State of the Art in Data Management for Precision Medicine & Genomics

March 8, 2017
2 pm – 3 pm ET
Housekeeping Issues

• All participants are muted
  • To ask a question or make a comment, please submit via the chat feature and we will address as many as possible after the presentations.

• Audio and Visual is through www.readytalk.com
  • If you are experiencing technical difficulties accessing audio through the web, there will be a dial-in phone number displayed for you to call. In addition, if you have any challenges joining the conference or need technical assistance, please contact ReadyTalk Customer Care: 800.843.9166.

• Today’s slides will be available for download on the eHI Resource page at:
  https://www.ehidc.org/resources/eventsummaries
Agenda

• Welcome and Introductions
  – Claudia Ellison, Program Director, eHealth Initiative

• Discussion & Comments
  – Virginia Balcom, Vice President, PHEMI Systems
  – Jim Buntrock, Vice Chair of Information Management and Analytics, Mayo Clinic
  – Josh Peterson, MD, MPH, Vanderbilt University School of Medicine
  – Paul Terry, MD, CEO and CTO, PHEMI Systems

• Questions & Answers
Overview of eHealth Initiative

• Since 2001, eHealth Initiative (c6) and the Foundation for eHealth Initiative (c3) have conducted research, education and advocacy to demonstrate the value of technology and innovation in health.

• Serve as the industry leader convening executives from multi-stakeholder groups to identify best practices to transform care through use of health IT.

• The missions of the two organizations are the same: to drive improvement in the quality, safety, and efficiency of healthcare through information and technology.

• Our work is centered around the 2020 Roadmap. The primary objective of the 2020 Roadmap is to craft a multi-stakeholder solution to enable coordinated efforts by public and private sector organizations to transform care delivery through data exchange and health IT.
Roadmap to Transforming Care

- RESEARCH
  Information Gathering, Surveys, Interviews

- CONVENE
  - Exec Roundtables, Committees, Webinars, Workgroups

- OUTPUTS & RECOMMENDATIONS
  Guidance, Education, Reports
eHealth - Convening Executives to Research & Identify Best Practices

- Data Analytics
- Data Access and Privacy
- Interoperability
- Patient and Provider Technology Adoption
Together Facing the Challenges of Change. eHealth Initiative’s 2017 Annual Conference & Member Meetings will bring together the most influential leaders from across the healthcare spectrum to discuss critical issues related to the use of data and technology to improve healthcare for all Americans.

www.ehidc.org/events
State of the Art in Data Management for Precision Medicine & Genomics

An eHI research report highlighting the issues, strategies, and challenges being faced by innovators in precision medicine and genomics. The findings shared in this report provide insight on how clinical and genetic data is used and managed, as well as the challenges providers face in genomics research and precision medicine.

Virginia Balcom
PHEMI Systems
vbalcom@phemi.com
Agenda

- Highlights from the Report
- Precision Medicine Initiatives at the Mayo Clinic
- Precision Medicine Initiatives at Vanderbilt University
- Common data challenges in Precision Medicine
- Questions and Answers
Our Guest Speakers

Jim Buntrock
Vice Chair of Information Management and Analytics
Mayo Clinic

Josh Peterson, MD, MPH,
Vanderbilt University School of Medicine

Dr. Paul Terry
CEO & CTO
PHEMI Systems
The Study

- Providers were identified based on criteria that assesses their involvement in genomics research and use.
- Interviewed by eHI to share insights on how they are using big data, their involvement with genomics and precision medicine, and what challenges they are facing in managing, storing, using and analyzing the data.
- Study Objectives
  - To understand the state of data management in precision medicine from research to clinical implementation.
  - To understand if organizations are adopting newer technologies (Hadoop, others) to handle the data demands of precision medicine.
State of the Art in Data Management for Precision Medicine & Genomics

Study Findings – Innovators leveraging clinical and genomics data to strengthen core competency of caring for the patient

