5
2. LEFT - Upper arm/elbow: - moderate - 5
4. RIGHT - Shoulder: - severe - 7
5. RIGHT - Lower arm/wrist/hand: - moderate - 4.5
7. LEFT - Hip: - moderate - 4
8. LEFT - Upper leg/knee: - extreme - 9
10. RIGHT - Hip: - moderate - 4
11. RIGHT - Upper leg/knee: - extreme - 9
12. RIGHT - Lower leg/ankle/foot: - extreme - 9
13. Neck/cervical spine: - moderate - 5
14. Upper back/thoracic spine: - extreme - 9
15. Lower back/lumbo-sacral spine: - extreme - 9
16. Head /headache: - moderate - 5
18. RIGHT - Jaw: - severe - 7
19. Chest: - moderate - 4
20. Stomach ache / Abdominal pain: - severe - 7



Diagnoses

Veteran with multiple symptoms including chronic pain, fatigue, IBS, sleep difficulties, as well as memory complaints and depression, meets working IOM criteria for chronic multi-symptom illness (CMI). In Veterans of ODS/S, CMI is referred to commonly as Gulf War Illness (GWI).

Psychiatric

4. Posttraumatic stress disorder
6. Mild major depression
11. Major depressive disorder

Somatic

1. Irritable bowel syndrome with diarrhea
2. Hyperlipidemia
3. Gastroesophageal reflux disease
5. Low back pain
7. Disorders of bursae and tendons in shoulder region
9. DISC DEGENERATION NOS
10. Myalgia
12. Wheezing
13. Abdominal Pain of the Right Lower Quadrant
14. Fibromyalgia
15. Health Maintenance (ICD-9-CM V65.9)
16. Dysuria
17. Hypertrophy (Benign) of Prostate
18. Insomnia, unspecified
19. Shoulder pain
20. Insomnia due to anxiety and fear



CASE PRESENTATION - 2

- 47 Year Male Veteran
- PCP referred Vet for "Veteran was deployed to Saudi Arabia 1990-1991. Diagnosed with sarcoidosis in 2006. Currently has multisystem complaints of episodes of dizziness, headaches, GI upset, loose stools, respiratory disease, sleep disturbance. We would like to know if current health issues are related to his Gulf War deployment."
- Marines Corps: 11/1989-11/1993.
- Combat location:
 - Saudi Arabia, Kuwait: 8/2/1990 to 4/1/1991, 7th Marines, part of First Marine Division
 - -Had several shots, took PB tablets, saw a lot of insects/flyies. Had probs with diarrhea (hot food with flies all over the food). Wore MOPP gear most of the time, had to wear masks x 3. Did not see SCUD missiles. His vehicle was the first through the mine-field. Hit mine which exploded and pushed his vehicle back. Was at the big tank fight, saw some horrendous things. Drove through oil-well fire smoke. Got into Kuwait City. Was there for a few days (poor memory for details).
 - Somalia: 12/5/1992 - 5/5/1993. - no injuries, but was exposed to considerable trauma.
 - Developed problems with dizziness while in Somalia. Initially occurred 1-2 x per month. Now occurs every day. Had episode of "room spinning", now just an occasional episode of unsteadiness. On boat returning; noticed both knees swelling. The associated pain caused difficulty walking up and down stairs on ship.
 - In Marine Corps, had shortness of breath issues, got harder to run, got progressively worse. First went to civilian doctors. When it got serious, he went to VA in 2006, dx sarcoidosis. Sarcoid is under control with steroids. Biopsy proven x 2
- VETERAN's TOP Four HEALTH CONCERNS:
 1. GI (acid reflux and other GI issues, including hiatal hernia)
 2. Respiratory (sarcoid and asthma)
 3. Pain - Musculoskeletal (joint aches)
 4. Neurologic ("dizzy spells")
- Weight: 245 lbs; BMI: 32.3



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PAIN LEVELS - WORST IN PRIOR MONTH

Specific location and Pain Levels \geq 4:

1. LEFT - Shoulder: - severe - 8
2. LEFT - Upper arm/elbow: - moderate - 6
3. LEFT - Lower arm/wrist/hand: - severe - 8
4. RIGHT - Shoulder: - extreme - 9
5. RIGHT - Lower arm/wrist/hand: - moderate - 5
6. RIGHT - Lower arm/wrist/hand: - extreme - 9
7. LEFT - Hip: - moderate - 5
8. LEFT - Upper leg/knee: - moderate - 6
9. LEFT - Lower leg/ankle/foot: - severe - 7
10. RIGHT - Hip: - moderate - 5
11. RIGHT - Upper leg/knee: - severe - 7
12. RIGHT - Lower leg/ankle/foot: - severe - 8
13. Neck/cervical spine: - moderate - 4
14. Upper back/thoracic spine: - moderate - 4
15. Lower back/lumbo-sacral spine: - severe - 7
16. Head /headache: - moderate - 4
20. Stomach ache / Abdominal pain: - severe - 7



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Diagnoses

GI - diarrhea is longest standing problem. Cause could be infectious. However, given later development of chronic pain and chronic fatigue, there may be a component of chronic multi-symptom illness (CMI), which in ODS/S Veterans is commonly referred to as Gulf War Illnesses (GWI).

