PANEL 7: STREAMLINING CLINICAL WORKFLOW, TRANSPORTABILITY TO OTHER SYSTEMS, CLINVAR SUBMISSIONS?

Genomic Medicine VIII

This meeting will help NHGRI and its Genomic Medicine Working Group (GMWG) examine our genomic medicine portfolio in light of evolving scientific knowledge and opportunities.

June 8-9, 2015
Rockville, Maryland

Panel members

- Mike Gaziano, M.D., Ph.D.
  - Brigham and Women's Hospital
- Stephen Kingsmore, MBChB, BAO, DSc, FRCPath
  - Children's Mercy Hospital
- Erin Ramos, Ph.D., MPH
  - NHGRI
- Howard McLeod, PharmD
  - Moffitt Cancer Center

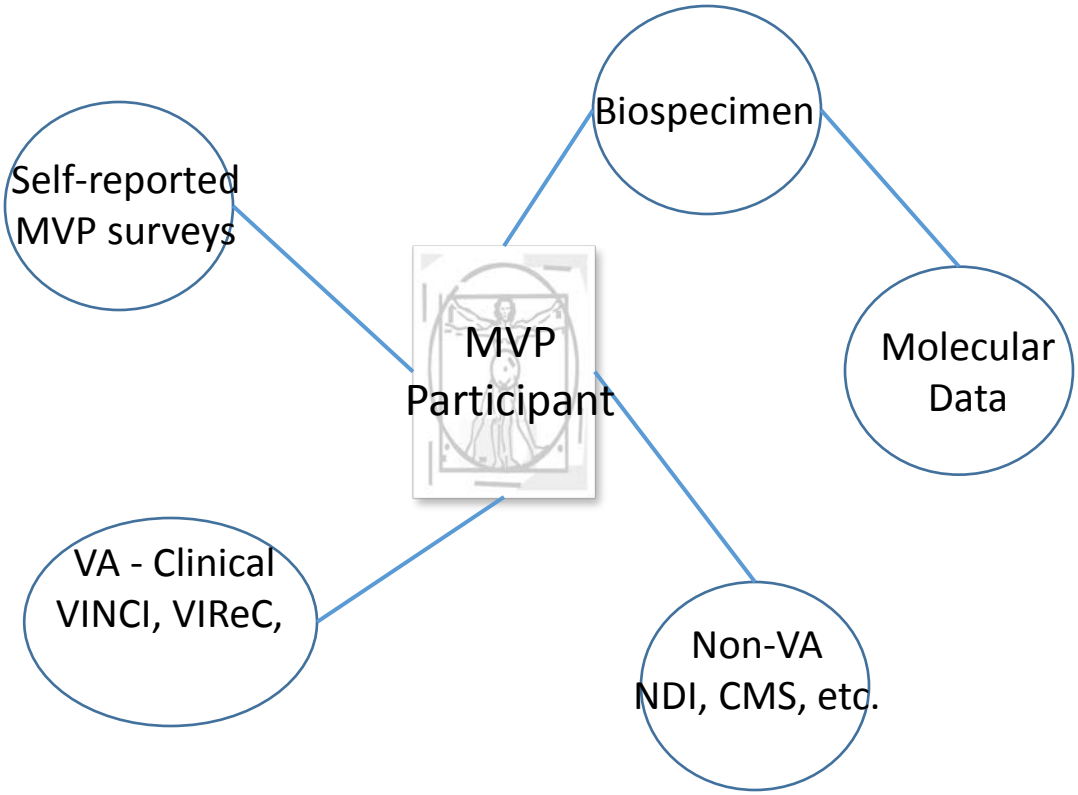
* Genomic Medicine Working Group Member

1. Importance and Impact for Genomic Medicine Implementation

- The quantity of data generated for each patient makes the practice of medicine unmanageable if using brain power alone.
- There are complexities in the generation, annotation, interpretation, implementation, and application of genomic results
- Patient clinical use patterns requires an ability for transport of clinical data across practices
- There is a need to bidirectional sharing of genomic data with databases (i.e., ClinVar)

