eMERGE Network
electronic medical records & genomics

Return of Genomic Results
Current Applications and Challenges

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On Behalf of the ROR Work Group
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GroupHealth · Marshfield Clinic · University of Washington · Essentia Health · Mount Sinai School of Medicine · Geisinger · The Children's Hospital of Philadelphia · Mayo Clinic · Boston Children's Hospital · Northwestern University · Cincinnati Children's Hospital Medical Center · Vanderbilt University

eMERGE ROR

Co-chairs	Workshop Panel members
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CHOP	John Connolly, Hakon Hakonarson, Brendan Keating
CCHMC/BCH	Armand Antommaria, John Harley, Ingrid Holm, Melanie Myers, Bahram Namjou, Cassandra Perry, Cindy Prows, Sander Vinks, Wendy Wolf
Geisinger	Glenn Gerhard, David Ledbetter, Agnes Sundaresan, Gerard Tromp, Marc Williams
Group Health/UW	Gail Jarvik, David Crosslin, Kelly Ehrlich, Malia Fullerton, Carlos Gallego, Kathy Leppig
MCEIRH/PSU	Murray Brilliant, Terrie Kitchner, Cathy McCarty, Marylyn Ritchie
Mayo	Richard Sharp, Iftikhar Kullo, Jen McCormick,
Mount Sinai	Erwin Bottinger
Northwestern	Steve Persell, Laura Rasmussen-Torvik, Maureen Smith, Cathy Wicklund
Vanderbilt	Kyle Brothers, Ellen Clayton, Julie Field, Tracy McGregor, Dan Roden, Quinn Wells
NIH/NHGRI	Lucia Hindorff, Rongling Li, Rochelle Longbottom, Teri Manolio, Jackie Odgis, Erin Ramos

EVOLUTION OF ROR IN EMERGE

Genetics inMedicine | SPECIAL ARTICLE

Return of individual research results from genome-wide association studies: experience of the Electronic Medical Records and Genomics (eMERGE) Network

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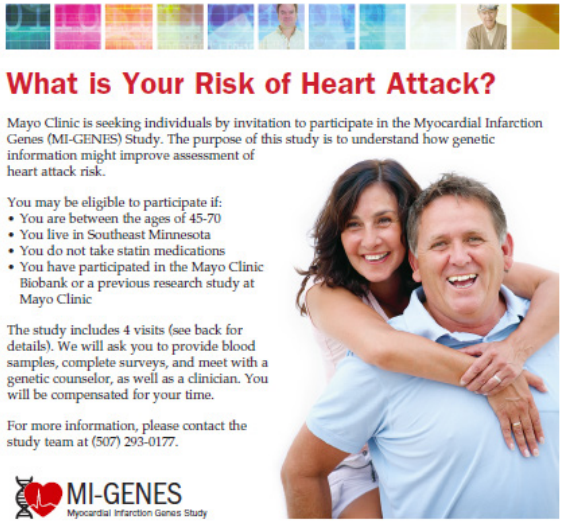
- ROR in the context of the EHR
- ROR in the context of age
- Evidence of clinical validity and actionability
- Appropriate methods for ROR
- Diversity of opinion across sites
- Input from lay community, advisory bodies