Veteran also has severe PTSD related to both ODS/S and Somalia.

Chronic pain began after Somalia, so there is concern for an infectious basis which may be impossible to determine. So, pain could be related to GWI also as later development of chronic pains is frequently seen in ODS/S Veterans.

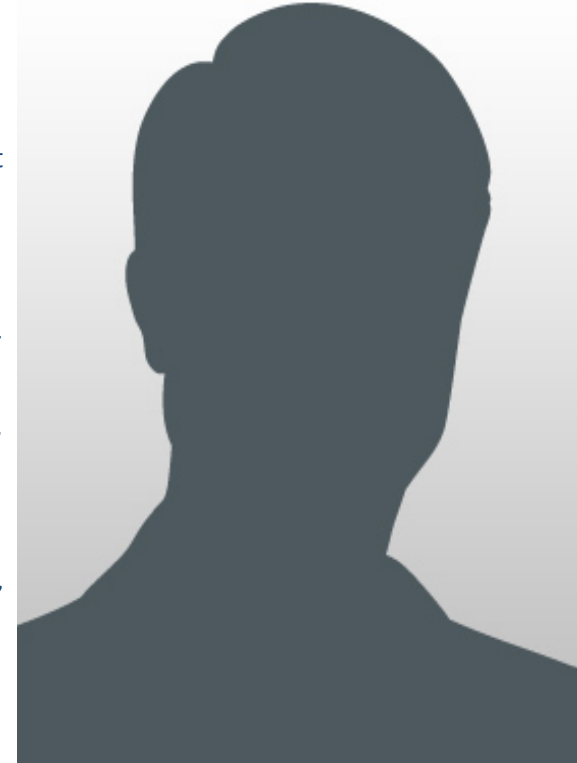
Development of sarcoid with no family history has no clear explanation, but could also be related to exposures in the Middle East and Somalia.

Asthma development has become relatively common. Pulmonary and Rheumatology both are unclear about the relationship between sarcoid and asthma. In any case, having 2 such conditions makes each harder to treat.



CASE PRESENTATION - 3

- 53 year old FEMALE Veteran (accompanied by identical twin)
- Employment Status: Employed Full-Time
-
- SERVICE CONNECTED 70%: NEUROSIS, GEN ANX DIS 30%, ECZEMA 10%, MULTIPLE SCLEROSIS 30%, CHRONIC FATIGUE SYNDROME 30%
- PCP referred Vet for "Polyarthralgia Chronic fatigue, Memory loss and concentration issues - can barely go through 8 hrs. at work, has to write things down."
- Army: 9/20/1988 to 1/27/1993
- Operation Desert Storm/Desert Shield: 12/18/1990 to 5/18/1991 - flew to King Fahd Airbase. Then went to Cement City for 2 weeks, then stayed at Base Camp at King Fahd Airbase, working as nurse (8th Evacuation Hospital) until May. Oil well smoke got so bad in mornings, pitch black, could not see hand in front of face. After cease fire, did make unofficial visit to Kuwait. Saw the Highway of Death, saw many burning oil wells, trashed tanks. Also experienced MST from an NBCOIC.
- Military Exposures: Anthrax Vaccine, Biological warfare agents, Chemical alarms/MOPP4 (put MOPP gear on frequently - up to 3 times per night - when air war started through cease fire - did have one experience where eyes were burning, took long-time to get all-clear), Chemical weapons (nerve agents, sarin, blistering agents, etc.), Fog oils, Insect bites (in location with many insects), Insecticides, pesticides, Loud noises, exposed to peeling paint (had to wash trucks at end of war - no protection), Prophylactic meds (pyridostigmine PB - given order to start taking when Operation Desert Storm started, until cease fire - twice per day).
- While in Saudi Arabia, had GI probs from PB tabs. ENT scoping for bad allergies, nasal passages inflamed, given meds. On return from deployment - had some probs readjusting (avoided socialization, difficulty making decision). In February, 1992, started experiencing extreme fatigue, along with night-sweats, memory and concentration difficulties, had hair coming out in clumps, metallic taste in her mouth, tinnitus, diffuse joint pain, weight-loss, photo-phobia, and headaches every day. These symptoms have waxed and waned over the last 25 years, now has various symptoms at various times, but has daily headaches.
- VETERAN's TOP THREE HEALTH CONCERNS:
 1. Mood (Depression/Anxiety)
 2. Pain - Musculoskeletal(Polyarthralgia)
 3. Fatigue



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PAIN LEVELS - WORST IN PRIOR MONTH

Specific location and Pain Levels \geq 4:

1. LEFT - Shoulder: - moderate - 6
2. LEFT - Upper arm/elbow: - moderate - 4
3. LEFT - Lower arm/wrist/hand: - moderate - 4
4. RIGHT - Shoulder: - extreme - 9
5. RIGHT - Lower arm/wrist/hand: - extreme - 9
6. RIGHT - Lower arm/wrist/hand: - extreme - 9
7. LEFT - Hip: - moderate - 6
8. LEFT - Upper leg/knee: - moderate - 5
9. LEFT - Lower leg/ankle/foot: - moderate - 5
10. RIGHT - Hip: - moderate - 5
11. RIGHT - Upper leg/knee: - moderate - 5
12. RIGHT - Lower leg/ankle/foot: - moderate - 4
13. Neck/cervical spine: - severe - 8
14. Upper back/thoracic spine: - severe - 8
15. Lower back/lumbo-sacral spine: - severe - 8
16. Head /headache: - moderate - 6
17. LEFT - Jaw: - moderate - 5
18. RIGHT - Jaw: - moderate - 5
19. Chest: - moderate - 4
20. Stomach ache / Abdominal pain: - moderate - 4



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Diagnoses

Veteran of Operation Desert Shield/Storm with major complaints of chronic pain (polyarthralgia), chronic fatigue, memory loss and concentration issues, skin problems. Has also had problems with depression and sleep and c/o gait instability. Pt has dx of GERD, but has probable Irritable Bowel Syndrome. Having this constellation of symptoms meets Institute of Medicine working criteria (2013) for Chronic Multi-symptom Illness (CMI). In Veterans of Operations Desert Shield/Storm, this is commonly referred to as Gulf War Illness (GWI).

Depression - moderate

PTSD - moderate



Figure 1: Registered FLAIR images of the identical twins facilitate the comparison of white matter hyperintensities (arrowed) on same slice.

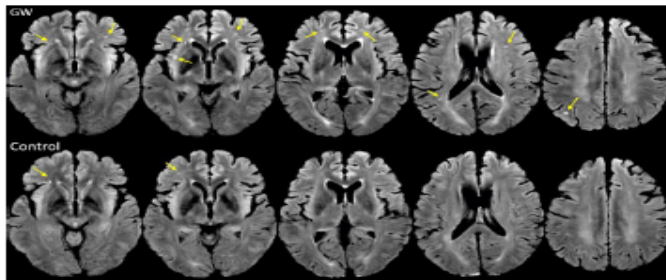


Figure 2: Regions of greater differences from averaged twin imaging for each MRI modality: row-1: greater atrophy (>3% from mean) of the GW-twin (hot) and the Control-twin (cold); row-2: greater MD increase (>5% from mean) of the GW-twin and the Control-twin (cold); row-3: greater FA reduction (>10% from mean) of the GW-twin (hot) and the Control-twin (cold); row-4: greater FD reduction (>15% from mean) of the GW-twin (hot) vs. the Control-twin (cold).

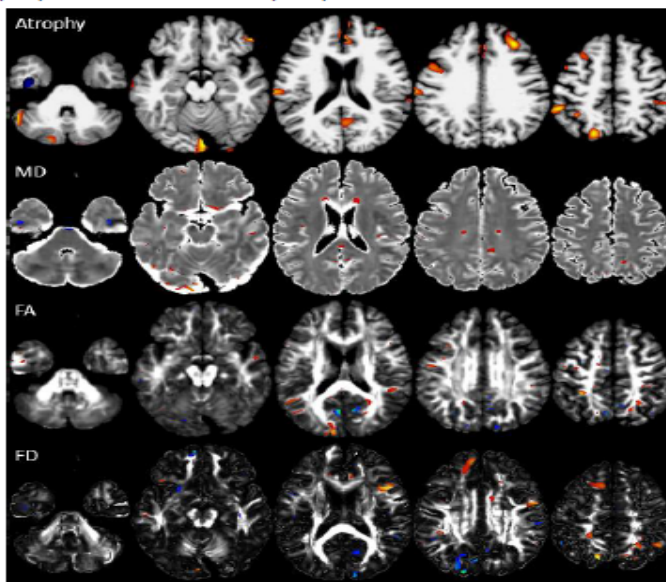
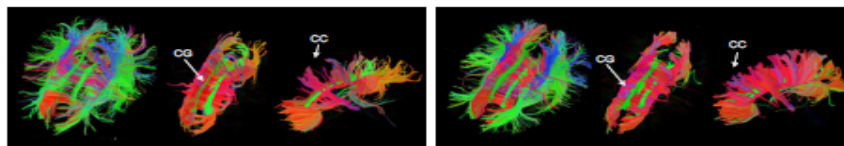


Figure 3: Diffusion tensor tractography of overall brain fibers, cingulum bundle (CG) and corpus callosum (CC) in a GW-twin (left) and Control-twin (right) pair. Colors indicate fiber orientations: red=left-right; green=anterior-posterior; blue=inferior-superior.