• All of those interviewed are interested in incorporating precision medicine to bring genomics to the point of care
• Providers are **just starting** to integrate genomics into clinical practice
• Providers understand that simply collecting genomic data is inadequate and that to derive value from it, they **must turn the data into knowledge** that informs clinical decisions and allows them to deliver personalized care.
Study Findings – Diverse Use Cases Emerging as Pioneering Providers find new ways to derive value from genomic data

Genetic underpinnings of disorders, using DNA, plasma, and serum samples from more than 40,000 patients

- Predict patients likely to develop cancer for early intervention
- Use adverse drug reactions to infer associations between metabolic pathways, drugs, and acquired disorders
- Matching genes to drugs targeted to that gene for oncology decision support
- Use age-related macular degeneration risk factors for prevention
- Intermediate decision support with gene annotations
- Immunotherapy at proteomic level
- Reporting, benchmarking, predictive analytics

**Precision Medicine Initiative Cohort**
1 million+ volunteers

- Inform medication prescription, based on relationship between adverse events and genetic variants
- Analyzing very large datasets to identify clinically significant genetic variations
- Use metabolic pathways, drugs, and acquired disorders
- Medical devices and monitors

**Moon Shots**
>165 immunotherapy clinical trials
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Study Findings – The Top Data Management Challenges Providers are Facing

- Increasing participation in clinical trials
- Moving from competing to collaborating – sharing data
- Exploring new data storage solutions, such as cloud
- Adopting new technologies: Hadoop
- Managing patient registries
- Acquiring data in a ready state for analysis
- Extracting value from unstructured data, non-clinical data, and leveraging metadata
- Balancing privacy, appropriate de-identification, and clinical and research needs
- Managing risk, management, privacy, and security
- Making data available for real-time clinical support
- Shortage of specialized skills, especially data science skills
- Better tools needed to make the most use of big data.
- Interoperability with EMRs

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Data Management and Analytic Strategies
Mayo Clinic Center for Individualized Medicine

eHealth Initiative

James Buntrock
Vice Chair, Information Technology
Mayo Clinic
Disclosures

- Mayo Clinic works with several health information technology companies
- Mayo Clinic is evaluating PHEMI technology

About me,
- I am a technologist.
- I am not a clinician, geneticist, bioinformatician, or molecular biologist.
The Center for Individualized Medicine will **integrate, develop** and **deploy** new individualized medicine **products and services** that continually differentiate our practice **for every life Mayo touches**.
Translational Programs
From Promise to Practice

Microbiome
Epigenomics
Pharmacogenomics
Biomarker Discovery

Clinomics
Need for a robust **Infrastructure**

- Biobank & Biorepositories
- Sequencing
- Information Technology
- Biomedical Ethics
- Education
- Biomedical Informatics
Genomics Processing – High Level

- **Sequencing**
  - Data Generation
- **Primary**
  - Base calling
  - QC
- **Secondary**
  - Assembly
  - Alignment
  - Annotations
- **Tertiary**
  - Annotations
  - Visualization
  - Statistics
- **Interpretation/Reporting**
  - Research
  - Clinical

IT Infrastructure/Data Management
(Storage, Workflow, Compute, Interfaces, Delivery)
# Aspects of Clinical Application of Genomics

## Patient / Provider Centered
- Specialty Clinics
- Per Visit/Test Functionality
- Visualization for Provider and Patient
- Multi-Provider Role (Generalist, Geneticist, Oncologist, Specialist)
- Focus deployment

## Big Data / Large Scale Data Management
- Large Data sets
- Storage and management of trillions of variants
- Cross-patient inquiry
- Lab Management

## Related Areas
- Analytic Dashboard
- Biomarker Discovery
- System of Record
- Unique Service Delivery
Advanced Diagnostic
Individualized Medicine Clinic

Bringing it all together ...
Systems of Genomic Medicine: Pharmacogenomics at VUMC

