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**

eHEALTH INITIATIVE

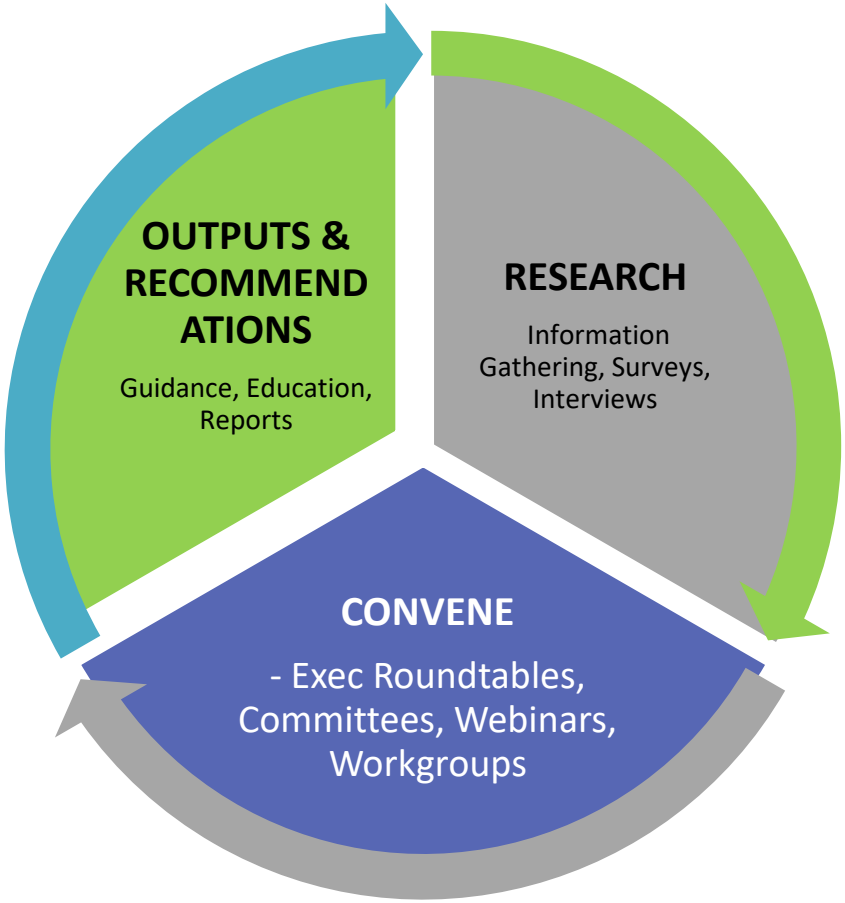
Agenda

- **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



eHealth - Convening Executives to Research & Identify Best Practices

- Data Analytics
- Data Access and Privacy
- Interoperability
- Patient and Provider Technology Adoption

eHI Member Meeting & Executive Networking
March 21 – 23, 2017

House of Sweden, 2900 K Street, N.W., WDC

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.

PHEMI® Big Data. Shared. Simply. Securely.

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

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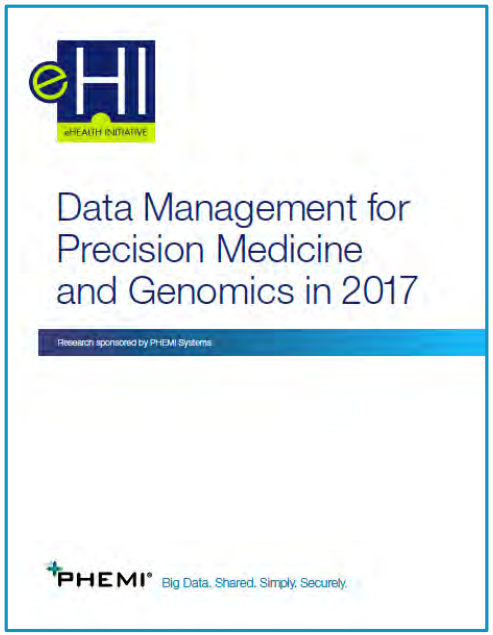
State of the Art in Data Management for Precision Medicine & Genomics

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

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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.

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

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

D3b
Center for Data-Driven Discovery in Biomedicine
addressing pediatric cancer

Use **adverse drug reactions** to infer associations between metabolic pathways, drugs, and acquired disorders

medical devices and monitors

Precision Medicine Initiative Cohort
1 million+ volunteers

Matching genes to drugs targeted to that gene for oncology decision support

Inform medication prescription, based on relationship between adverse events and genetic variants

Analyzing very large datasets to identify clinically significant genetic variations

Use age-related macular degeneration risk factors for prevention

Intermediate decision support with gene annotations

Moon Shots
>165 immunotherapy clinical trials

Immunotherapy at proteomic level

Reporting, benchmarking, predictive analytics

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

Study Findings – The Top Data Management Challenges Providers are Facing

- Increasing participation in clinical trials
- Moving from competing to collaborating – sharing data

- Acquiring data in a ready state for analysis
- Extracting value from unstructured data, non-clinical data, and leveraging metadata

- Exploring new data storage solutions, such as cloud

- Balancing privacy, appropriate de-identification, and clinical and research needs
- Managing risk, management, privacy, and security
- Making data available for real-time clinical support

- Adopting new technologies: Hadoop
- Managing patient registries

- 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

3/8/2017

Disclosures

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

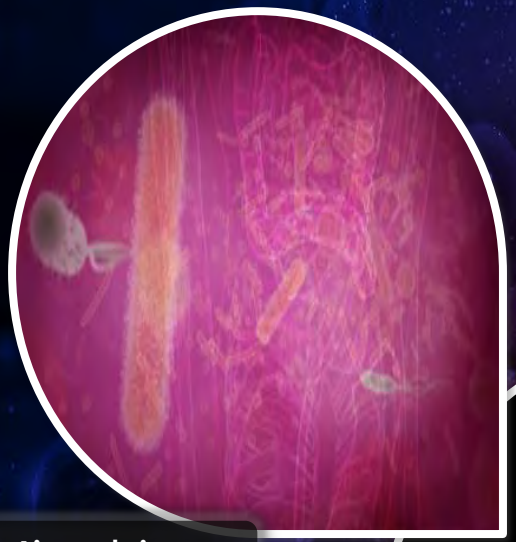
About me,

- I am a technologist.
- I am not a clinician, geneticist, bioinformatician, or molecular biologist.

