Million Veteran Program

Part I: Development & Use of Database

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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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• MVP will facilitate
  o Developing new diagnostic tests to enable disease prevention and earlier treatment
  o Personalize therapies to the Veteran's individual genetic characteristics and conditions, e.g. Pharmacogenomic customization
  o 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
  o Link genotype to phenotype
  o Complex, adult, multi-gene diseases possibly with strong environmental influences

• VA assets
  o Large HCS, Electronic Health Record, research embedded in clinical program

• Large population with substantial diversity
  • Enables rigorous examination of a variety of subpopulations
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
Genomics Survey Findings

• With VSO and Veterans’ collaboration, internet survey performed April 24 – May 5, 2008
  o N = 931

• 83% said program should be done

• Increased support associated with
  o Attitudes about research
  o Attitudes about helping and history of previous “altruistic behaviors”
  o Curiosity about genetics
  o Satisfaction with VA healthcare

• Important issues
  o Privacy
  o Safeguarding data
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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
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
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
Validating Use of Genomic Data in Healthcare
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
Point of Care Research

• Research designed to randomize clinical choices within the healthcare system at Point of Care
  - 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
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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Part II: Questions for Discussion

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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
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?
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