State of the Art in Data Management for Precision Medicine and Genomics

Josh F. Peterson, MD, MPH
March 8th, 2017

Associate Professor
Department of Biomedical Informatics
Department of Medicine
Vanderbilt University Medical Center

No conflict of interest disclosures
Managing Wave of Genomic Data
PREDICT Pharmacogenomics Model

Target Clinics

Prognostic Flag for Testing

Preemptively Tested

Reactive/Indication Testing

Genotyped for PREDICT

Genotyping

Genetic Risk

Clinical Application

CYP2C19 Variant

TPMT Variant

VKORC1 + CYP2C9

CYP3A5 Variant

Clopidogrel

Thiopurines

Warfarin

Tacrolimus

Has genetic risk variant

Exposed to new or recent prescription
Clinical Workflow

VUMC returning patient
Male, age 60
BMI = 34
Prior history of hypertension and atrial fibrillation

During clinic appointment, provider is notified in EMR that patient is likely to be prescribed target drug within 3 years and thus benefit from genotype-tailored prescribing.

PREDICT test ordered and genotype results delivered to EMR

Clopidogrel sensitivity: Poor Metabolizer – Reduced Antiplatelet Effect – gene result CYP2C19 *2/*3

1 year later

When writing Rx for clopidogrel, cardiologist caring for a patient after a stent is alerted in the e-prescribing system that patient is a poor metabolizer.

Patient leaves clinic appointment with Rx for appropriate drug.
Nomenclature and Interpretations

Tacrolimus and CYP3A5 interaction

<table>
<thead>
<tr>
<th>Gene</th>
<th>Nucleotide variation(^a):</th>
<th>Effect on CYP3A5 protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP3A5</td>
<td>6986A&gt;G 31611C&gt;T</td>
<td>Splicing defect</td>
</tr>
</tbody>
</table>

This result signifies that the patient has two copies of a non-functional allele (*3). Patients with this genotype are expected to require **standard tacrolimus dosing**. Please consult a clinical pharmacist for more specific dosing information.
Antiplatelet Drug Selection
Within E-Prescribing and Based on CYP2C19 variant

Drug-Genome Advisor
Intermediate Metabolizer - clopidogrel (Plavix) - Rare Risk Allele
Substitution recommended due to increased cardiovascular risks

If not otherwise contraindicated:
- Prescribe prasugrel (Effient) 10 mg daily
  - **Prasugrel should not be given to patients:**
    - history of stroke or transient ischemic attack
    - $\geq$ 75 years of age [Current patient age: 51]
    - with body weight $< 60$ kg [Current patient weight: 59.0 kg as of 10/12/2012]
- Prescribe ticagrelor (Brilinta) 90 mg twice daily
  - **Ticagrelor should not be given to patients:**
    - history of severe hepatic impairment
    - intracranial bleed

- Continue with clopidogrel (Plavix) prescription
  - **Primary override reason:**
    - Contraindicated for prasugrel or ticagrelor
    - Potential side effects
    - Provider/Patient opts for clopidogrel
    - Cost

Evidence Link

https://cdskb.org/
Warfarin Recommended Initial Dosing

This patient has been tested for CYP2C9 and VKORC1 genetic variants that can affect a patient's warfarin dosing requirements. The following dosing algorithm uses genetic and other patient information to estimate a weekly warfarin dose. This dosing recommendation ONLY applies to NEW starts of warfarin. If the patient has previously taken a stable dose of warfarin, please disregard this dosing recommendation.

- **Age:** 56
- **Weight (kg):** 77.1
- **Height (cm):** 175.3
- **Genetic Variants:** VKORC1 a/a; CYP2C9 *2/*2

Is the patient currently taking amiodarone? No
Is the patient currently taking Phenytoin, Rifampin, or Carbamazepine? No

**Recommended WEEKLY starting dose of warfarin: 16.8 mg/week**

The DAILY equivalent of this recommended starting dose is 2.4 mg/day.

