

RACGWVI: Presentation

Cooperative Studies Program (CSP 2006)

Million Veteran Program 029 Cohort: Deployment, GWI and COVID Health Outcomes



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Cooperative Studies Program (CSP 2006) Million Veteran Program (MVP 029) Cohort: Deployment, GWI and COVID Health Outcomes

Study Overview and Preliminary Findings Update

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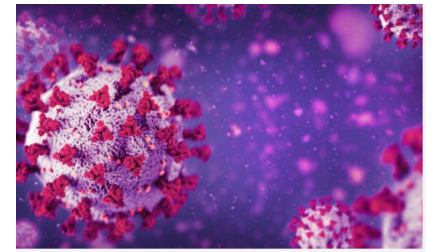


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COVID-19



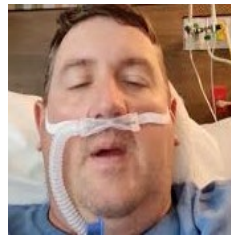
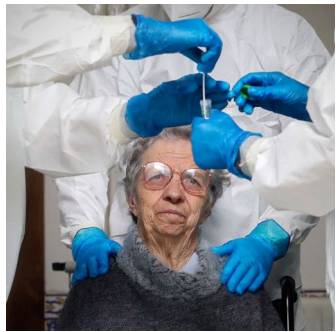
- 776 million COVID cases and 7.1 million COVID deaths officially reported globally[^]
- U.S. -- highest #s COVID cases (103 million) & deaths (1.2 million)
- Even with marked reduction in most serious COVID outcomes (hospitalization, ICU admission and deaths) --
 - COVID remained in top 10 leading causes of U.S. deaths in 2023

[^]World Health Organization 2023 data.who.int, WHO Coronavirus (COVID-19) dashboard > Cases [Dashboard].
<https://data.who.int/dashboards/covid19/cases>. Accessed thru 8/04/2024

COVID 19 -- a disease of disparities

Disproportionately impacting vulnerable populations:

- Well-established vulnerable: Elderly, obese, non-White, male, higher chronic disease burden (e.g., respiratory conditions like asthma/bronchitis/COPD, conditions impacting immune system, heart disease), socioeconomic disadvantage (e.g., less access to healthcare), alcohol abuse and smoking
- Emerging: air pollution/harmful airborne particulate exposure



Deployed Gulf War Veterans (GWVs)

- >695,000 deployed to 1990-1991 Persian Gulf conflict theater, well-known broadly exposed to hazardous agents ('toxic soup'):
 - *Airborne hazards*: oil well fires, diesel fuel, cross-contaminated blowing sands, occupational chemical and pesticide 'fumes', burn pits
 - *Neurotoxic/neuroinflammatory agents*: military grade pesticides, polyvaccination-anthrax/botulin vaccines, pyridostigmine bromide (PB) pills chemical weapons sarin/cyclosarin at Khamisiyah weapon site



Gulf War Illness (GWI)

- ~30% deployed GWVs developed Gulf War Illness (GWI):
 - Chronic medically unexplained multi-symptom condition
 - High burden condition--- GWI associated with ↓ Health-related quality of life and ↑ Risk for multiple medical chronic conditions (e.g., Coronary Heart Disease)
 - Prominence of neurological symptoms (e.g., pain, brain fog, sleep/autonomic symptoms, fatigue) + experimental research led to:

▶ ▶ ▶ **Paradigm---GWI as Chronic Neuro-immune**

Gulf War Veterans (GWVs) and COVID-19

- GWVs, their healthcare providers, researchers and advocates raised concerns that deployed and those with GWI may be especially vulnerable to COVID---
- *VA's Office of Research and Development Gulf War Research Program provided COVID supplement funds to conduct first study to evaluate potential GWV vulnerability to COVID employing*
- **The largest nationwide U.S. GWV cohort---the VA's CSP2006 Gulf War veteran study cohort**

CSP 2006 Original Gulf War Veteran Cohort

- CSP2006 ‘*Genomics of Gulf War Illness*’ (PI: D. Helmer, MD, MS; Co-PI: E. Hauser, PhD) -- included >109,000 Department of Defense-confirmed Gulf War era veterans identified among >550,000 enrolled in the VA’s Million Veteran Program (MVP) study cohort by June 2018