Results:

- Compared to Control-twin, GW-twin showed a few more white matter hyperintensity foci on T2WI and FLAIR that may be attributable to small vessel chronic ischemic changes (Figure 1).
- GW-twin globally had greater gray and white matter atrophy and CSF expansion than Control-twin (Table 1). Specifically, the distribution of the greatest atrophy involves anterior cingulate, frontal, parietal and some occipital gray matter areas (Figure 2).
- GW-twin had greater white matter microstructural alterations, manifested as reduced FA and increased MD on DTI than the Control-twin (Figure 2).
- Diffusion tensor fiber tracking showed reduced fiber streamlines of the anterior cingulate tract, and the frontal and parietal corpus callosum fibers in GW-twin when compared to the same fibers of the Control-twin (Figure 3).
- Control-twin showed greater atrophy and microstructural alterations than GW-twin only in focal regions in the occipital lobe and temporal pole (Figure 2).

Conclusions:

- In this case study we found that a combat-exposed twin with gulf-war related chronic illness had greater structural atrophy and microstructural alterations that consistently distributed in anterior cingulate, frontal and parietal brain regions compared to the control-twin without combat exposure.
- This pattern of intra-pair alterations may be environmentally driven but also could be associated with pathological characteristics of gulf war-related illness.
- Further MRI studies in larger twin samples are needed to differentiate the genetic and environmental factors associated with pathology.



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Gulf War Illness Findings

No Identified Diagnostic Entity

- **Somatic Medical** - normal x-rays of joints
- **Neurological** -
 - Peripheral electrophysiological abnormalities
 - Normal MRI, PET scans
 - Abnormal SPECT, MR spectroscopy
- **Psychiatric** –
 - depression
 - neuropsychological dysfunction – borderline
- **Possible relation to other conditions**
 - chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, TBI (traumatic brain injury – especially from blasts)



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Leading Causes Considered

- Chemical Weapons and other chemical exposures
 - Sarin and Cyclosarin, Pyridostigmine Bromide, Organophosphate Pesticides, other chemical pesticides, CARC - Chemical Agent Resistant Coating, fuel, decontamination solution, oil fires
- Infectious Diseases – disruption of microbiome
 - Leishmaniasis, travelers diarrhea, sandfly fever, malaria, and viscerotropic leishmaniasis found in 12 U.S. veterans
- Multiple vaccinations – immunological disorder
 - Anthrax vaccine containing squalene as an adjuvant
- Unknown poison, e.g., Aspartame/Methanol Poisoning
 - At 85 °F, aspartame breaks down into methanol which then breaks down into formaldehyde
- Biological Weapons
 - mycoplasma fermentans



Problem:

How to link all of the symptoms

- Currently , there is no identified biomarker or laboratory test

Research studies have found instances of differences related to GWI, but none can explain the variety of symptoms:

- mitochondrial function
- immune measures
- structures in the brain seen on MRI
- lipid metabolism
- protein expression
- microRNA signaling pathways
- markers of neuronal injury in blood and CSF



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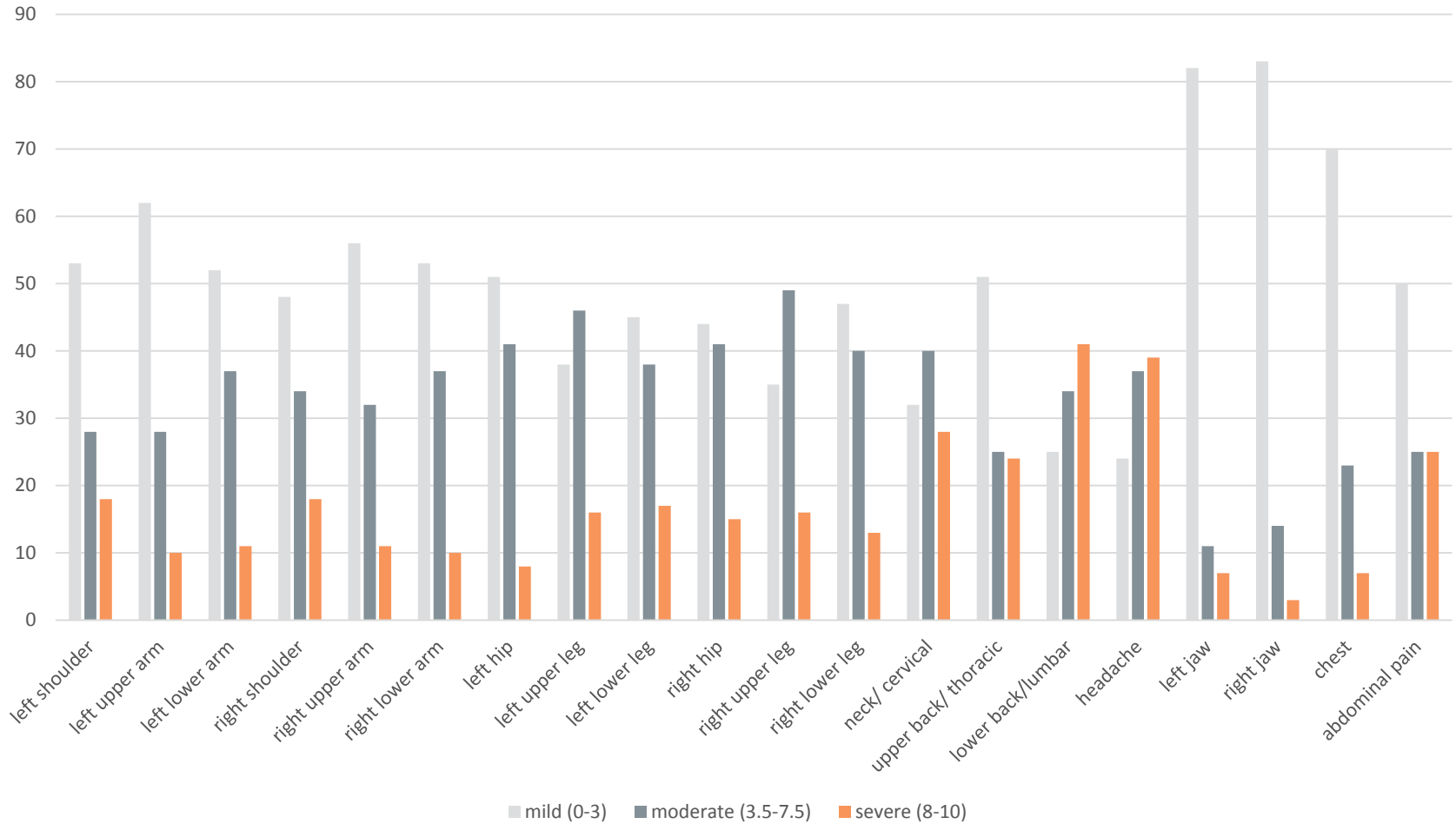
Care for the Symptoms of Gulf War Veterans