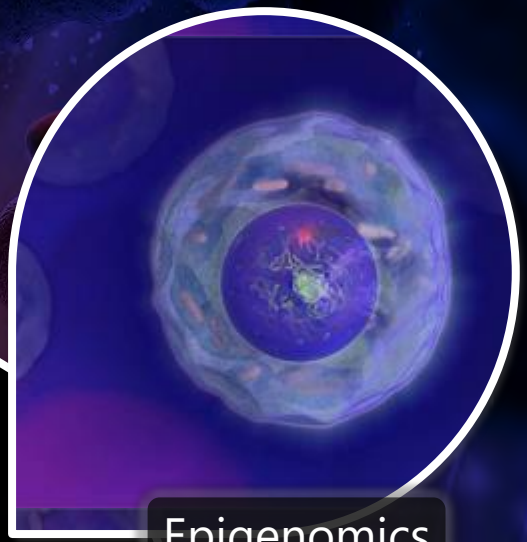
The Center for Individualized Medicine will ***integrate, develop*** and ***deploy*** new individualized medicine ***products and services*** that continually differentiate our practice ***for every life Mayo touches.***

Translational Programs

From Promise to Practice

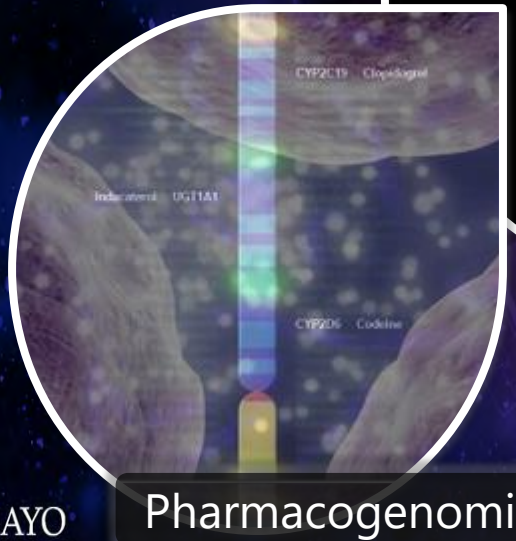


Microbiome



Epigenomics

Clinomics



Pharmacogenomics

Biomarker Discovery

The branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes

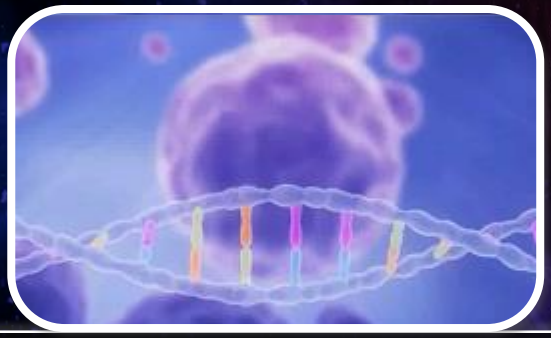
MAYO CLINIC

Need for a robust **Infrastructure**

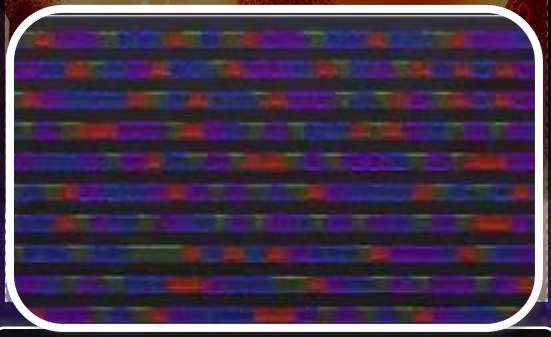
Biobank & Biorepositories

Biomedical Ethics

Education



Sequencing

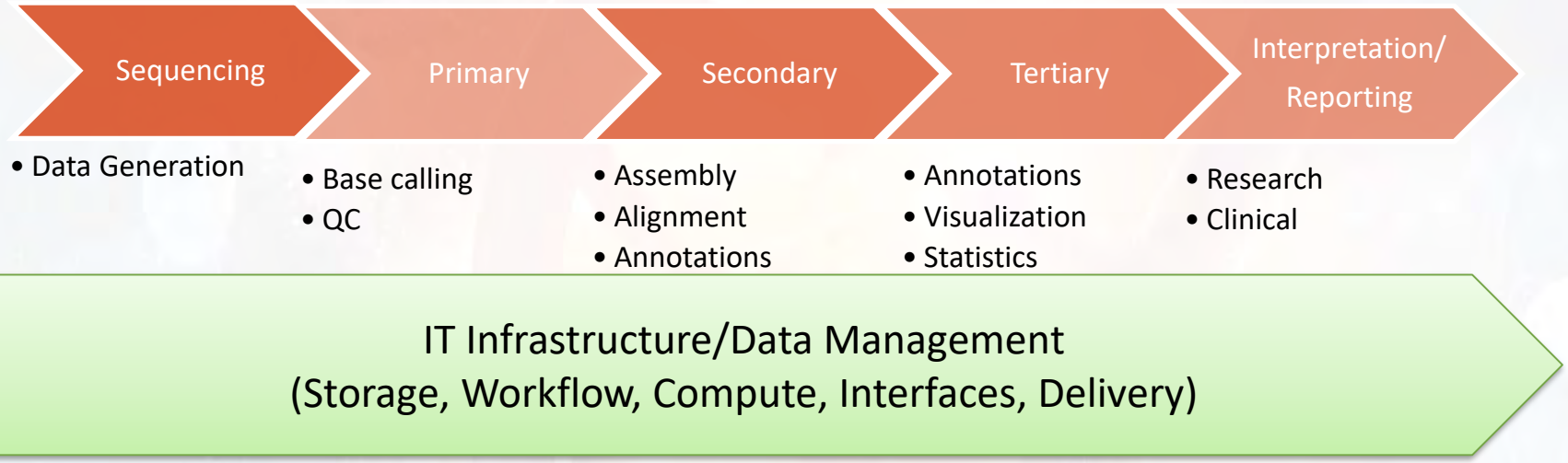