- Data > Information > Knowledge > Wisdom

Million Veteran Program (MVP) Data Universe



Other Data Sources

MVP Data

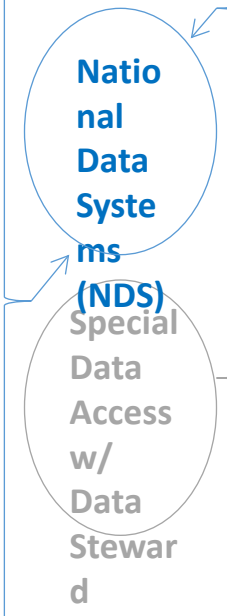
- Self-Reported Survey Data:
  - Lifestyle Survey Data (Personal Information, Well-Being, Activity, Health, Military Experience, Dietary Intak, Medication, Habits)
  - Baseline Survey (Health, Military Experiences, family medical history)
- Genetic Data
  - Genotype data
  - Sequence data

Other Data

- VA Healthcare System Data
- Other Data
  - National Death Index (NDI)
  - Centers for Medicare and Medicaid Services (CMS)
  - State Mortality Data

VA Data Sources

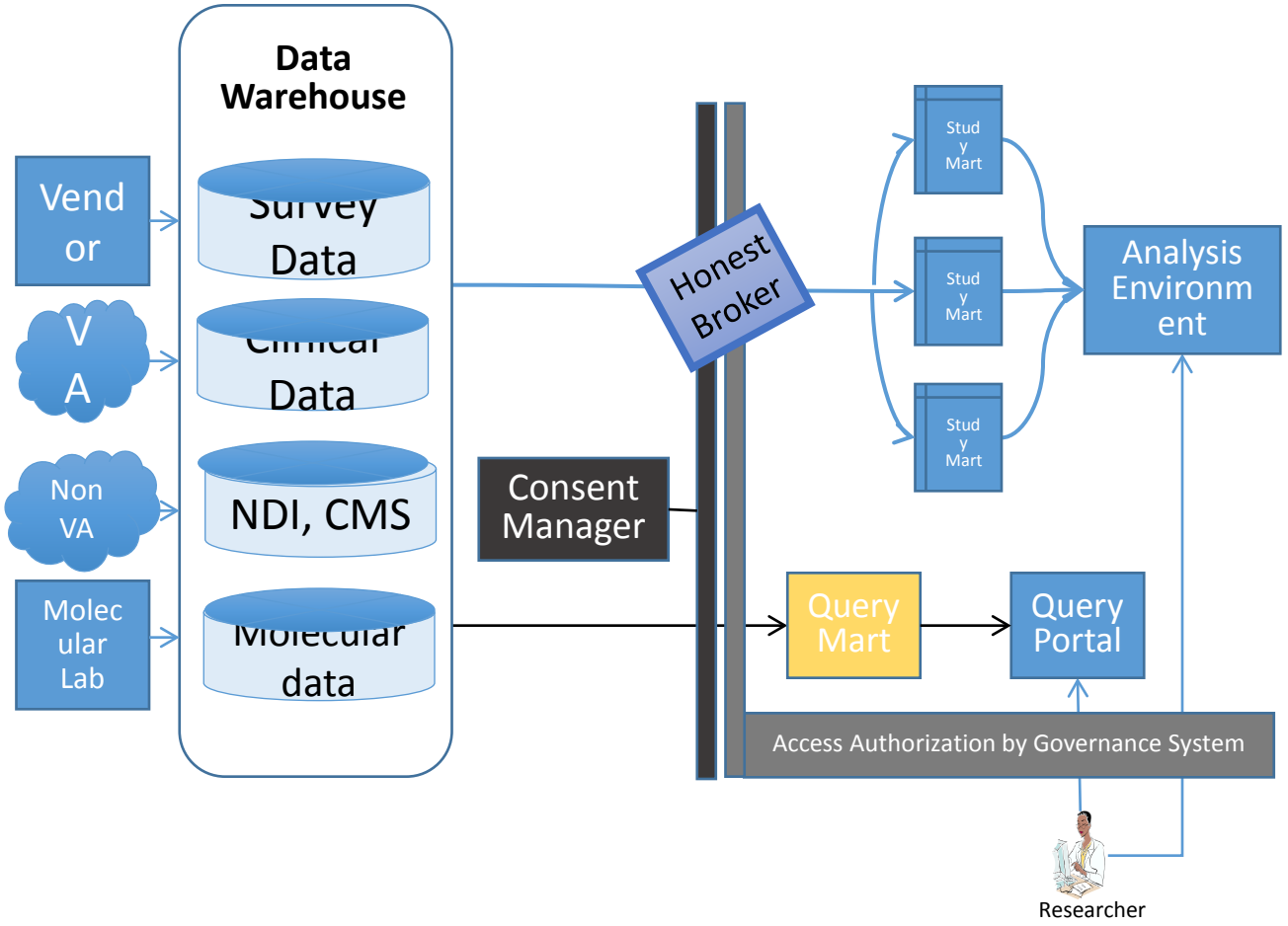
- Corporate Data Warehouse Databases
- National Patient Care Databases
- Vital Status
- Decision Support System
- National Data Extract
- Beneficiary Identification Records Locator (BIRLS) death file
- New England VISN-1 Pharmacy files
- Outpatient Clinic File (OPC)
- Patient Treatment File (PTF)
- Inpatient and Outpatient Hospitalizations