- **Pain – MSK**: Rehab/PT/exercise/CAM/acupuncture to help with pain management (?rTMS)
- **Cognition**: Neurocognitive assessment and directed interventions
- **Fatigue**: medical, endocrine evaluation, management, consider metabolic disorders, 24/7 routine, graded increase of exercise
- **GI**: referral to GI Clinic, Dietician for management of Irritable Bowel Syndrome (IBS) (low-FODMAP diet)
- **Respiratory**: Pulmonary or Cardiology for shortness of breath, autonomic dysfunction
- **Headache/migraine/Neurologic**: Neurology assessment for TBI, migraine, balance
- **Sleep**: Sleep clinic evaluation, sleep hygiene, 24/7 routine, exercise, CPAP as needed
- **Dermatologic**: Dermatology for management of skin problems
- **Mood/PTSD**: Evaluation, f/u by Mental Health, monitor for PTSD, depression, substance/opiate dependence and suicide risk

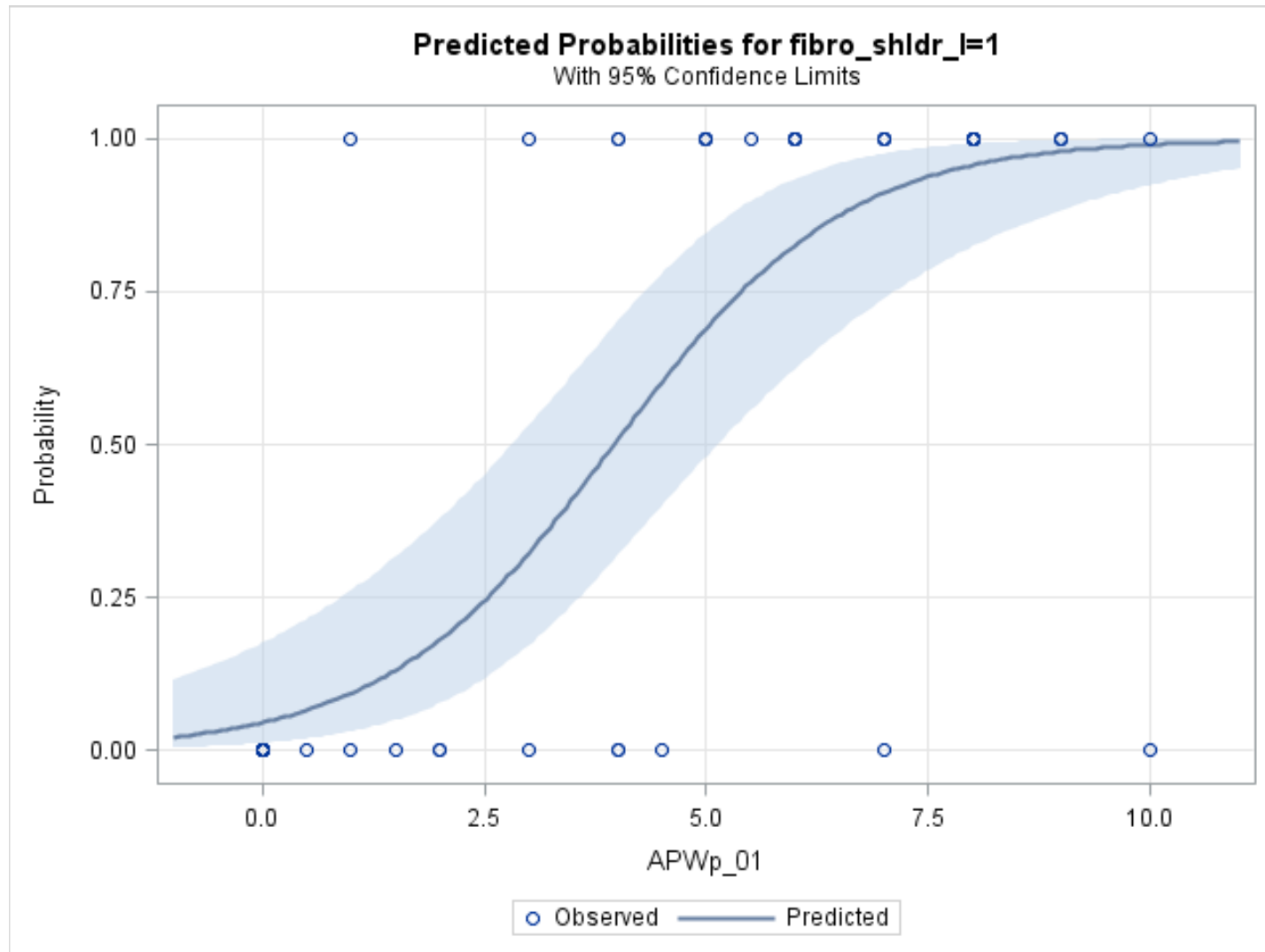


USING THE DIGITAL PAIN MATRIX

Location and Severity of Pain in 70 WRIISC Patients
by percent



COMPARING THE PAIN MATRIX TO THE FIBROMYALGIA SCALE



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THE PROBLEM OF CHRONIC PAIN

- Pain is a significant national health issue
- The Institute of Medicine reports that in 2011, the total annual financial costs to the US due to pain amounted to \$560 billion—more than the total financial costs due to cancer, heart disease, and diabetes combined
- Chronic pain is one of the most frequently reported symptoms of Veterans recently returning from combat, reported to be as high as 19.2%, high compared with the prevalence of fibromyalgia in the general population, which is about 2.1%.



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WHAT CAUSES CHRONIC PAIN?

Common in Post-Deployment Veterans:

- Osteoarthritis: related to over-use - common in Veterans (ankle, knee, hip, back, shoulder)
- Headache: common after traumatic brain injury
- Migraine: similar to post-traumatic headaches
- Back pain
- Fibromyalgia: frequently diagnosed, misdiagnosed, criteria are not clear, related to GWI?