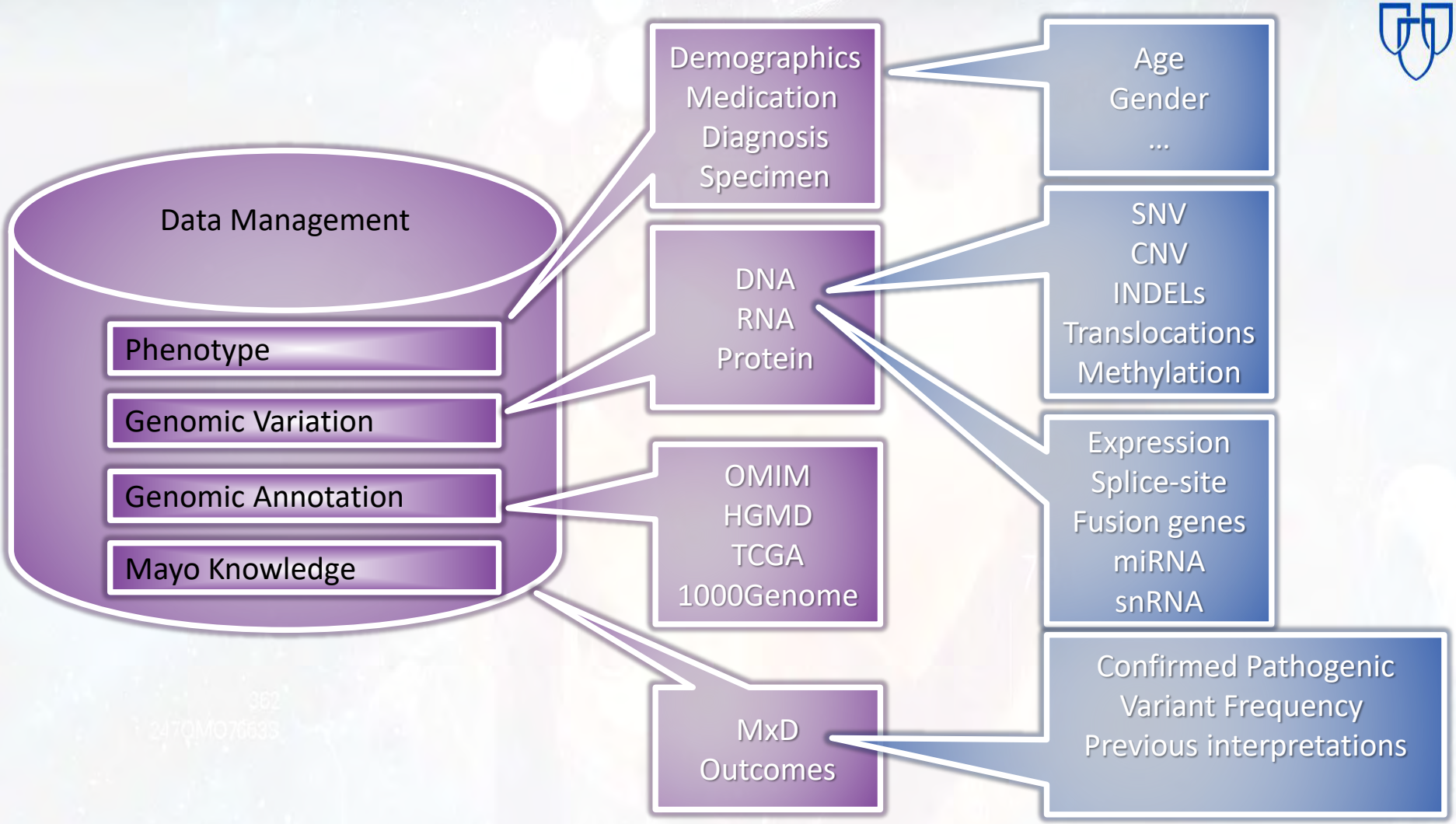
Information Technology

Biomedical Informatics

MAYO CLINIC

Genomics Processing – High Level




Data Management
Phenotype
Genomic Variation
Genomic Annotation
Mayo Knowledge
Demographics
Medication
Diagnosis
Specimen
DNA
RNA
Protein
OMIM
HGMD
TCGA
1000Genome
MxD
Outcomes
Age
Gender
…
SNV
CNV
INDELs
Translocations
Methylation
Expression
Splice-site
Fusion genes
miRNA
snRNA
Confirmed Pathogenic
Variant Frequency
Previous interpretations

Aspects of Clinical Application of Genomics

Patient / Provider Centered

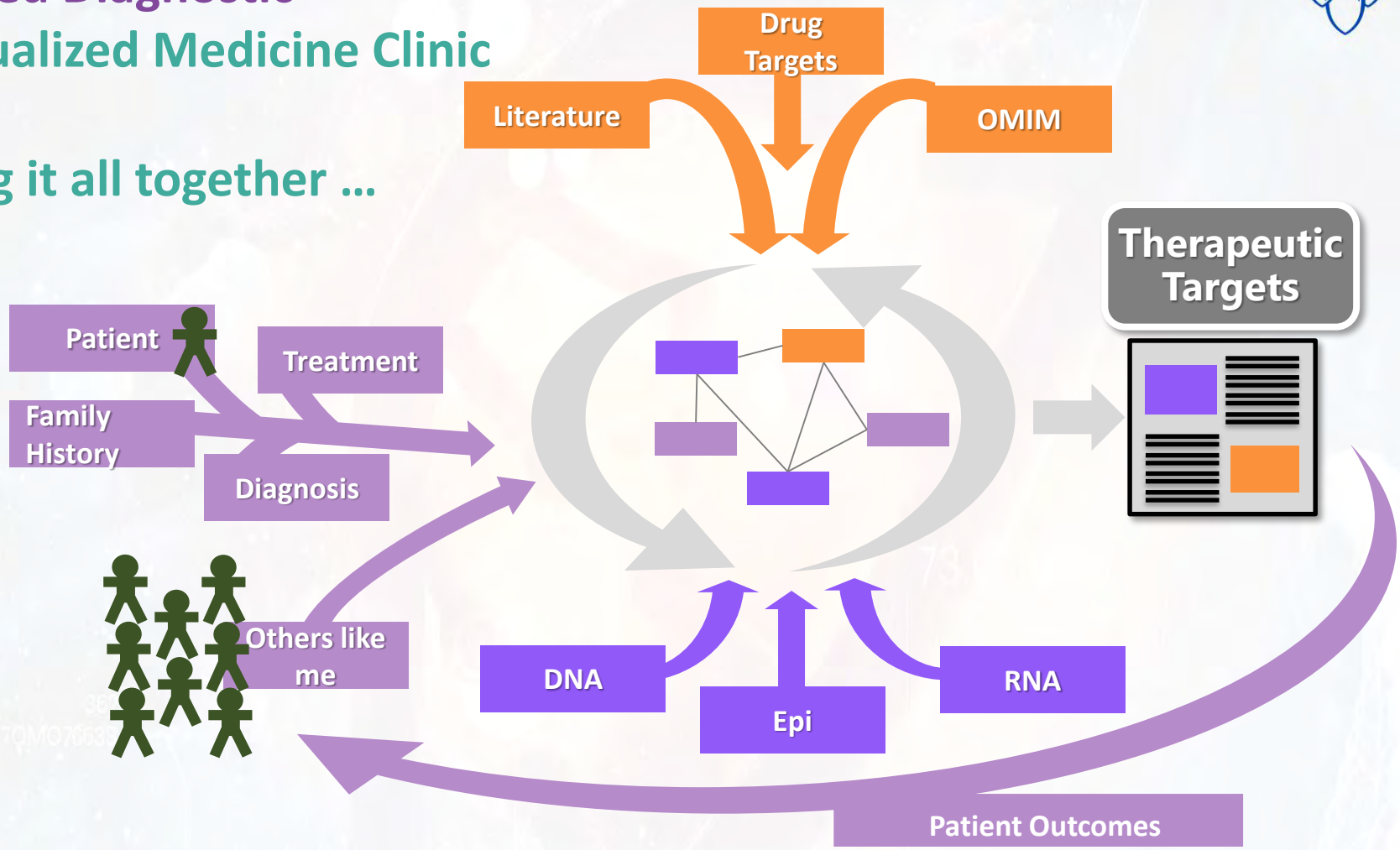
- Specialty Clinics
- Per Visit/Test Functionality
- Visualization for Provider and Patient
- Multi-Provider Role (Generalist, Geneticist, Oncologist, Specialist)
- Focus deployment