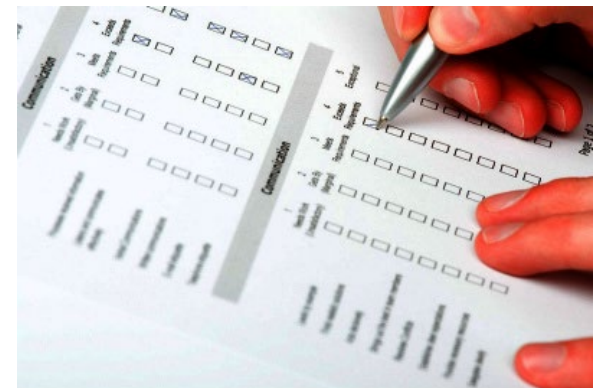
- MVP Study and Participants:

- >1 million veterans, 1 of 9 VA-users participates
- Complete baseline and lifestyle risk factor surveys
- Blood drawn for DNA extraction/genetic testing
- Provide access to their VA electronic health data



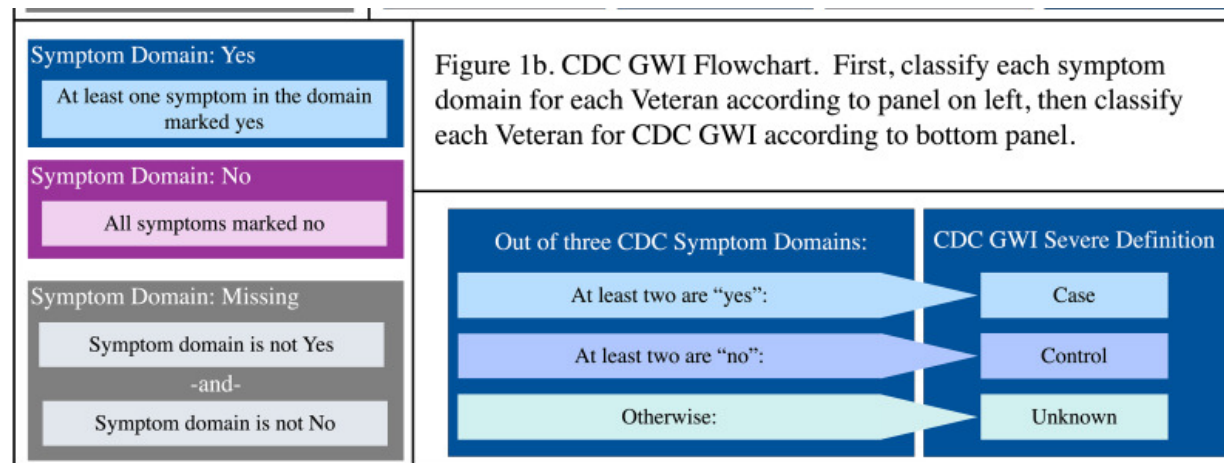
CSP 2006 Original Cohort Study Survey

- Mailed Gulf War veteran specific survey in June 2018 – mid-2019
 - Clinical Symptoms (duration, frequency, burden)
 - Medical and Risk Factor History
 - Military Exposures