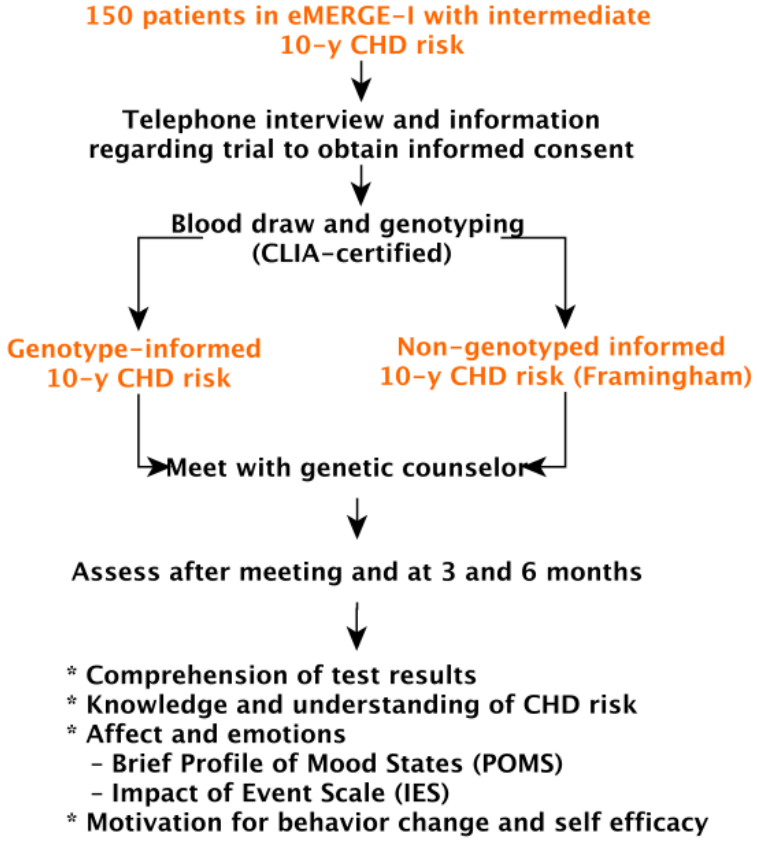
Phase II- Genomic medicine pilots

- **Genetic risk scores**
  - Essentia: 7 SNPs assoc with Macular degeneration
  - Mayo: 28 SNPs assoc with heart attack
- **SNPs**
  - Mount Sinai: *ApoL1* for hypertensive renal dz in AA
  - Northwestern: *HFE* and *FV*
- **WGS**
  - Geisinger: Whole genome sequencing in trios
- **PGx**
  - *CYP2D6* results to parents and providers
  - Hypothetical return of *CYP2D6*

An EHR-based genomic medicine pilot study

MI-GENES
Myocardial Infarction Genes Study



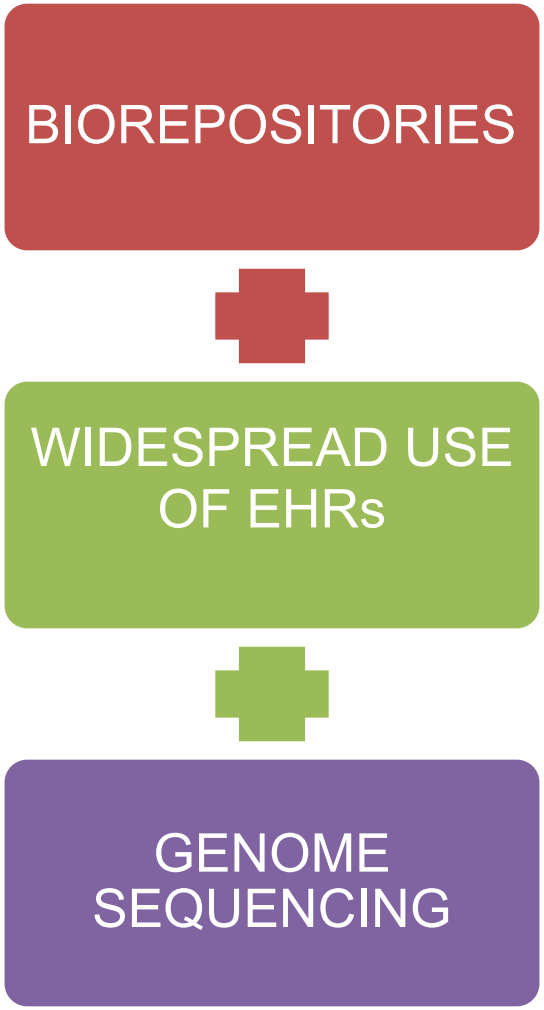


Phase II- Network-wide projects

- eMERGE PGx
- Copy number variation
- *HFE* variants

Site	C282Y/C282Y	C828Y/H63D	H63D/H63D	Sum
Geisinger	12	67	110	189
GHC/Seattle	17	60	72	149
Marshfield	15	52	87	154
Mayo	44	179	206	4
Mt. Sinai	1	12	29	42
Northwestern	19	64	81	164
Vanderbilt	39	152	141	332
Total	**147**	**586**	**726**	**1459**