Big Data / Large Scale Data Management

Large Data sets	Analytic Dashboard
Storage and management of trillions of variants	Biomarker Discovery
Cross-patient inquiry	System of Record
Lab Management	Unique Service Delivery

Advanced Diagnostic Individualized Medicine Clinic

Bringing it all together …



Systems of Genomic Medicine: Pharmacogenomics at VUMC

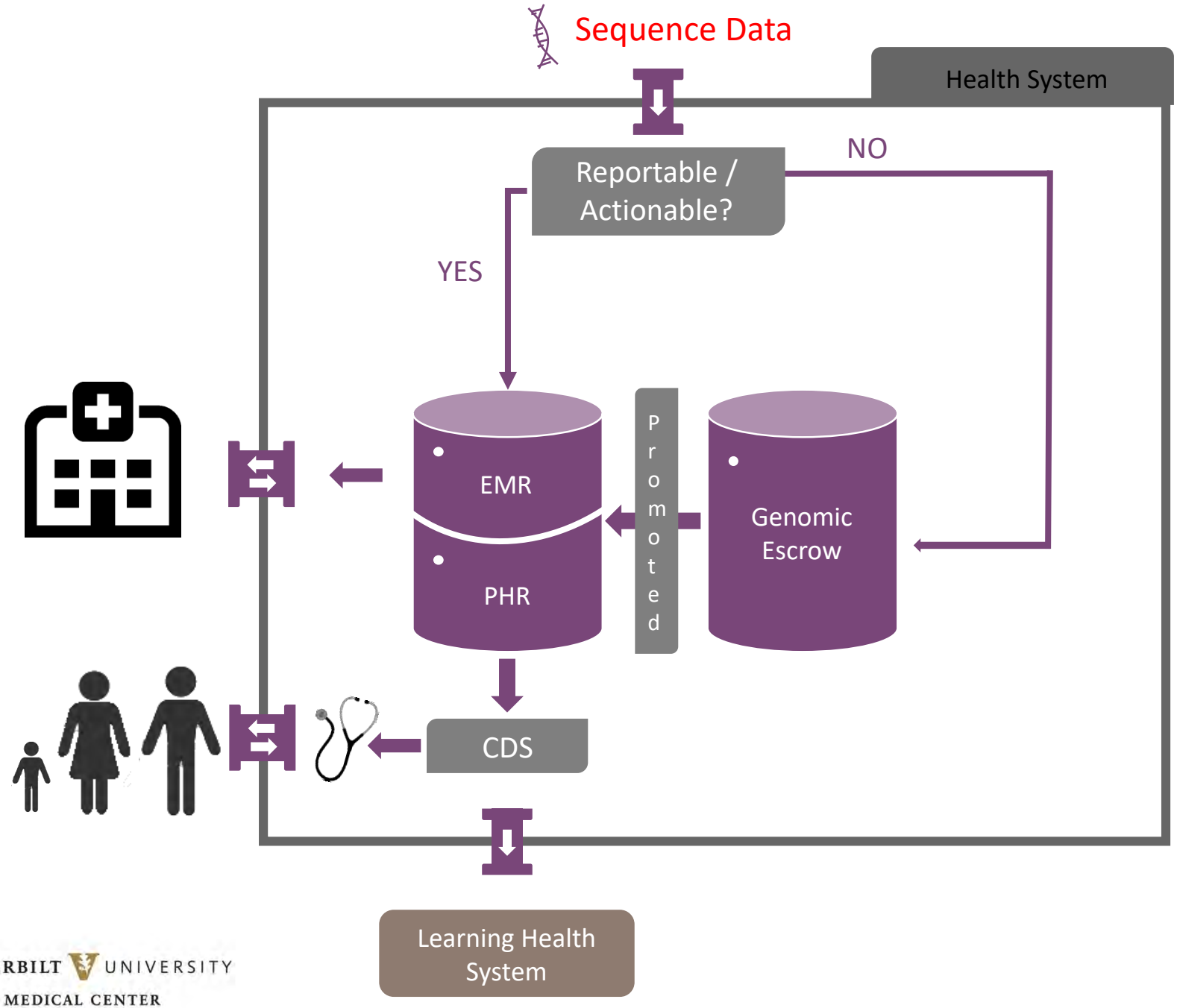
State of the Art in Data Management for Precision Medicine and Genomics

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



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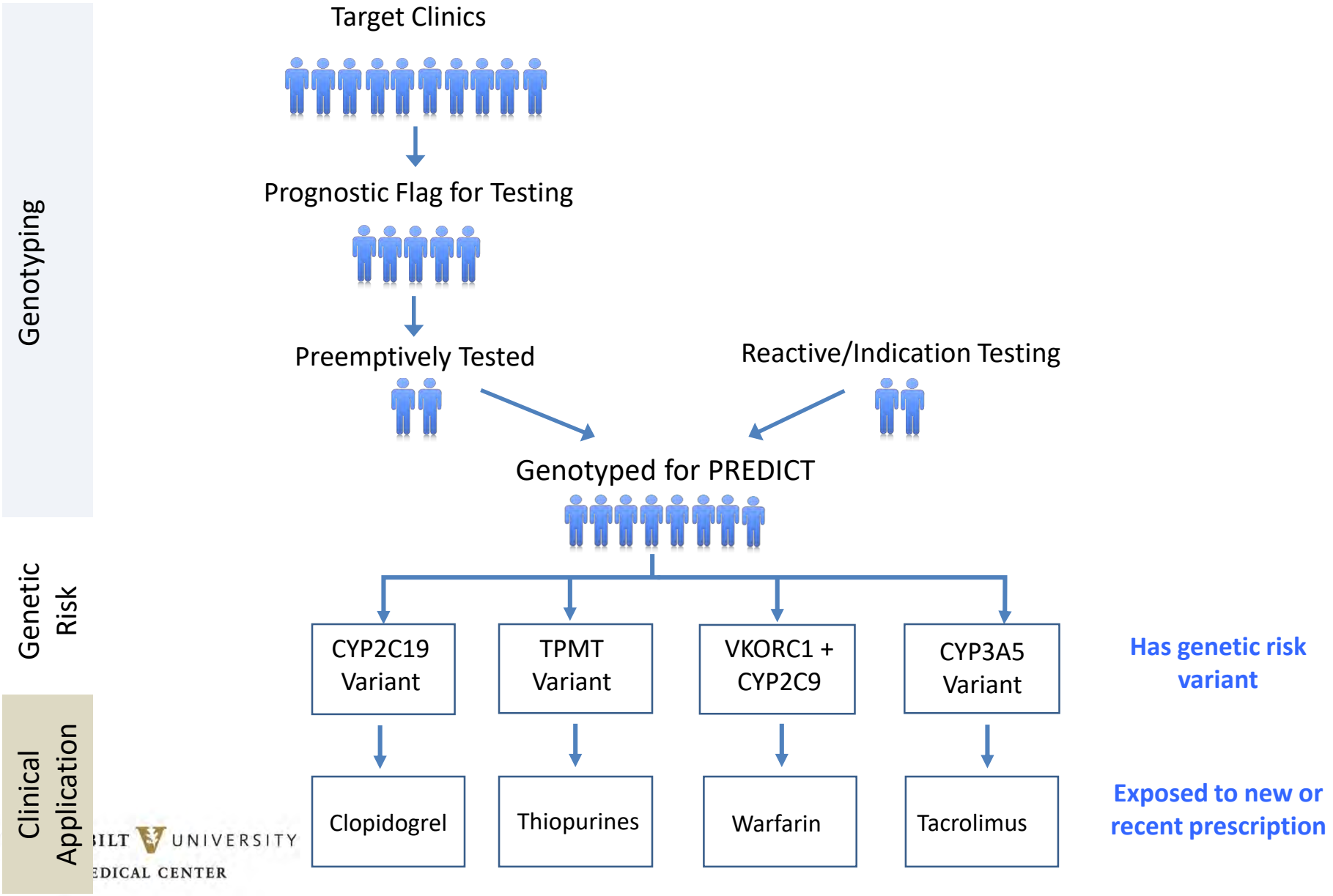
PREDICT Pharmacogenomics Model