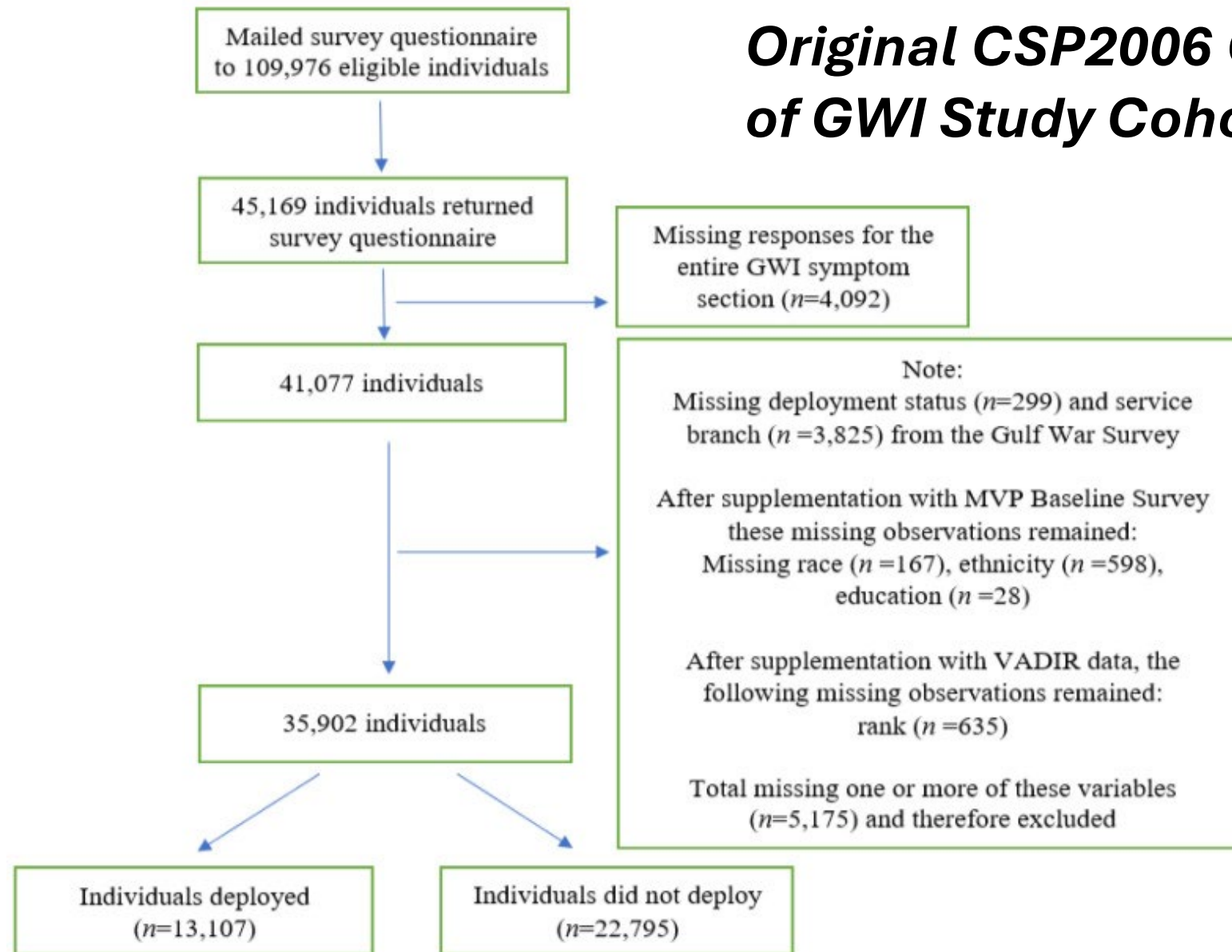
GWJ Determination in Original CSP2006 Cohort

- Used algorithm developed in another general Gulf War veteran cohort to participant survey responses[^]
- It applied National Academy of Sciences endorsed CDC (Fukuda) severe GWJ symptom-based case definition criteria to participant survey responses to classify GWJ case-status (GWJ+/GWJ-)



[^]Vahey J, et al. Life Sci. 2021 Oct 1;282:119808.

Original CSP2006 Genomics of GWI Study Cohort[^]



27% Met CDC Severe GWI criteria (GWI+)

[^]Duong *et al.* Int J Environ Res Public Health. 2022 Dec 24;20(1):258.

CSP2006 COVID Study: Cohort Expansion and Eligibility

- Added another >29,000 GWV enrolled in MVP after June 2018 thru 2019 (pre-pandemic)
- Removed >2500 cohort members who died before 3/1/2020

FINAL EXPANDED CSP2006 COVID STUDY COHORT—

136,871 Gulf War era veterans

COVID Testing and Outcomes



- VA's COVID Shared Data Resource (CSDR) to identify COVID testing/outcomes; began 3/1/2020
- Applies large data informatic methods and pre-defined algorithms to VA health and administrative record databases to identify all VA-users:
 - Tested for COVID
 - Diagnosed with COVID (i.e., COVID+)
 - Treatments and outcomes in those COVID+ (e.g., COVID-related hospitalization)
 - Specific medical, healthcare use, and risk factor data on veterans ever tested for or diagnosed with COVID



