85 Years of Discovery, Innovation, and Advancement

Million Veteran Program

Part I: Development & Use of Database

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Million Veteran Program

- **The Million Veteran Program will create a genomic database over 5-7 years of 1 million Veterans who are users of the VA healthcare system**

- **Database will have available**

  - DNA specimens and links to tissue specimens

  - Access to the VA Electronic Health Record

  - IT capability to identify patients for a variety of types of studies

  - Analytical tools

- **MVP is part of a larger initiative in genomic medicine by the VA**

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Million Veteran Program

- **MVP will facilitate**
  - Developing new diagnostic tests to enable disease prevention and earlier treatment
  - Personalize therapies to the Veteran's individual genetic characteristics and conditions, e.g. Pharmacogenomic customization
  - Conduct surveillance for early detection of military exposure and other deployment-related conditions and possibly link them to genetic susceptibilities
- **Overall establish how genetic information will be used in clinical medicine**
  - Link genotype to phenotype
  - Complex, adult, multi-gene diseases possibly with strong environmental influences
- **VA assets**
  - *Large HCS, Electronic Health Record, research embedded in clinical program*
- **Large population with substantial diversity**
  - Enables rigorous examination of a variety of subpopulations

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MVP/Genomic Medicine Initiative: Building Infrastructure

- **Genomic Medicine Program Advisory Committee (GMPAC)**
- **Biorepository (in Boston) to extract and store DNA from samples -** Expanding to 4 million samples
- **Special laboratories and contracts, e.g. Pharmacogenomics**
- **Equipment purchases**
- **Central IRB**
- **IT infrastructure to enable research use of databases**
  - High performance environment and secure platform for storing and analyzing genetic and health information
  - Coordinate central recruitment, scheduling and enrollment for studies using MVP database
  - Software analysis and reporting tools for all projects
  - Natural language processing
- **Veterans Consultation Project – Survey**

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Genomics Survey Findings

- **With VSO and Veterans' collaboration, internet survey performed April 24 – May 5, 2008**
  - N = 931
- **83% said program should be done**
- **Increased support associated with**
  - Attitudes about research
  - Attitudes about helping and history of previous "altruistic behaviors"
  - Curiosity about genetics
  - Satisfaction with VA healthcare
- **Important issues**
  - Privacy
  - Safeguarding data

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Million Veteran Program Enrollment Process

- **Receive letter of invitation to MVP**
- **Respond to the letter**
- **Read and sign an informed consent and HIPAA authorization in VAMC**
- **Fill out health and behavior surveys**
- **Provide contact info**
- **Provide a blood sample**
- **Get an optional health assessment**
- **Allow secure access to VA and VA-linked medical and health information**

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Protection of Veteran's Samples and Data

- ## Security

  - o Veteran's samples and health data will be labeled with a code instead of the name or other personally identifying information

  - o Samples will be stored in a central, secure biorepository and data will be stored in a central, secure database

  - o All analyses will be performed behind a secure firewall

- ## VA Central Institutional Review Board review

  - o Initial and ongoing review of all aspects of MVP study design, implementation, and operation

  - o Access to data and samples for any database project will be granted only after rigorous scientific peer review and specific *new* IRB approval

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Research Using MVP Database

Research Using MVP Database

- **Identification and validation of genomic associations**

- **Genomic customization of treatment – observational studies to be validated by clinical trials (including trials conducted by the VA Cooperative Studies Program)**

- **Population surveillance (illnesses following deployment, for example)**

- **Studies validating the effectiveness of using genomic data in the healthcare system**

Using MVP Database Research Approaches to Validation

- **Observational Studies**

  o Retrospective and prospective database analysis

  o Natural experiment but confounding factors and bias are issues

  o Stratification, Regression analysis, Case control, Matching, Propensity scores, Instrumental variables, etc

- **Randomized Clinical Trials**

  o Trials performed under strict "laboratory" conditions

  o Confounding factors addressed by randomization

  o Rigorous but limits in generalizability and applicability of RCT protocols and issue of expense and time

- *Point of Care Research – Hybrid being piloted in VA*

  o Natural experiment with randomization

  o How VA can contribute to general research capability

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Point of Care Research

- **Research designed to randomize clinical choices within the healthcare system at Point of Care**

  o *Choices that are part of care but have equipoise*

- **At Point of Care, when a patient identified by MVP software sees clinician, EHR reminder will inform that patient is a suitable research subject**

- **Clinician in routine visit decides whether the patient so identified should be randomized and, if so, enters the patient into the study**

- **Randomized study is then conducted by the patient's clinician within the healthcare system using healthcare system resources and with findings recorded in patient's EHR**

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Point of Care Research Examining Use of Genomic Data

- **Point of Care Research examining use of genomic data** *Hypothetical example - Decision-making via genetic testing when initiating Warfarin therapy*

- **Arms of study might be**
  - Hospital laboratory initiation and monitoring follow-up with *clinician-determined dosing*
  - Hospital laboratory initiation followed by home PT monitoring with *clinician-determined dosing*
  - Hospital laboratory initiation with clinician-determined dosing followed by hospital lab monitoring with *computer-assisted dosing*
  - Hospital laboratory initiation followed by home PT monitoring with *computer-assisted dosing*
  - *Initial dosing using genetic testing, followed by any of above*

- **Direct healthcare system data obtained**

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Issues to Consider

- **Technical issues with regards to specimen handling and analysis**
- **Issues associated with data sharing**
- **Return of research results to Veterans**
- **Implications for health care systems**

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Specimen Handling and Analysis

- **The cost of whole genome sequencing is dropping rapidly. Should VA make sequencing the "standard for analysis?"**
  - o Level of coverage? (80%, 90%, more?)
  - o Depth of sequencing (40X, 200X?)
  - o Cost vs. value?
  - o Begin now or wait for lower costs and increased reliability?

- **How should VA approach the issues of providing specimens to researchers, or instead the resulting data?**

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Data Sharing

- **How can VA make data from MVP widely available to the community while protecting Veterans?**

Re-identification Risk

- **What risks of re-identification must be mitigated to provide individualized genomic information and/or health record information to the research community?**

Return of Results

- **Should VA develop a strategy that would allow return of individualized results to Veterans?**

Implications for Health Care Systems

- **How can health care systems prepare to deal with a possible deluge of information?**

Conclusions

- **The Million Veteran Program will create a substantial database of genomic and healthcare data**

- **Research deriving from this database at all levels of study will address issues for the benefit of Veterans and all Americans**

- **VA has the appropriate assets, has created an infrastructure and has established a logistical structure to accomplish these ends**

- **Database enrollment is proceeding well**

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