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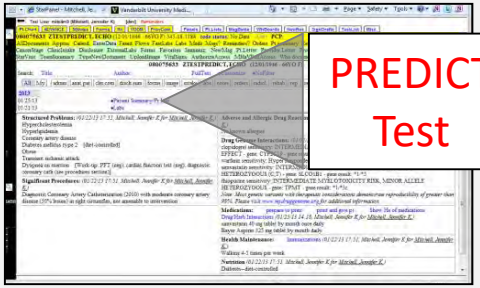
Clinical Workflow

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

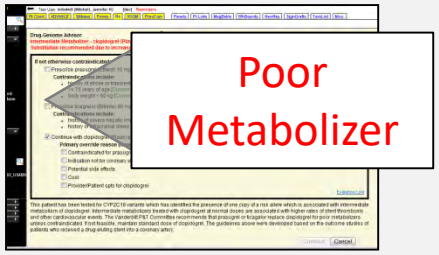


During clinic appointment, provider is notified in EMR that patient is likely to be prescribed target drug within 3 years and thus benefit from genotype-tailored prescribing.

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

Result

Gene	Nucleotide variation[a]:	Effect on CYP3A5 protein
CYP3A5	6986A>G 31611C>T	Splicing defect

Genotype & Phenotype

CYP3A5 *3/*3 → Tacrolimus Poor metabolizer

Interpretation

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
- >= 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

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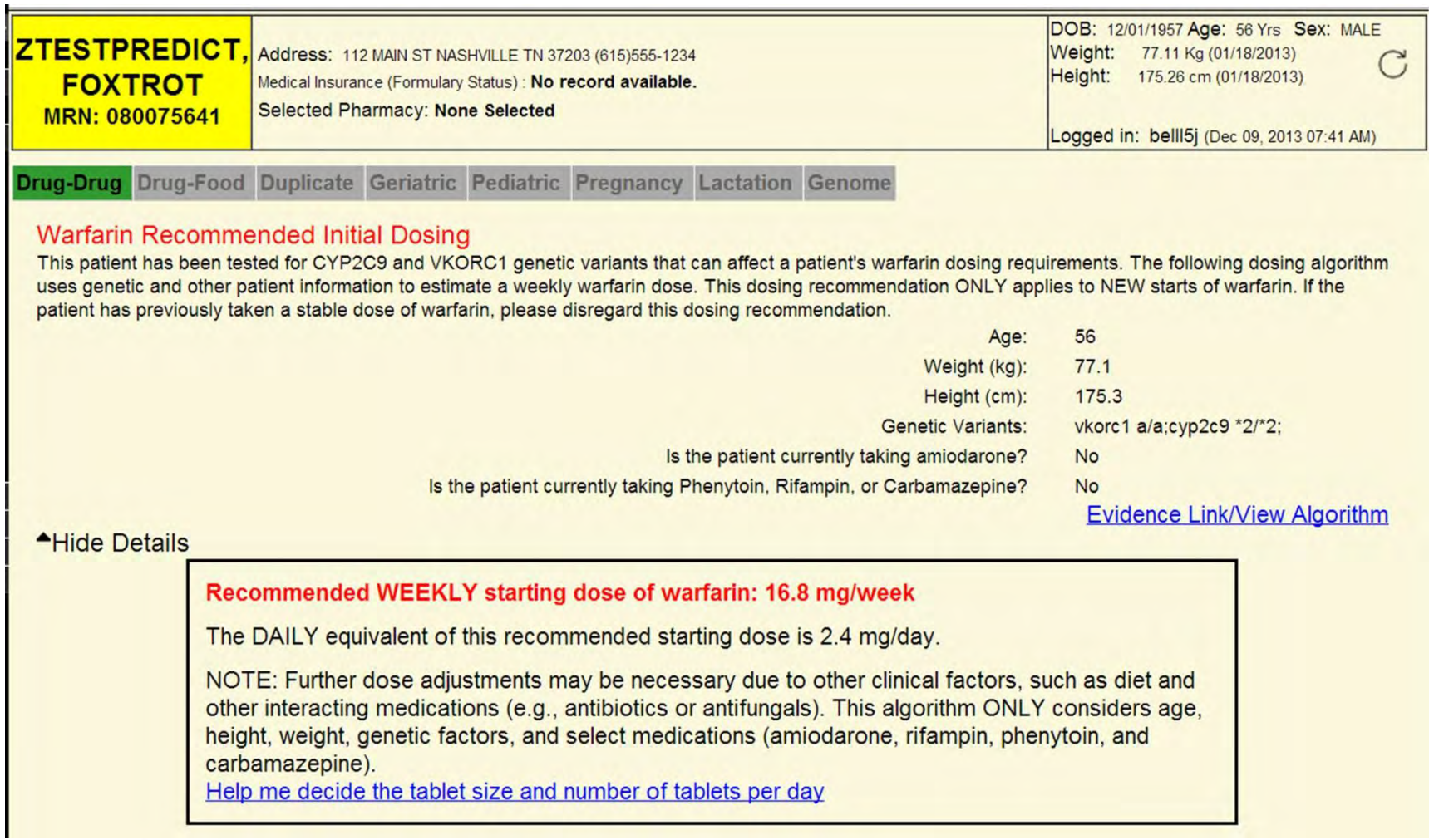
https://cdskb.org/