COVID Data We Used from VA CSDR

- A) **Ever COVID tested**--VA PCR/antigen laboratory tested for COVID between 3/1/2020-12/31/2020
- B) **COVID+** --Lab confirmed COVID+
- C) **COVID-** -- All lab test results were confirmed COVID- (i.e., never COVID+)
- D) **COVID-related hospitalization** -- newly hospitalized ≤ 14 days after lab test confirmed COVID+
- E) **COVID-related ICU admission** – new ICU admission ≤ 14 days after tested COVID+ or during COVID hospitalization
- F) **COVID-related death** – died in ≤ 30 days of lab test confirmed COVID+
- G) **Potential confounders** --e.g., BMI, Elixhauser comorbidity score, smoking, VA healthcare use during 2 years prior to COVID test date

Study period 3/1/2020-12/31/2020

- Pre-vaccine and Pre-Paxlovid (oral antiviral medication) period
- Best picture of background host susceptibility to a novel viral respiratory pathogen
- *Important potential implications for:*
 - Clinical care and disease surveillance in GWVs with COVID
 - Next novel respiratory viral pathogen

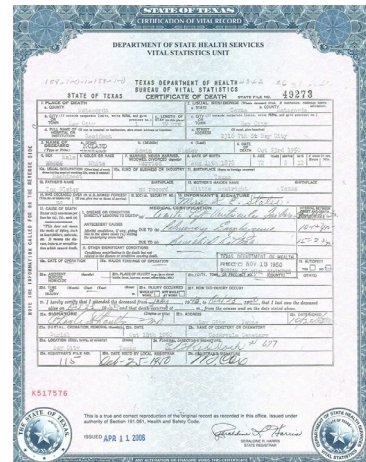
Key Analyses

Among ever COVID tested (VA lab-confirmed COVID status and data in VA's CSDR):

- Prevalence of COVID Outcomes—e.g., calculated and compared COVID outcome rates (e.g., test positivity rate) in deployed and non-deployed and deployed GWI+ vs. deployed GWI-
- COVID outcome risk models---logistic regression used to assess if deployed (or deployed with GWI) had significantly increased risk of any COVID outcome after adjusting for other risk factors ('confounders')
 - *Outcomes:* testing positive, and COVID-related hospitalization, ICU admission, and mortality)
 - *Confounders:* age, race/ethnicity, gender, Elixhauser comorbidity level (key) + other military service variables, healthcare use, BMI, smoking, geographic region

Additional Data Source & Analyses: National Death Index

- 1) Includes all official death certificates in U.S. ('gold standard')
- 2) *Data on mortality including if death was COVID-related available for entire cohort (including those who never tested for COVID in 2020 and thus are not included in VA COVID Shared Data Resource [CSDR])
- 3) Calculated total proportion deaths due to COVID and average age at death among those dying with COVID





Preliminary Provisional Results Update*

**Highlights Pending Manuscript
Scientific Peer Review and
Publication Submission
Requirements*



Background characteristics COVID-tested GWVs

Among the 26,141 lab tested Gulf War era veterans (GWVs) in CSP2006 in 2020

Mean age was 60 years old

81% Male

55% White (not Hispanic)