- Nerve damage, neuropathy: many post-deployment cases, causes unclear (GWI)
- Irritable bowel syndrome versus GERD
- Specific injury that has long since healed



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CHRONIC PAIN SYNDROMES

- **Chronic Regional Pain Syndrome (CRPS)**
(described as the most painful long-term condition)
 - **Type 1: Reflex Sympathetic Dystrophy (RSD)**
 - No demonstrable nerve lesions
 - **Type 2: Causalgia**
 - Related to specific nerve injury – presumable sympathetic nerve pathways
- **Chronic Pervasive Pain Syndrome (CPPS)**
 - **Consider Tardive Dysautonomia**
 - possibly NGF related – excess connections
 - Difficult to determine histopathologically
 - » excess, not lack



MANAGEMENT OF PAIN - PHARMACOLOGIC

- **Avoid narcotics, tranquilizers, central anti-cholinergics**
 - May consider opioid blocking agent – naltrexone
- **Consider anti-depressants with anti-pain effects**
 - With anti-cholinergic effects: Nortriptyline, doxepin (stabilize GI symptoms)
 - Without anti-cholinergic effects: duloxetine, bupropion (for nicotine users especially)
 - Anti-convulsant agents: gabapentin, pregabalin
- **Numerous adrenergic agents – alpha, beta, etc.; melatonin**



MANAGEMENT OF PAIN – NON-PHARMACOLOGIC

- **Exercise – low-impact, non-exhausting, graded**
 - Gradually increase to over 150 minutes/week
 - Swimming (need more use of Masters Swimming Programs – free to Vets: www.usms.org)
 - Low-impact aerobic exercises - elliptical exercise machines
 - Stretching and resistance routines, Pilates
- **Complementary Modalities:**
 - Yoga,
 - Tai Chi
 - Massage Therapy
- **Acupuncture**



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rTMS FOR THE TREATMENT OF CHRONIC PAIN

- **What is Transcranial Magnetic Stimulation?**
 - rTMS is a method of non-invasive brain stimulation that is done on an outpatient basis
 - The participant is awake and alert during treatments that last approximately 20 minutes
 - rTMS is an FDA-approved treatment for depression (focus – Left prefrontal cortex)



