

# VETERANS HEALTH ADMINISTRATION

## Measuring Chronic Multisymptom Illness (CMI) in 1990-1991 Gulf War Veterans: Case Definitions and Challenges.

Presentation for: NAESM

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Date of briefing: 4/3/24



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- I have no conflicts to report.



# History of 1990-1991 Gulf War

- On January 16, 1991, President George H. W. Bush announced the start of what would be called Operation Desert Shield and Storm—a military operation to expel occupying Iraqi forces from Kuwait.
- A massive ground invasion followed on February 24, 1991. Coalition forces swiftly drove Iraq forces from Kuwait, advanced into Iraq, and reached a cease-fire on February 28.
- US forces suffered only 146 casualties, but the chronic disease that followed is estimated to be in the hundreds of thousands.



# Initial Reporting

- Soon after the end of the 1990-1991 Gulf War, Veterans began to report a variety of symptoms and illnesses- “Mystery Illness”
  - Joint pain
  - Fatigue
  - Headache
  - Memory loss
  - Sleep disturbance
  - Rash
  - Difficulty concentrating
- April of 1994: NIH Technology Assessment Workshop
  - What is the evidence for the increased incidence of symptoms/illness attributable to service in the 1990-1991 Gulf War?
  - What are the components of the most practical working case definition?
  - What are the etiologies of these symptoms/illnesses?
  - What future research is necessary?



# CMI Case Definitions: A History

- Efforts to characterize Gulf War illness into a case definition have produced several different definitions
  - Haley et al., 1997
  - Spencer et al., 1998
  - Fukuda et al., 1998
  - Steele, 2000
  - Bourdette et al., 2001
  - Gray et al., 2002
  - Kan et al, 2009
  - Iannacchione et al., 2011
  - Barth et al., 2021
- Studies that describe a deployment-related illness-but no case definition
  - DeFraithe et al., 1992
  - Wolfe et al., 2002
  - Kang et al., 2002
  - Young et al., 2003
  - Levine et al., 2006



# CMI Case Definitions: A History

- While all are slightly different from each other in terms of symptom severity, the types of symptoms, the number of symptoms required, and exclusionary medical conditions, ***all the proposed definitions require the symptoms to be chronic and, at minimum, include symptoms from the following domains: pain, fatigue, and neurocognitive***
- What do all the case definitions NOT include
  - Exposure
  - Dose
  - Duration
  - Frequency
  - Onset parameters
  - Exclusionary criteria
  - Confirmatory laboratory test/value



# CMI Case Definitions: Measurement

- Primary data collection-surveys, symptom inventories, checklists
  - Can get more granularity on onset, chronicity, severity
  - Recall bias

Symptom		SYMPTOM SEVERITY (circle)		
		Mild	Moderate	Severe
<b>PAIN SYMPTOMS</b>				
Joint pain	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
Generalized muscle pain	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score: Pain Symptoms _____		
<b>FATIGUE SYMPTOMS</b>				
Excessive fatigue	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
Unrefreshing sleep	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score Fatigue Symptoms _____		
<b>NEUROCOGNITIVE SYMPTOMS</b>				
Difficulty concentrating/remembering	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
Headache	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score Neurocog Symptoms _____		
<b>GASTROINTESTINAL SYMPTOMS</b>				
Diarrhea	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
Stomach pain	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score GI Symptoms _____		
<b>RESPIRATORY SYMPTOMS</b>				
Shortness of breath/cough	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
Sinus congestion/runny nose	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score Respiratory Symptoms _____		
<b>DERMATOLOGICAL</b>				
Skin rash	<input type="checkbox"/> Yes <input type="checkbox"/> No	1	2	3
		Score Derm Symptoms _____		



# CMI Case Definitions: Measurement

- Secondary data collection-medical records data, identify ICD codes that represent the various symptoms and illnesses
  - Less detailed
  - Prevalence tends to be lower than self-report
  - If there are comorbid conditions can't always determine what illness is responsible for what symptom
  - Over 50 ICD-10 codes that capture symptoms that have been reported in the peer-reviewed literature as disproportionately affecting 1990-1991 Gulf War Veterans
  - Codes for diagnoses
    - Myalgic encephalomyelitis/Chronic fatigue syndrome
    - Fibromyalgia
    - Irritable bowel syndrome
    - Major depressive disorder





# CMI Case Definitions: Measurement

## VA HOME Machine Learning GWI Case Definition Project

- Machine learning methods were applied to the Department of Defense and Department of Veterans Affairs administrative and healthcare data to:
  - Identify baseline predictors of deployment to the 1990-1991 Gulf War
  - Identify interactions between deployment and baseline characteristics predicting GWI
  - Predict risk for GWI among Gulf War and Gulf Era Veterans
  - Calculate differences in risk for GWI among Gulf War Veterans
  - Identify factors associated with differences in deployment-related risk for GWI.