88% Enlisted

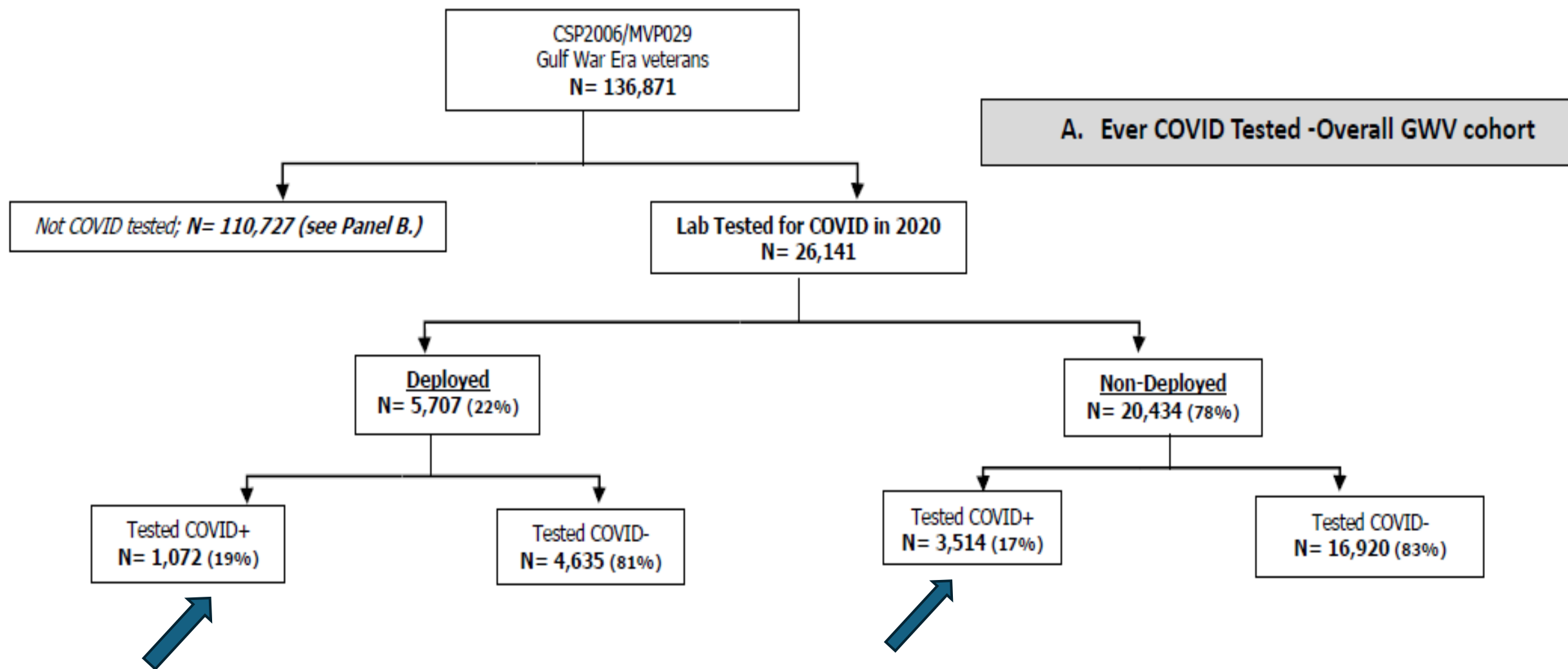
54% Army

55% obese (BMI \geq 30)

45% lifetime non-smokers

>99% had used VA healthcare in prior year

Figure 1: Study flow diagram detailing COVID-testing and vital status in N=136,871 veterans with confirmed service in 1990-1991 Persian Gulf War era according to deployment status during the first 10 months of the VA COVID pandemic (3/1/2020-12/31/2020).



Summary Preliminary Provisional Results:

- *Deployment overall was not associated with increased risk of COVID outcomes evaluated after accounting other risk factors*
 - Though suggestive possible signal being investigated---a shift toward relatively younger ages at death among few dying of COVID in 2020
- *Deployed with GWI had suggestive potential increased risk for only one COVID outcome*
 - Given small number plus changes in virus characteristics and new treatments and vaccines, confirmatory studies needed

Other Ongoing COVID Research in CSP2006

Are there differences between deployed Gulf War veterans and those with GWI+ with respect to:

1. **COVID Vaccine Effectiveness:** (i.e., how well vaccines worked in preventing COVID outcomes including testing positive or having a COVID-related hospitalization, ICU admission or death from 2021 onwards)
2. **COVID Vaccine Safety:** (i.e., how likely it was to experience rare known serious vaccine side-effects like anaphylaxis, heart inflammation and blood clots post-vaccination?)
3. **Long COVID Burden:** (i.e., were risks of developing long COVID after infection similar after accounting for other known risk factors like age and vaccination?)

Acknowledgments:

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****Very importantly, we would like to thank the >140,000 1990-1991 Gulf War era veterans participating in the MVP!!****

Your data counts and is making global impacts on health while helping support research important to your fellow Gulf War veterans and other veteran and military populations!