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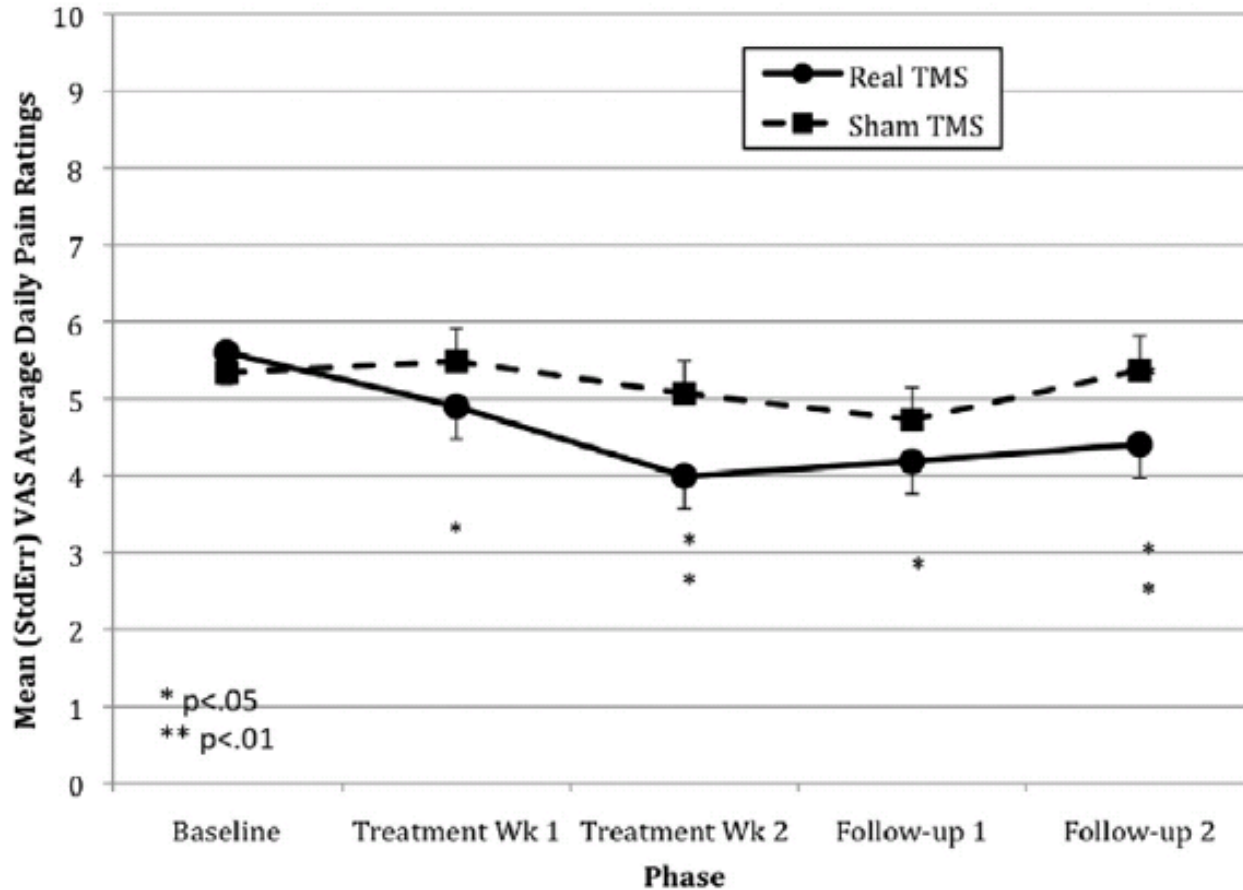
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TMS EFFECT ON VISUAL ANALOG SCALE (VAS) IN FIBROMYALGIA PATIENTS

Worst pain



No pain

Left prefrontal rTMS reduces fibromyalgia pain (Short et al., Pain, 2011)