NOTE: Further dose adjustments may be necessary due to other clinical factors, such as diet and other interacting medications (e.g., antibiotics or antifungals). This algorithm ONLY considers age, height, weight, genetic factors, and select medications (amiodarone, rifampin, phenytoin, and carbamazepine).

[Help me decide the tablet size and number of tablets per day](Evidence Link/View Algorithm)
PREDICT Results in the Patient Portal

Personalized Medicine

Each person responds differently to medicines. Your genes play a role in how you respond to medicines. Based on your history, your provider has ordered a test to learn more about which drugs are right for you. Having this information can help predict and prevent bad drug side effects.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Does your genetic test result affect your response to medicines?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel/Plavix®</td>
<td>Yes</td>
</tr>
<tr>
<td>Simvastatin/Zocor®</td>
<td>Yes</td>
</tr>
<tr>
<td>Tacrolimus®</td>
<td>Yes</td>
</tr>
<tr>
<td>Thiopurine Therapy®</td>
<td>Yes</td>
</tr>
<tr>
<td>Warfarin/Coumadin®</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The Clopidogrel Test

Show less >

Clopidogrel (sounds like "kloh-PID-oh-gral") is a blood thinner used to prevent clots that can cause a heart attack or stroke. Your genes can affect how well the drug works. This genetic test identifies how well you may respond to clopidogrel.

Your Risk

Show less >

Sometimes clopidogrel does not prevent harmful strokes or clots as well as it should because of your genes. Your provider, often with the results of a lab test, can determine if clopidogrel is the right medicine for you.

The results of your test show that you have two versions of the gene that may put you at increased risk for this negative outcome.

More About Clopidogrel

Show more >

More About Your Risk

Show more >
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Integrating a Wide Variety of Heterogeneous Data

Molecular You Solution
- Early warning system
- Prevent, delay, mitigate
- Quarterly molecular screening
- Grow to 25,000 patients
- 15+ varied data sources
- Integrate “omics” with clinical data
- Longitudinal study
Ability to Extract Data from Complex Data Sources

Semi-Structured

XML Lab Results Reader

Structured

<table>
<thead>
<tr>
<th>Name</th>
<th>Visibility</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Non PHI</td>
<td>4.82</td>
</tr>
<tr>
<td>Patient PHN</td>
<td>PHI</td>
<td>994-859-9326</td>
</tr>
<tr>
<td>Collection Date</td>
<td>Non PHI</td>
<td>2013-02-06</td>
</tr>
<tr>
<td>Facility ID</td>
<td>Non PHI</td>
<td>BCB Van East</td>
</tr>
<tr>
<td>Patient Name</td>
<td>PHI</td>
<td>Sullivan, Ian</td>
</tr>
</tbody>
</table>

Source File

Data Processing Function

Analytics-Ready Digital Assets
Interactive Genomic Analytics

- Annotate known genetic variations using reference data sets (ClinVar, dbSNP, UCSC Known Genes)
- Join genotype data with clinical data collections and omics reference data
- Analyze data using PHEMI’s Genomics API
- Build interactive visualization using Zeppelin notebooks
- Use Spark API & Machine Learning library for advanced analysis and modeling
- Export to R & Bioconductor or external databases
Integration of Data Science Tools

- Predictive Modeling
- Risk Modeling
- Anomaly Detection
- Categorization
- Semantic Analysis
- Natural Language Processing, etc.
Discussion

Jim Buntrock
Vice Chair of Information Management and Analytics
Mayo Clinic

Josh Peterson, MD, MPH,
Vanderbilt University School of Medicine

Dr. Paul Terry
CEO & CTO
PHEMI Systems
Thank you for Participating

For more information about eHI and its programs and services, please go to our website at www.ehidc.org or please contact:

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Slides are available at [www.ehidc.org/resources](http://www.ehidc.org/resources)