

### Considerations in the return of genetic results: Lessons from the Million Veteran Program

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#### Disclosures

Dr. Vassy is an employee of the U.S. Department of Veterans Affairs (VA). His views do not represent those of the VA or the U.S. Government.



# Veterans Health Administration (VHA)

Largest integrated health care system in the US

- Caring for >9M Veterans in every U.S. state and territory
- 18 geographically defined Veterans
  Integrated Service Networks (VISNs)
- >1200 healthcare facilities, including 171 medical centers and 1,112 outpatient facilities
- Policy decided at VHA level; management and practice implemented at regional facility levels



# VHA Office of Research & Development

- Intramural research program for VA investigators
  - \$882 million budget in FY2022
- Organized into 4 major services:
  - Biomedical Laboratory R&D Service
  - Clinical Science R&D Service
  - Health Services R&D Service
  - Rehabilitation R&D Service
  - Major programs:
    - Cooperative Studies Program (CSP)
    - Million Veteran Program (MVP)



# **VA Million Veteran Program**



- Launched in 2011, MVP is a national VA research program and one of the world's largest programs on genetics and health
- Designed to advance precision health care by learning how genes, lifestyle, and military experiences and exposures affect health and illness
  - Curated and standardized datasets in secure, centralized computing environments to expedite scientific discovery
  - Pipelines to translate findings into the clinic to benefit Veterans and all people

![](_page_4_Picture_6.jpeg)

![](_page_5_Picture_0.jpeg)

Veterans enrolled (22K+ joined online)

Slide courtesy of Sumitra Muralidhar

![](_page_5_Picture_3.jpeg)

The world's largest genomic database

Linked to a health care system Largest cohort of people with African American ancestry (~150K) 650K+

Genotyped samples

![](_page_6_Figure_0.jpeg)

Genome-wide association study of alcohol consumption and use disorder in 274,424 individuals from multiple populations

nature genetics

Genome-wide association analysis of venous thromboembolism identifies new risk loci and genetic overlap with arterial vascular disease

OPEN https://doi.org/10.1038/s41467-019-12576-w

International meta-analysis of PTSD genome-wide association studies identifies sex- and ancestryspecific genetic risk loci

Caroline M. Nievergelt et al.#

LETTERS ps://doi.org/10.1038/s41591-019-0492-5

medicine

Genome-wide association study of peripheral artery disease in the Million Veteran Program

Genome-wide association study of posttraumatic stress disorder reexperiencing symptoms in >165,000 US veterans

## **Relevant comparisons to NHANES for RoR**

#### Similarities

- National in scope
- Designed as a research (not clinical) program
- Return of genetic results not a part of initial design or consent

#### Differences

• Linked to a single national healthcare system

![](_page_7_Picture_7.jpeg)

# **Considerations for RoR within MVP**

- Consent
- Analytic validity
- A research program within a healthcare system
  - Responsibility to return?
  - Process to bridge research/clinical divide

![](_page_8_Picture_6.jpeg)

## **MVP Return of Results**

Familial hypercholesterolemia (FH)

- Recontact of participants with suspected FH-associated variant on MVP array
- Clinical confirmation
- Delivery of telegenetic counseling intervention to Veterans and clinical recommendations to PCP
- n>100 enrolled to date

**Metastatic prostate cancer (mPC)** 

- Recontact of participants with mPC to facilitate germline testing / confirmation for BRCA variants
- Inform targeted treatment
- Genetic counseling and cascade testing
- *n*>500 consented to date

## Future considerations for genetic RoR in MVP

- Learning best practices and Veteran and provider feedback from current ongoing pilots
- Expanded list of genes/conditions, pharmacogenomics
- New national or regional service delivery models to connect research to clinical care: expert consultation to local providers

![](_page_10_Picture_4.jpeg)

# Thank you

Thank you to the Veterans, MVP staff, and collaborators who make this research possible.