Warfarin Dosing Advisor



ZTESTPREDICT, FOXTROT
MRN: 080075641

Address: 112 MAIN ST NASHVILLE TN 37203 (615)555-1234
Medical Insurance (Formulary Status) : **No record available.**
Selected Pharmacy: **None Selected**

DOB: 12/01/1957 Age: 56 Yrs Sex: MALE
Weight: 77.11 Kg (01/18/2013)
Height: 175.26 cm (01/18/2013)

Logged in: bellI5j (Dec 09, 2013 07:41 AM)

Drug-Drug | Drug-Food | Duplicate | Geriatric | Pediatric | Pregnancy | Lactation | Genome

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

Evidence Link/View Algorithm

▲Hide Details

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

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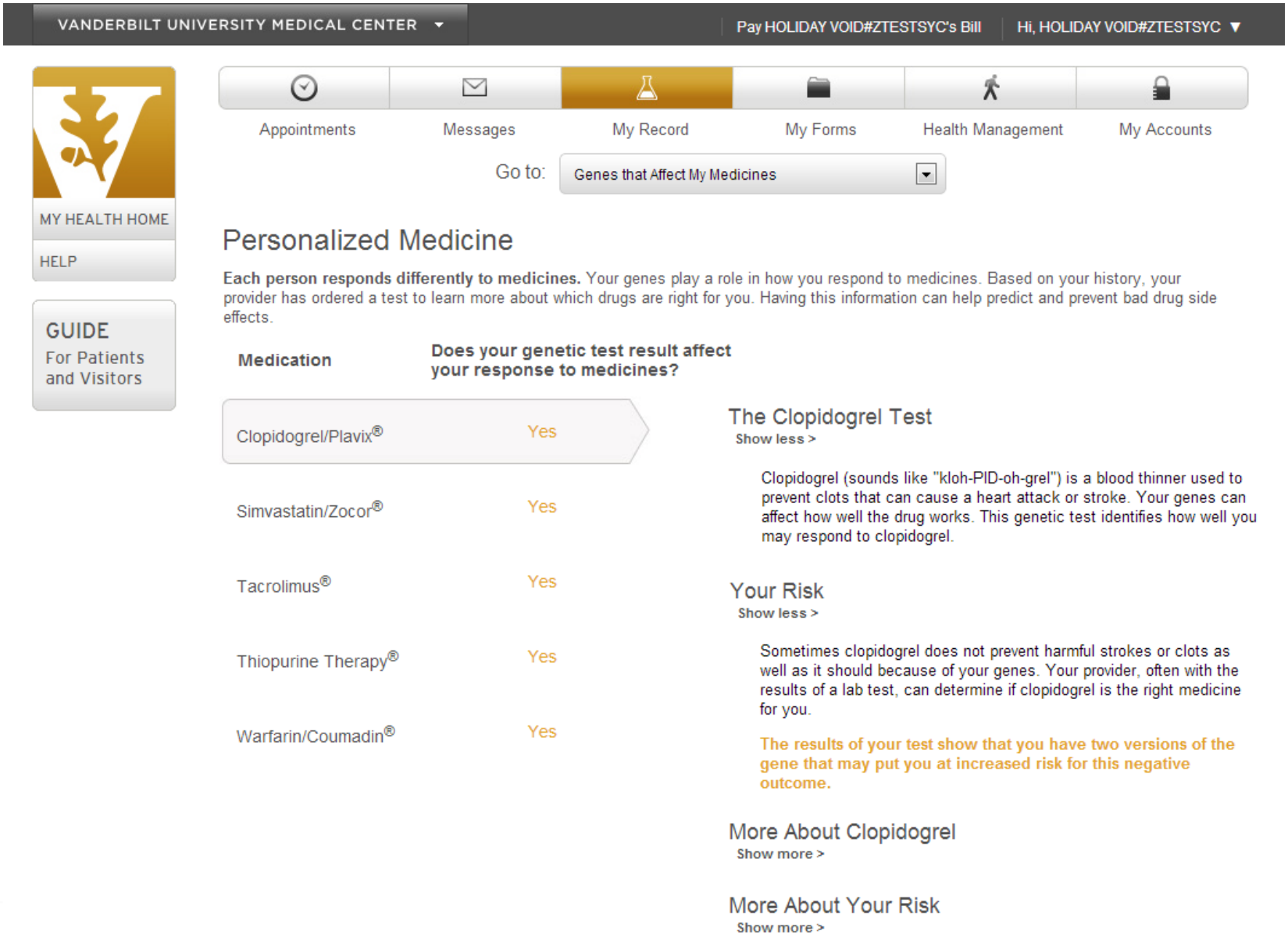
PREDICT Results in the Patient Portal