- Clinic Inpatient and Outpatient Visits
- Diagnosis (ICD-9) codes
- Procedure (CPT) codes
- Pharmacy data and laboratory data

- Pharmacy Benefit Management (PBM) system database
- OEF/OIF and OND Roster
- VA Clinical Assessment Reporting and Tracking (CART)
- Veterans Affairs Surgical Quality Improvement Program (VASQIP)
- Veterans Affairs Central Cancer Registry (VACCR)

System Architecture



2. Related Research Programs

NIH/NHGRI

- *Precision Medicine*
  - http://www.nih.gov/precisionmedicine/workshop-summary.pdf
- Clinical Sequencing Exploratory Research (CSER)
  - http://www.genome.gov/27546194
- Electronic Medical Records and Genomics (eMERGE)
  - http://www.genome.gov/27540473
- ClinGen
  - http://clinicalgenome.org/
- Implementing Genomics in Practice (IGNITE)
  - http://www.genome.gov/27554264

3. Barriers and Opportunities

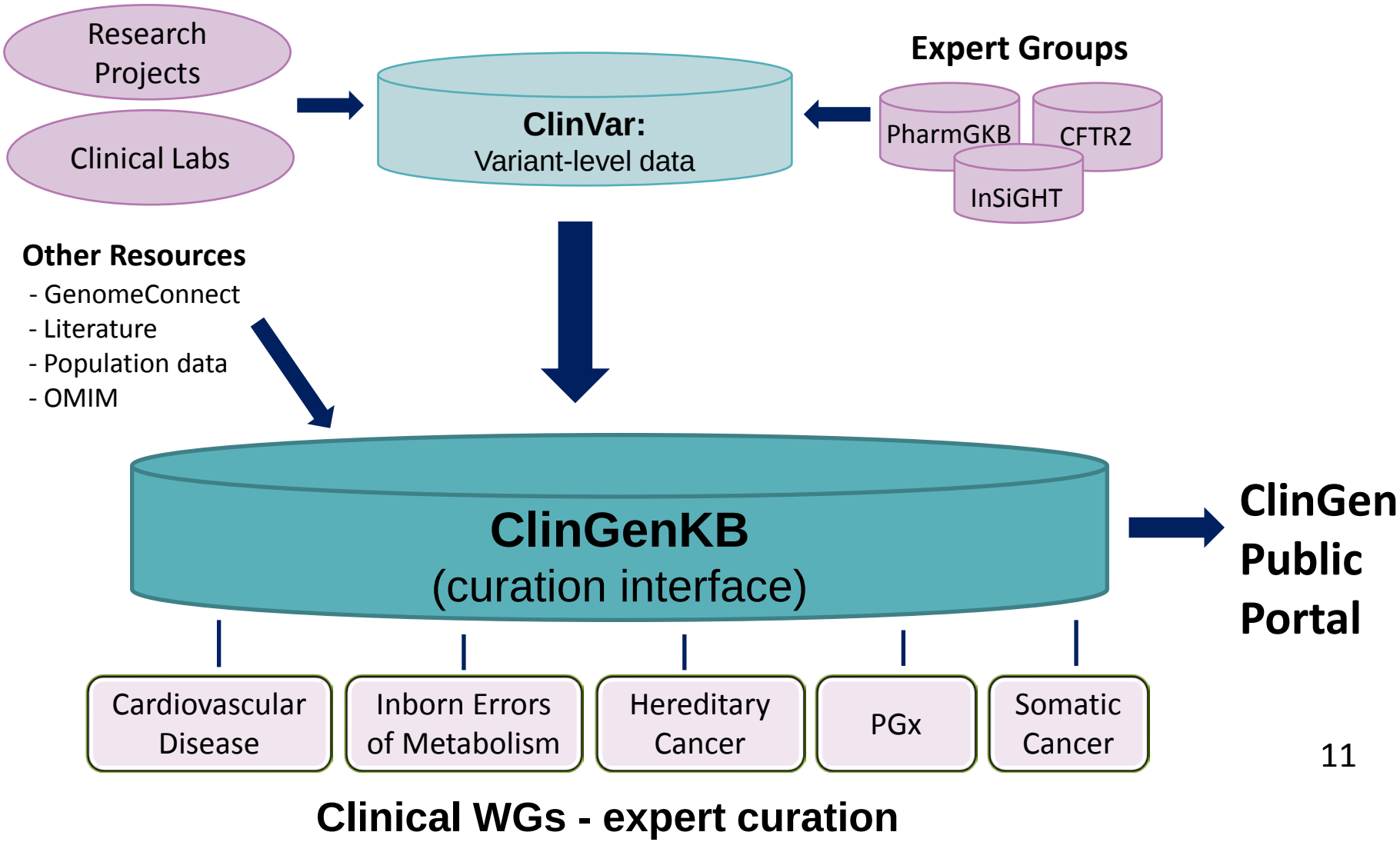
- Curation of EHR data, including uniqueness to each given EHR
  - eMERGE making progress, but there is a lot to do
- Many EHR elements are not biologically driven constructs
  - Cancer moving from organ specific to molecular similarity
- Few practical analytics to aid use of EHR data
- There is a need to invest in EHR mapping
  - 3,000 variables with word albumin across VA system
  - Differences in how each clinical group uses ICD9 codes

