



**THE MILLION VETERAN PROGRAM (MVP):  
IMPROVING THE LIVES OF AMERICA'S VETERANS**

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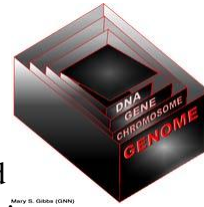
**OUTLINE**

- describe aspects of **genetics** and **genomic biobanks**
- report on the **VA Million Veteran Program**, as a major initiative of the VA Office of Research & Development
- discuss how the VA Million Veteran Program is designed to **improve the health of, and healthcare for, Veterans**

## GLOSSARY

### Selected terms

- **DNA** (deoxyribonucleic acid) carries genetic info
- **gene** is a sequence of “base pairs” within DNA
- **chromosome** organizes DNA/genes as a linear strand
- **genome** refers to (all) genetic material and their function



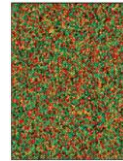
### Specific resource

- **genomic biobank** refers to collection of specimens/data



### Common research approaches

- **genotyping** characterizes selected elements of DNA
- **sequencing** identifies an exact pattern of base pairs for either part of, or the entire (“whole”), genome



## BACKGROUND

### Overview of heredity in humans

- long-standing awareness that DNA affect health & disease
- 46 chromosomes;  $\approx 20,000$  genes;  $>3$  billion “base pairs”
- coding of proteins by 1-2% “exome” portion of genome; non-coding 98-99% portion of genome is *not* “junk DNA”
- **genomic technology** is advancing rapidly (e.g., genomewide association analysis [GWAS], and genomic sequencing); need “mega-cohorts” (very large #s) to provide broad results

## EXAMPLES OF GENOMIC RESEARCH

Genotyping: *Nature* 2007;447:661 [**identified genes as risk factors**]

Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls

Exome-sequencing: *PNAS* 2009;106:19096 [**enabled diagnosis**]

Genetic diagnosis by whole exome capture and massively parallel DNA sequencing

Whole-genome seq'ing: *Sci Transl Med* 2011;3:87re3 [**informed Rx**]

Whole-Genome Sequencing for Optimized Patient Management

## ONGOING GENOMIC BIOBANKS

- **Europe** (selected examples):
  - Banco Nacional de ADN [Spain]
  - Biobank Hungary
  - Biohealth Norway
  - Danubian Biobank Consortium
  - Estonian Genome Project
  - Generation Scotland
  - Genome Austria Tissue Bank
  - GenomEUtwin
  - German Biobank Registry, KORA-gen
  - National Biobank Program [Sweden]
  - Sequencing Initiative Finland
  - UK DNA Banking Network & British Biobank

### ONGOING GENOMIC BIOBANKS (cont'd)

- **North America** (selected examples):
  - Database of Genotypes & Phenotypes (National Center for Biotechnology Information)
  - Genome Canada & pediatric consortium
  - Mayo Clinic Biobank
  - Nat'l Children's Study (NIH)
  - Nat'l Health & Nutrition Exam. Surveys (CDC)
  - Personalized Med. Res. Project (Marshfield Clinic)
  - Research Program on Genes, Environment, & Health (Kaiser Permanente, Northern CA)
  - Translational-Genomic Research in the African Diaspora (Howard University)
  - Vanderbilt University BioVU
  - Veterans Affairs Million Veteran Program

### ASPECTS OF GENOMIC BIOBANKS

#### Examples of ongoing “mega-cohort” biobanks

- UK Biobank: ≈500K; decentralized health records
- Vanderbilt University BioVU: ≈175K; “opt-out” model
- Kaiser Permanente project: ≈200K; patients migrate in/out
- China Kadoorie Biobank: ≈500K; w/ Univ. of Oxford
- **VA Million Veteran Program**: ≈290K; *to be described*

## ‘WHY THE VA?’

### Advantages of VA environment

- national “pool” of long-term (and altruistic) beneficiaries
- centralized electronic health record
- existing research infrastructure & expertise
- “location” of research in integrated VA healthcare system

### Relevance to (all) Veterans

- Veterans have unique military exposures and health outcomes
- VA research & clinical program focuses on Veterans’ health
- [Note: results can also benefit non-Veterans]

## MILLION VETERAN PROGRAM (MVP)

### Overarching goal

- assemble a large, well-characterized source population of Veterans with DNA samples & linkage to electronic health record (EHR) information, as an **infrastructure** for multiple future research uses

### Specific objectives

- enroll **up to 1,000,000 Veterans** over 5-7 years
- administer general **questionnaire**; collect blood and extract **DNA**; link to **VA EHR** (and create information technology system)
- create policies and procedures for **laboratory and clinical scientists to access & utilize (de-identified) data**

## MVP 'DAILY UPDATE'

Status as of 15 Jul 2014

- |                                       |                |
|---------------------------------------|----------------|
| • Invitations mailed                  | 2,447,669      |
| • Baseline surveys received           | 387,250        |
| • <b>Consent forms (and blood)</b>    | <b>290,159</b> |
| • “Yes” reply (initial 2.1M mailings) | 17.8%          |

## SCOPE OF MVP

Operational aspects of the Million Veteran Program

- recruit using **opt-in**/decline model; invitational letter will be sent to ≈6 million Veteran Health Administration beneficiaries
- initial enrollees at vanguard sites in 2011 → **50 sites** as of 2014
- myriad of issues regarding conduct of “team science” within existing (non-genomic) VA research infrastructure: **scientific; administrative; technical; regulatory; ethical; societal**

## SITES FOR MVP ENROLLMENT



Note: **new sites** are launched to replace depleted sites; capability for **web-based enrollment** is under-development

## MVP: SCIENTIFIC ASPECTS

MVP is being designed as a “platform” to help:

- develop new diagnostic and monitoring tests
- provide basis for identifying new therapies
- link genetic susceptibilities, military exposures, and health
- study the full spectrum of health & disease (e.g., cancer, cardiovascular, mental health, pulmonary, “longevity”)
- help personalize treatment based on genetic characteristics
- *[Not cloning or genetic engineering]*

### MVP: ADMINISTRATIVE ASPECTS

VA Central Office: e.g., Office of R&D, Coop Studies Prgm

Coordinating Centers: e.g., Boston & West Haven “Epi” Centers

Special units: Lab for 4M specimens; genomic “IT” platform

VA sites: steady-state of 50 VA medical centers; (web pending)

“The field”: e.g., Veteran Service Organizations, local media

Veteran enrollees: [focus of entire program]

### MVP RESEARCH TEAM (PARTIAL LIST)

#### VA Central Office

- **T. O’Leary**; J. Breeling; K. Hill; G. Huang; J. Moser;  
S. Muralidhar; R. Przygodzki; K. Schaa
 

<u>Boston</u>	<u>West Haven</u>
• M. Gaziano, Co-PI	• J. Concato, Co-PI
• M. Brophy	• D. Anderson
• J. Deen	• M. Aslan
• L. Fiore	• D. Cavaliere
• L. Hansen	• P. Guarino
• D. Morin	• R. LaFleur
• G. Muldoon	• L. Mancini
• S. Pyarajan	• L. Piscitelli
• C. Shannon	• J. Russo
• S. Whitbourne	• F. Sayward
- [multiple other staff, including at sites & support units]



### MVP: **TECHNICAL ASPECTS**

#### Genomic analysis

- genotyping and sequencing done by contracted vendors

#### Genomic Information System for Integrated Sciences (GenISIS)

- coordinate central recruitment and scheduling
- receive & store genetic data; link to pertinent health data
- create & maintain secure information technology platform
- [Note: data remain on VA servers, behind VA firewall]

### MVP: **REGULATORY ASPECTS**

- VA Cooperative Studies Program Guidelines and Standard Operating Procedures (SOPs) are followed
- Good Clinical Practices (GCP) apply, to safeguard participants' welfare and assure validity of results
- Regulatory agencies have applicable rules and policies to be followed

### MVP: **ETHICAL ASPECTS**

- Obtain and document informed consent and HIPAA (Health Insurance Portability & Accountability Act) authorization
- Timely handling of safety data, requests to withdraw
- Establish and maintain confidentiality regarding participants' genomic and non-genomic data
- Thoughtful use of “resource” provided by Veterans
- Monitor changing concepts of what-is-ethical

### MVP: **SOCIETAL ASPECTS**

#### **Veterans' attitudes regarding a database for genomic research**

The promise of new treatments and preventative measures, and respondents' curiosity about the role of genes in their health and the health of their relatives and fellow veterans, resonate as important factors that largely seem to outweigh concerns about privacy, mistreatment, or the use of limited VA health-care dollars. Although these concerns are real and must be addressed, the surveyed population seems to believe that the benefits of a GMP database will largely outweigh the burdens, if study designers can protect participants' information from misuse and offer as much transparency as possible.

*Genetics in Medicine* • Volume 11, Number 5, May 2009

### PERSPECTIVE OF VETERANS WHO ENROLL

- **Any VHA beneficiary can volunteer** to provide blood sample, have medical records accessed, complete Baseline & (optional) Lifestyle questionnaires
- Understand potential benefits and risks; complete **informed consent** and enrollment process after study is explained
- Recognize (per study document) that: *Testing on your sample including DNA (genetic tests) or other molecules derived from it will be done for research purposes. Because the results have no clear meaning at this time, we will not report these genetic test results to you or your doctor. The genetic test results will not be placed in your electronic medical record.*

### CHARACTERISTICS OF MVP ENROLLEES

<u>Age:</u>	<50 yrs	13.8%	<u>Branch:</u>	Army	50.6%
	50-69 yrs	58.7%		Navy	21.2%
	≥70 yrs	27.5%		Air Force	16.7%
<u>Sex:</u>	Male	91.9%		Marines	10.1%
	Female	8.1%		Nat'l Guard	0.5%
<u>Race:</u>	White	77.5%		Coast Guard	0.8%
	African-Amer	18.5%		[other]	0.1%
	[other]	3.3%	<u>Era:</u>	thru 6/1950	5.3%
	[Native]	0.7%		7/50-1/55	5.0%
<u>Ethnicity:</u>	Hispanic	5.4%		2/55-7/64	7.1%
				8/64-4/75	41.0%
				5/75-7/90	11.8%
				8/90-current	10.0%
				[multiple]	19.8%

Note: based on N≤275,806 enrollees

## INITIAL USES OF MVP

### Projects linked to, or embedded within, MVP

- “Genetics of Functional Disability in **Schizophrenia & Bipolar Illness**” (N≈9,300 Veterans enrolled as “case” patients)
- “Genomics of **Posttraumatic Stress Disorder**” (N≈10,000 Veterans in MVP population to be identified as “case” patients)
- “**Request for Applications**” from VA intramural investigators [planned for Spring 2015]
- Ultimate goal of enabling **personalized medicine** for Veterans

## INFORMATION AVAILABLE TO VETERANS

MVP information booklets, pamphlets, newsletters, and web site  
(at <http://www.research.va.gov/MVP/default.cfm>)



## SUMMARY

**MVP is an evolving VA-based resource that will inform:**

- why some Veterans are at greater risk for developing illness
- how to help prevent certain illnesses in the first place
- why treatments can work well for some Veterans but not others
- [to-be-identified] based on peer-reviewed ideas from scientists
- how VA can **incorporate genomic information in patient care**