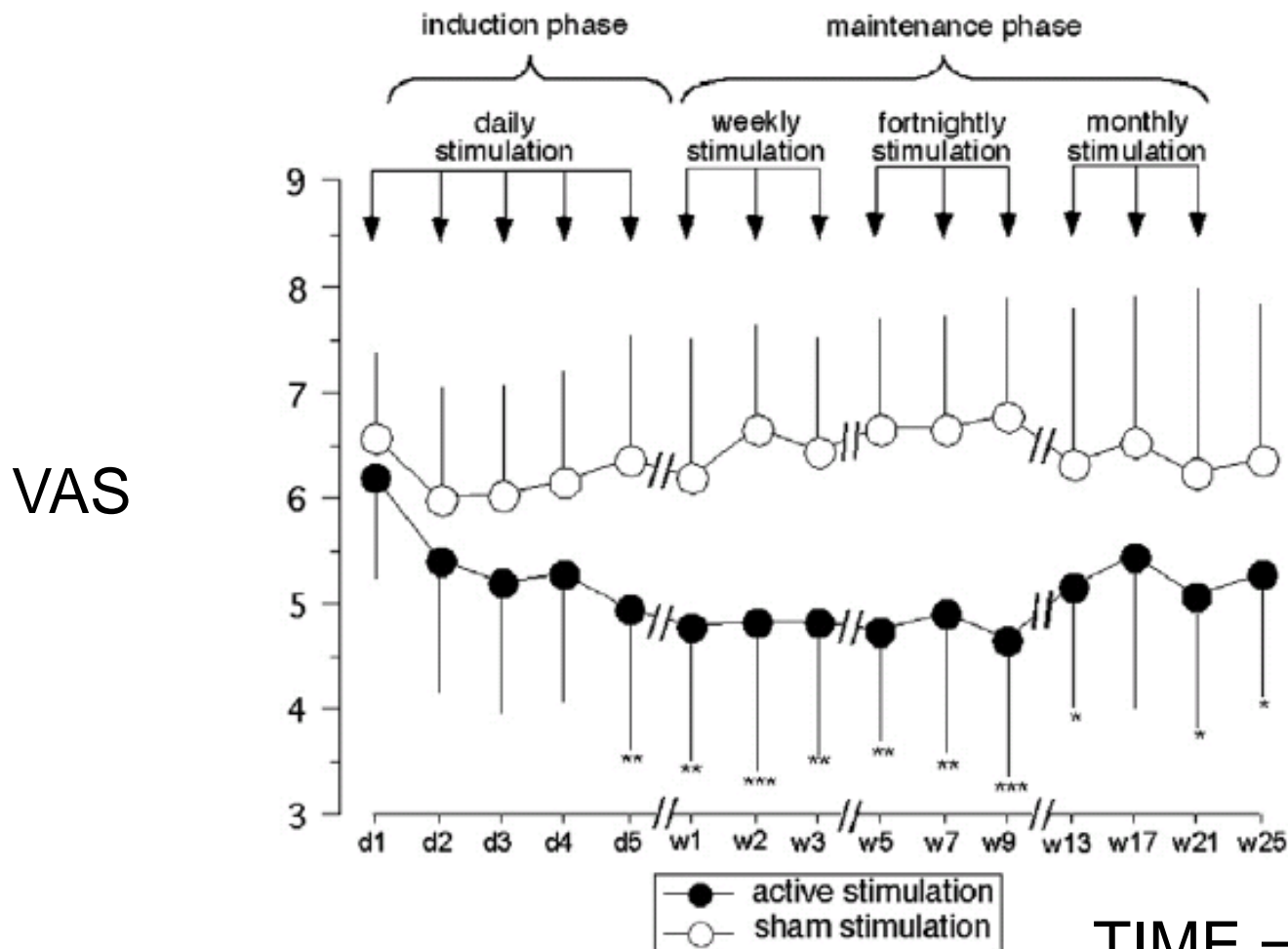
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TMS EFFECT ON VISUAL ANALOG SCALE (VAS) IN FIBROMYALGIA PATIENTS



TIME = 6 months

Long-term maintenance of rTMS analgesia in fibromyalgia (Mhalla et al., Pain, 2011)

Make Veterans Fit Again

- Focus on fitness – chasing the post-boot-camp dream:
 - Weight
 - Healthy diet (for IBS, dieticians recommend low-FODMAP diet)
 - Exercise under direction of Physical Therapy
 - Learn to swim
 - Learn to increase exercise intensity and compete
 - Low impact – swimming – plan to introduce Veterans to Masters Swimming programs: www.usms.org
 - Development of Masters Swim Teams in VA
 - Complimentary and Alternative Medicine (CAM)
 - Yoga, mindfulness, Pilates
 - Dr. Bayley will present some result on a WRIISC CA yoga clinical trial next
- Best approach to reduce pain, fatigue, bowel instability



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- Jennifer Jennings
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The screenshot shows the homepage of the War Related Illness and Injury Study Center (WRIISC). The header includes the VA logo and the text "VA > Health Care > War Related Illness and Injury Study Center". The main title is "War Related Illness and Injury Study Center". A navigation menu on the left lists: "War Related Illness and Injury Study Center (WRIISC)", "WRIISC Home", "About Us", "Clinical Services", "Referrals", "Research", "Education", "Fellow/Mentorships", "Veteran Viewpoints", "FAQ", "Calendar", "Site Map", "Contact Us", "Public Health", and "More Health Care". The main content area features a video player with a play button, a photo of four people, and a section titled "Our Clinical Services" with the text: "We provide clinical evaluations and other services for post-deployment Veterans and support for VA clinicians. Learn more >". Below this is a section titled "About the WRIISC" with the text: "The War Related Illness and Injury Study Center (WRIISC) is a National VA Post-Deployment Health Resource. The WRIISC focuses on the post-deployment health concerns of Veterans and their unique health care needs. The WRIISC develops and provides post-deployment health expertise to Veterans and their health care providers through clinical programs, research, education, and risk communication." To the right of this text is a sidebar with the WRIISC logo and three buttons: "REFER A VETERAN", "VOLUNTEER FOR RESEARCH", and "VETERAN VIEWPOINTS". Below the main content is a "News and Announcements" section with two items: "Update for Gulf War Veterans 2014" and "SAVE THE DATE: VA Post Deployment Health Champions Train the Trainer Workshop Wednesday - Thursday, May 7 and 8, 2014, EES Conference Center, Crystal". At the bottom right of the sidebar is a "CONNECT WITH VHA" link.