4. Potential Synergies

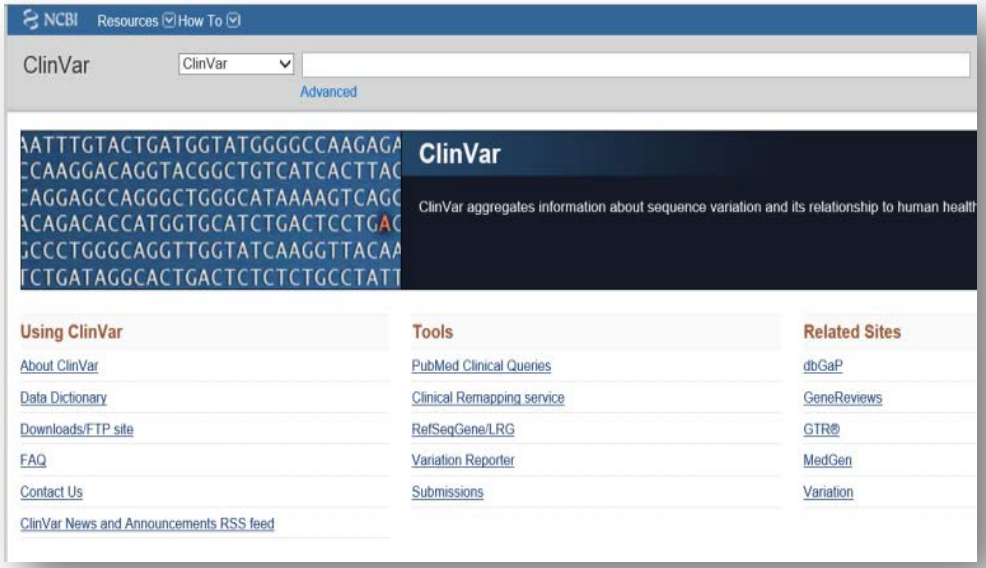
NIH-centric

- Precision Medicine
  - http://www.nih.gov/precisionmedicine/workshop-summary.pdf
  - ***RFI on the Precision Medicine Cohort http://grants.nih.gov/grants/rfi/rfi.cfm?ID=44***
- Implementing Genomics in Practice (IGNITE)
  - http://www.genome.gov/27554264
- ClinGen
  - http://clinicalgenome.org/
- eMERGE