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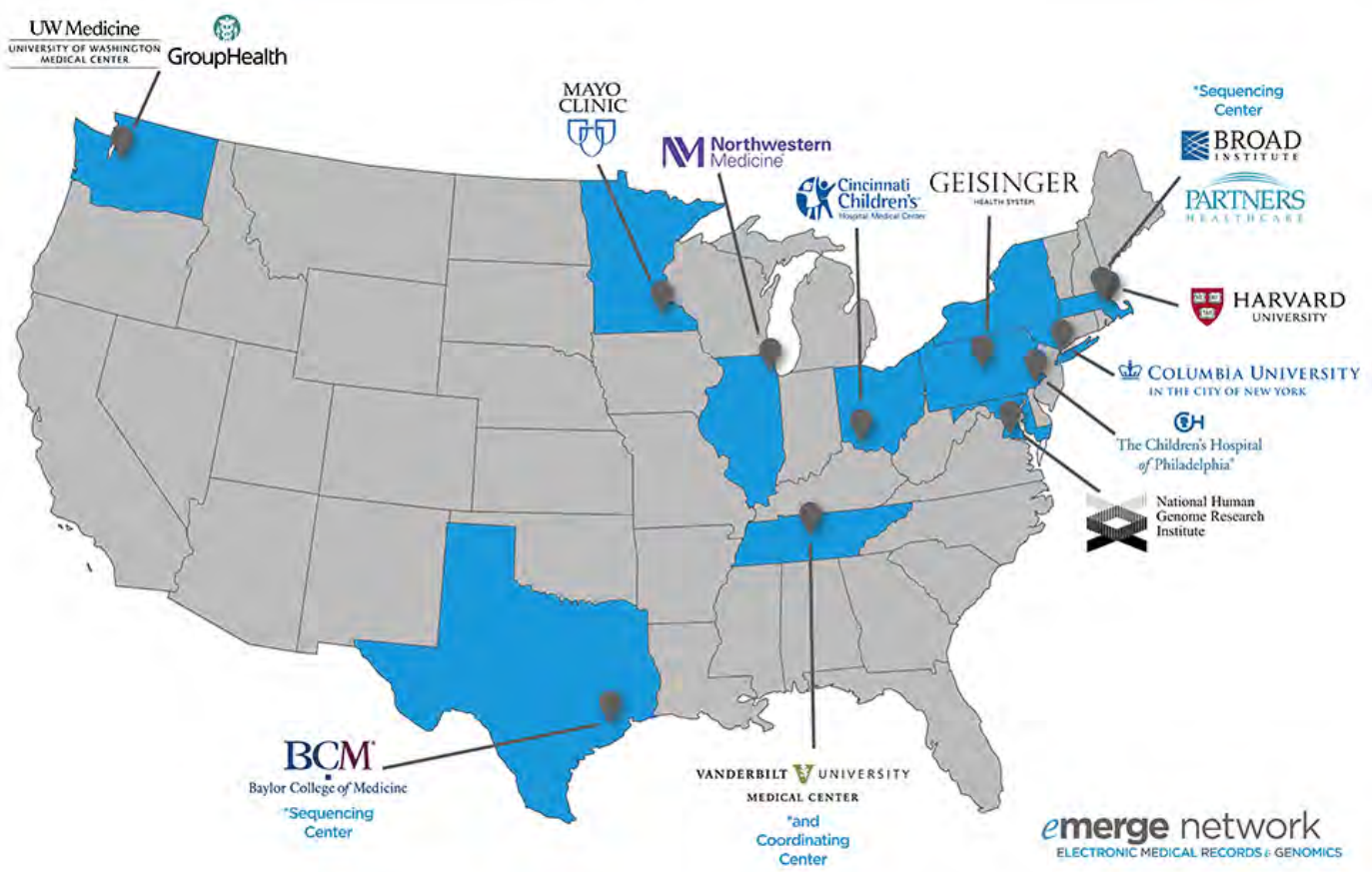
Genomic Medicine Case Studies

emerge network
ELECTRONIC MEDICAL RECORDS & GENOMICS



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https://emerge.mc.vanderbilt.edu

State of the Art in
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eHi research report highlighting the issues, strategies, and challenges being faced by innovators in precision medicine and genomics

The report will be sent to all registered attendees after the webinar.

Report Sponsored by

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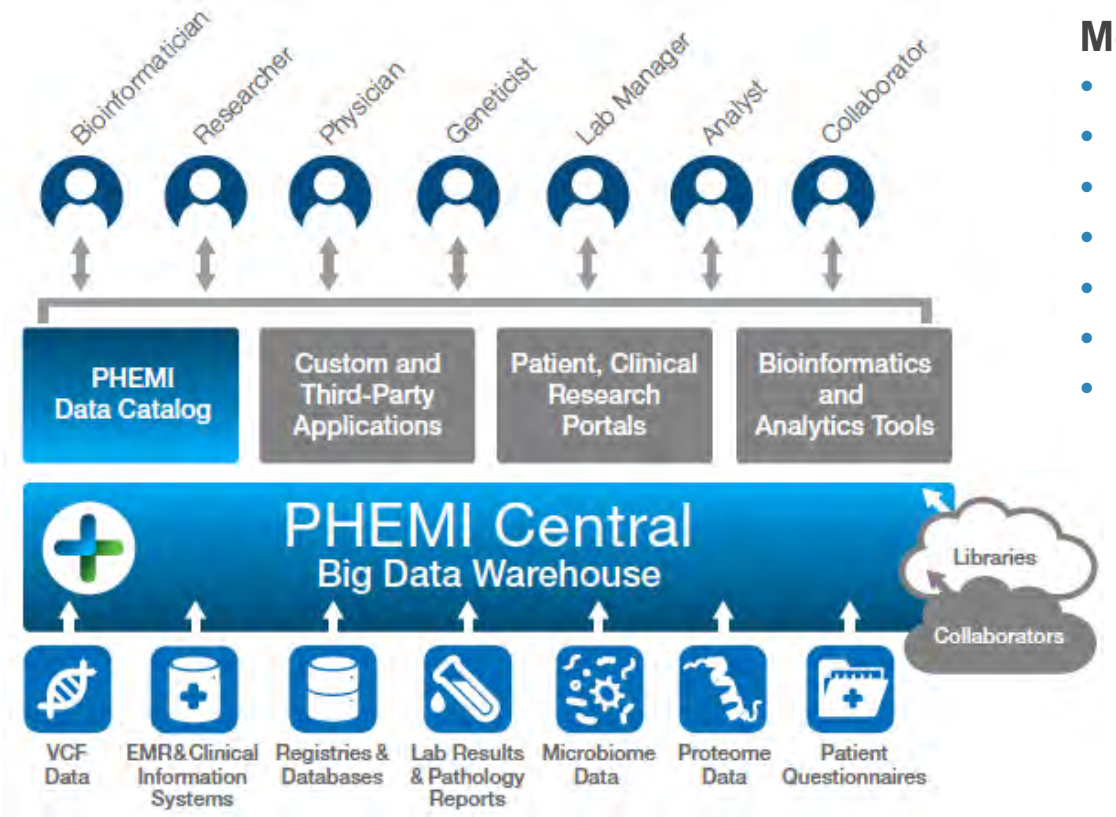
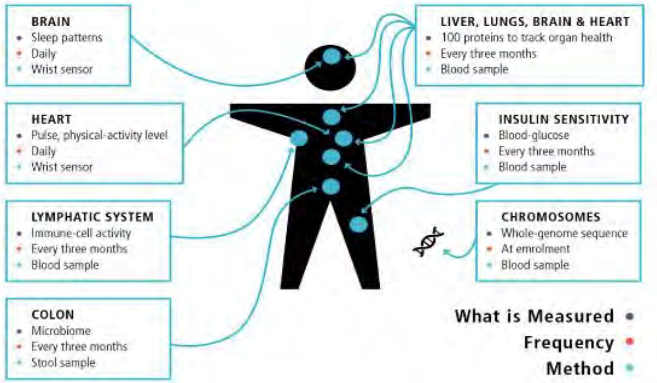
Integrating a Wide Variety of Heterogeneous Data



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



PHEMI

Ability to Extract Data from Complex Data Sources

Semi-Structured

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      ei="994859326"
      ln="Sullivan"
      fn="Ivan"/>
  <rq rk="1"
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      ocd="2003-02-09T01:39:59"
      rd="2003-02-12T13:42:25"/>
  <ph>
      <dr ty="or"
          name="Dr. Alan Shepard"
          id="4"/>
  </ph>
  <fa fi="BCB_VAN_EAST"
      fn="BC Biomedical East Vancouver"/>
  <ts si="CHEM">
    <tg ph="Investigation of Carbohydrate Metabolism">
        <lt ph="Glucose Tolerance">
            <ti ph="Glucose 1h"
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                tk="7916"
                hf="N">
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                af="False"
                si="0"
                rs="F"
                rv="4.82"
                nr="4.0-11.0"
                ru="mmol/L"
                bc="GT6"
                lo="14756-1"
                vt="N">
```

Source File

XML Lab Results Reader

```
private LogicalInsertRow generateRow(Document doc) throws ParseException {
    LogicalInsertRow row = new LogicalInsertRow();
    Element root = doc.getRootElement();
    Element pa = root.getChild("pa");
    Element rq = root.getChild("rq");
    Element dr = root.getChild("ph").getChild("dr");
    Element fa = root.getChild("fa");
    Element bgRe = root.getChild("ts").getChild("tg").getChild("lt").getChild("ti").