# CMI in Post 9/11 Veterans

- Smith et al., 2014
  - Self-reported symptoms from participants in the Millennium Cohort Study (MCS) components (2001-2008) compared to self-reported symptoms in a cohort of subjects from the 1991 Gulf War, much less symptom reporting in the MCS group.
- McAndrew et al., 2016
  - Self-reported symptoms among participants in the HEROES Project. One-year post-deployment symptoms were assessed using the CDC criteria of CMI; 46.7 percent reported symptoms consistent with CMI, and 10.8 percent reported symptoms consistent with severe CMI.



# CMI in Post 9/11 Veterans

- Mohanty et al., 2018
  - Cross-sectional study included 501,996 males and 69,611 females from the OEF/OIF/OND Roster provided by the Department of Defense who had encounters in any VHA facility nationwide after their last deployment end date from fiscal years 2002–2011. Defined CMI as one (ICD-9-CM) coded diagnosis of chronic fatigue syndrome, fibromyalgia, or irritable bowel syndrome. The prevalence of CMI was 4.2% in males and 8.4% in females.
  
- Porter et al., 2020
  - CMI/GWI over time in MCS among 1990-1991 Gulf War Veterans, 1990-1991 Gulf War Era Veterans, and Veterans who did not serve during 1990-1991 Gulf War (so OEF/OIF/OND). The prevalence of CMI/GWI increased over time in all three groups, with the 1990-1991 Gulf War Veteran group reporting the highest prevalence during the study period.



# CMI Case Definitions: Challenges

- CMI case definitions were developed from studies of 1990-1991 Gulf War Veterans, not in the post-9/11 Veteran population. While both cohorts deployed to Southwest Asia these populations **are different** from each other
  - Duration of conflict
  - Blast injury/TBI
  - Types of exposures
  - Technology and safety gear
- Still have the issue that Veterans who never deployed still report symptoms and meet the criteria for CMI
- Treatment



# CMI Case Definitions: Challenges

- Benefits issues
  - VA presumes chronic, unexplained symptoms existing for 6 months or longer are related to Gulf War service without regard to cause
  - The presumptive illnesses must have appeared during active duty in the Southwest Asia theater of military operations OR by December 31, 2026, and be at least 10 percent disabling.
    - ME/CFS
    - Fibromyalgia
    - Functional gastrointestinal disorders –IBS, functional dyspepsia, and functional abdominal pain syndrome.
    - ***Undiagnosed illnesses***
      - Symptoms that may include but are not limited to- abnormal weight loss, fatigue, cardiovascular disease, muscle and joint pain, headache, menstrual disorders, neurological and psychological problems, skin conditions, respiratory disorders, and sleep disturbances.



# CMI Case Definitions: Challenges

38 CFR 3.317 (1994) Undiagnosed/medically unexplained illness	CDC (CMI) Fukuda et al, 1998	Kansas (GWI) Steele, 2000
Fatigue Sleep disturbances	Fatigue	Fatigue and Sleep
Neurological signs/symptoms Neuropsychological signs/sym Headache	Mood Cognition	Neurological Mood Cognition
Muscle pain Joint pain	Musculoskeletal (pain)	Pain
Gastrointestinal signs/symptoms		Gastrointestinal
Respiratory signs/symptoms		Respiratory
Skin signs/symptoms		Skin
Cardiovascular signs/symptoms		
Abnormal weight loss		
Menstrual disorders		
CFS IBS FM		



# Summary

- CMI/GWI has caused significant morbidity in the 1990-1991 Gulf War population
- No objective diagnostic test, clinicians/researchers must rely on symptom reporting
- Data sources for symptom information include VHA medical records, VBA claims data, research studies/surveys, and Department of Defense medical records

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