ClinGen Data Flow

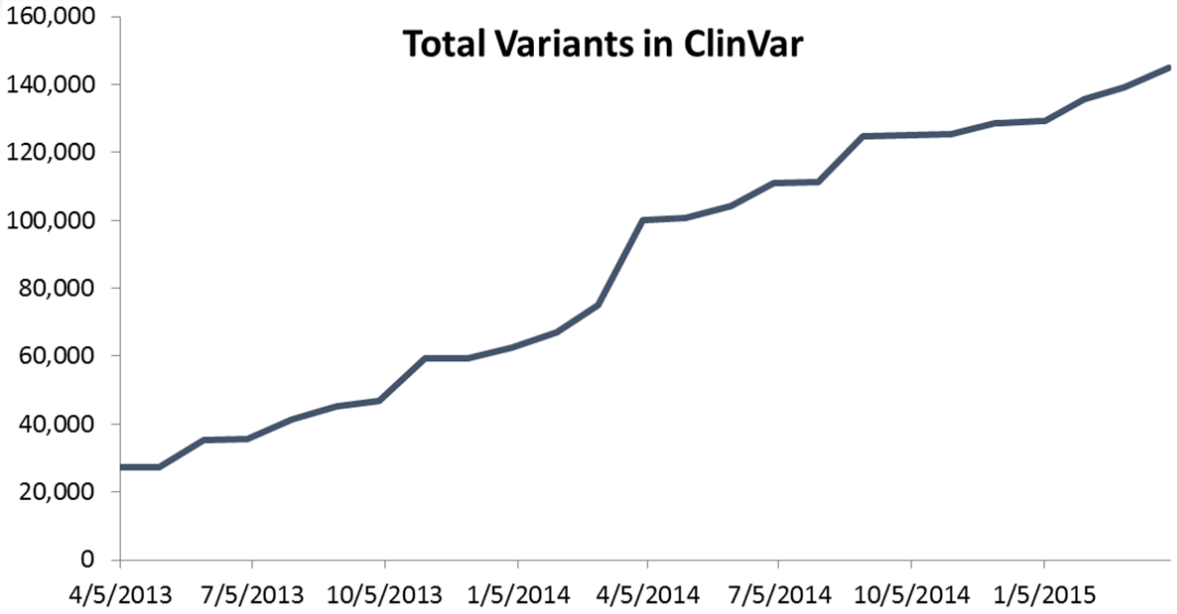


ClinVar: ClinGen's Variant Repository



>315 ClinVar submitters
>172,000 submissions
>118,000 unique interpreted variants

ClinVar Content Continues to Climb



Courtesy of Melissa Landrum

ClinVar submitters with >50 interpreted variants

Submitter	# of Variants
Expert Consortia and Professional Organizations	
International Society for Gastrointestinal Hereditary Tumours (InSiGHT)	2362
Clinical and Functional Translation of CFTR (CFTR2)	133
American College of Medical Genetics and Genomics (ACMG)	23
Clinical Laboratories	
International Standards for Cytogenomic Arrays (ISCA) Consortium	14440
Partners Healthcare Laboratory for Molecular Medicine	12040
GeneDx	11038
University of Chicago Genetic Services Laboratory	7158
Emory University Genetics Laboratory	6944
Ambry Genetics	4150
Sharing Clinical Reports Project for BRCA1 and BRCA2	2147
Laboratory Corporation of America (LabCorp)	1390
ARUP Laboratories	1374
InVitae	1134
Blueprint Genetics	651
U. Washington CSER Program with Northwest Clinical Genomics Laboratory	646
University of Washington Collagen Diagnostic Laboratory	411
Children's National Medical Center GenMed Metabolism Laboratory	317
Baylor College of Medicine	235
Pathway Genomics	189
Counsyl	112
Greenwood Genetic Center Diagnostic Laboratories	80
U. of Pennsylvania School of Medicine Genetic Diagnostic Laboratory	68
Research Programs and Locus-Specific Databases	
Breast Cancer Information Core (BIC)	3734
Royal Brompton Hospital Cardiovascular Biomedical Research Unit	1346
Muilu Laboratory, Institute for Molecular Medicine Finland	840
ClinSeq Project, National Human Genome Research Institute, NIH	425
Lifton Laboratory, Yale University	389
PALB2 Leiden Open Variation Database	242
Dept of Ophthalmology and Visual Sciences, Kyoto University Hospital	171
King Faisal Specialist Hospital and Research Centre Developmental Genetics	105
Dept Zoology, M.V. Muthiah Government College, India	58
Aggregate Databases	
Online Mendelian Inheritance in Man (OMIM)	25044
GeneReviews	4006