    String patientId = pa.getAttributeValue("pk");
    add(row, "patient_pk", patientId, NON_IDENTIFIED);

    add(row, "patient_last_name", pa.getAttributeValue("ln"), DE_IDENTIFIED);
    add(row, "patient_first_name", pa.getAttributeValue("fn"), IDENTIFIED);
    add(row, "patient_phn", pa.getAttributeValue("ei"), IDENTIFIED);
    add(row, "patient_last_name", mask(pa.getAttributeValue("ln")), DE_IDENTIFIED);
    add(row, "patient_first_name", mask(pa.getAttributeValue("fn")), DE_IDENTIFIED);
    add(row, "patient_phn", mask(pa.getAttributeValue("ei")), DE_IDENTIFIED);

    add(row, "rq_id", rq.getAttributeValue("rk"), NON_IDENTIFIED);
    Date receivedDate = parseISO8601(rq.getAttributeValue("ord"));
    Date collectedDate = parseISO8601(rq.getAttributeValue("ocd"));
    Date reportedDate = parseISO8601(rq.getAttributeValue("rd"));
    add(row, "rq_received_datetime", receivedDate, NON_IDENTIFIED);
    add(row, "rq_collected_datetime", collectedDate, NON_IDENTIFIED);
    add(row, "rq_reported_datetime", reportedDate, NON_IDENTIFIED);

    String doctorId = dr.getAttributeValue("id");
    add(row, "doctor_name", dr.getAttributeValue("name"), NON_IDENTIFIED);
    add(row, "doctor_id", doctorId, NON_IDENTIFIED);
```

Data Processing Function

Structured

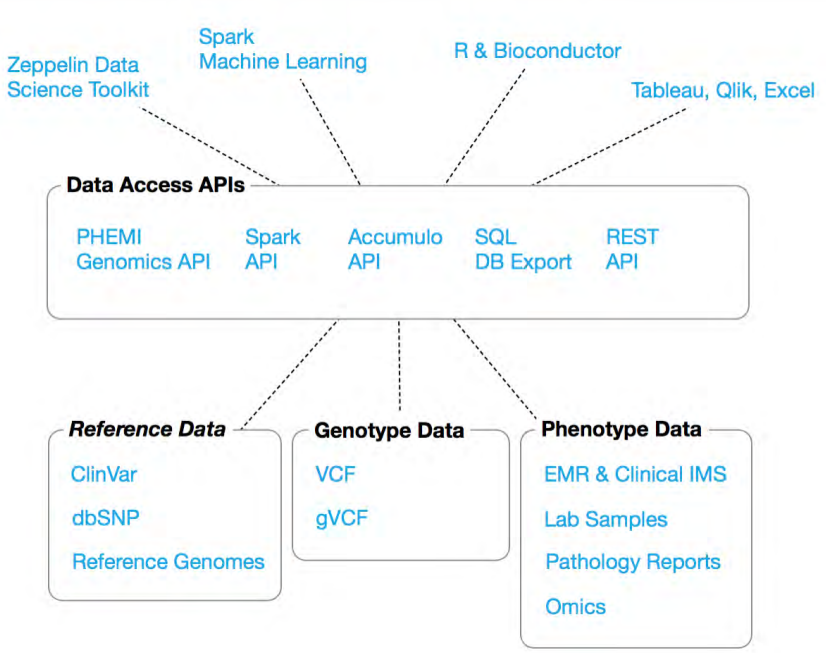
Name	Visibility	Value
Glucose	Non PHI	4.82
Patient PHN	PHI	994-859-9326
Collection Date	Non PHI	2013-02-06
Facility ID	Non PHI	BCB Van East
Patient Name	PHI	Sullivan, Ian

Analytics-Ready Digital Assets

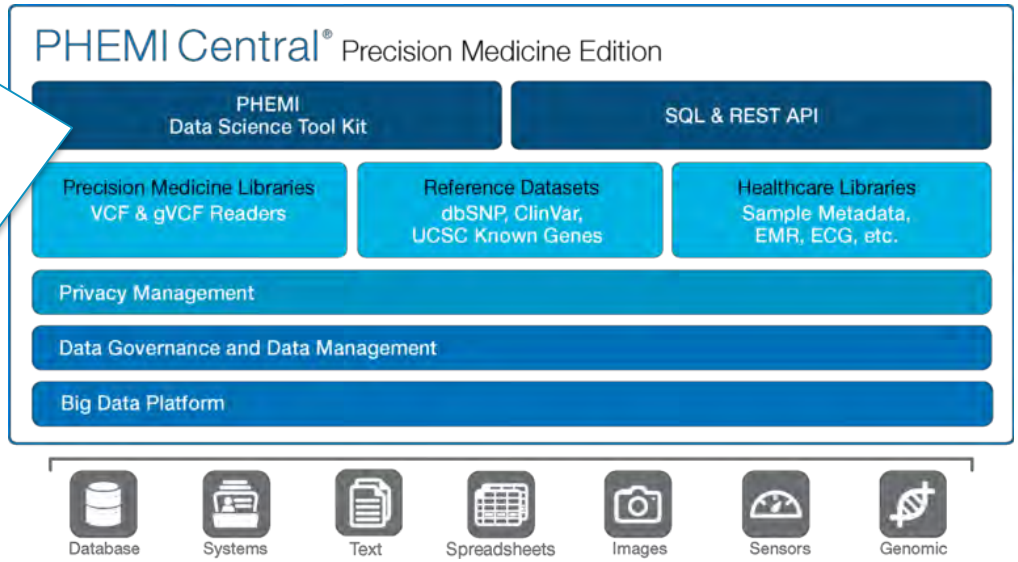
PHEMI

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...

PHEMI

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

eHEALTH INITIATIVE

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:

- Claudia Ellison
  - Claudia.Ellison@ehidc.org
  - 202-624-3280

This webinar was made possible through the generosity and support of PHEMI!

Slides are available at www.ehidc.org/resources

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