(*Courtesy: of Heidi Rehm*)

Gene-Disease Validity Classification*

Definitive	Repeatedly demonstrated in research & clinical settings.
Strong	Excess of pathogenic variants in cases vs. controls & supporting experimental data.
Moderate	≥3 unrelated probands with pathogenic variants & supporting experimental data.
Limited	<3 probands w/ pathogenic variants.
No Evidence Reported	"Candidate" genes based on animal models or disease pathways, but no pathogenic variants reported.
Disputed	Significant evidence *refuting* a role for gene in this disease.
Evidence Against	Evidence refuting the role of the gene significantly outweighs any supporting evidence.

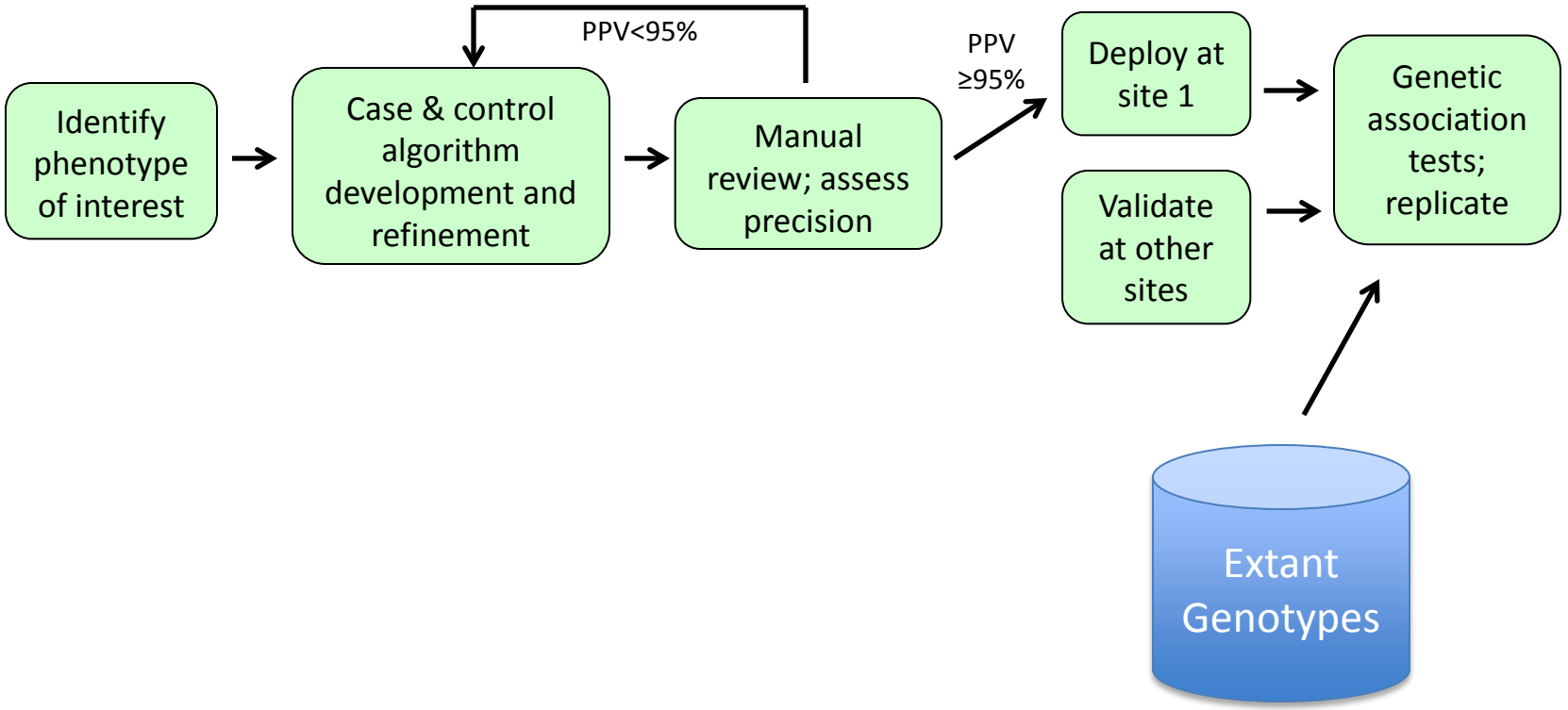
Jonathan Berg

Co-Chairs

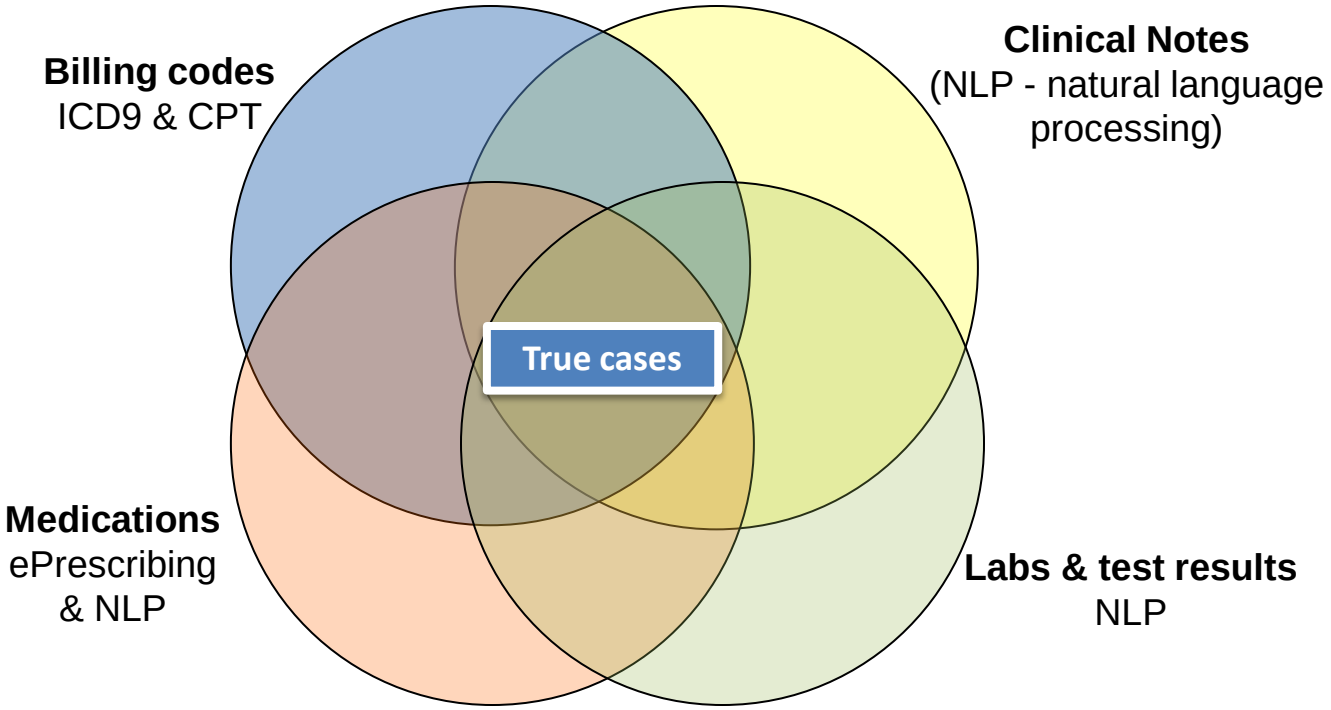
Christa Martin

***Detailed criteria available online:**
http://www.clinicalgenome.org/knowledge-curation/gene-curation/

Approach to EHR phenotyping



What we've learned - Finding phenotypes in the EMR



5. Training Opportunities

Not a lot of NIH focus on training EHR scientists

Main Points for Panel 7

- NHGRI should not (and cannot) and doesn't need to solve all EHR work flow and transportability issues
- Tools designed for billing (most EHRs) are not going to meet all genomic medicine needs

- The new Precision Medicine Initiative will require effort in informatic workflow, analytics across EHR systems, two-way interactions with databases
- Training is not organized on a national level. There are individual centers (e.g., vanderbilt), but there is an opportunty to work across ICs to create an EHR focus