FUTURE DIRECTIONS


BIOREPOSITORIES
WIDESPREAD USE OF EHRs
GENOME SEQUENCING

ROR: Unique potential of eMERGE

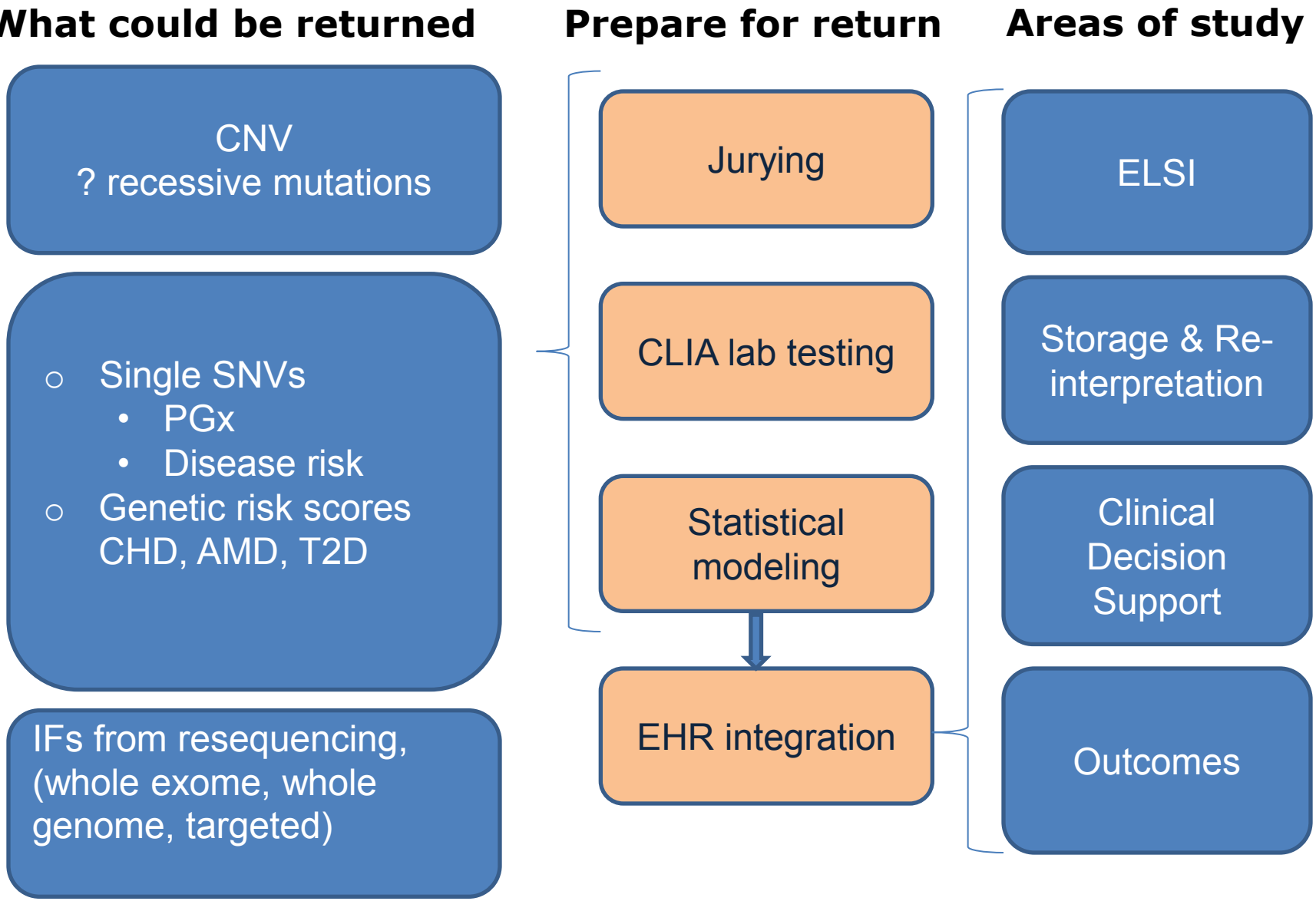
- EHR-based genomic discovery
  - ‘Longitudinal’ phenotypes
  - Pleiotropy (PheWAS)
- EHR based genomic implementation
  - Storage, visualization and integration
  - Decision support
  - Incidental findings
  - Outcomes
- The learning EHR

ROR - Discovery

- Incidental findings
- Mechanism and timing of ROR
- Consent
- Patient preferences
- CLIA confirmation
- Documentation in EHR
- Family members
- Pediatric setting

Jarvik et al, Manuscript in preparation, joint CSER and eMERGE effort

ROR - Implementation



Potential projects

- **WES (n = 1000 each site)**: phenotypes, penetrance, pleiotropy, pediatric considerations
- **Targeted sequencing** for the 56 ACMG genes to determine pathogenicity, penetrance, informing kin, etc.
- **Clinically indicated panels:** cardiomyopathies, pediatric syndromes
- **High-density genotyping** - common and rare variants

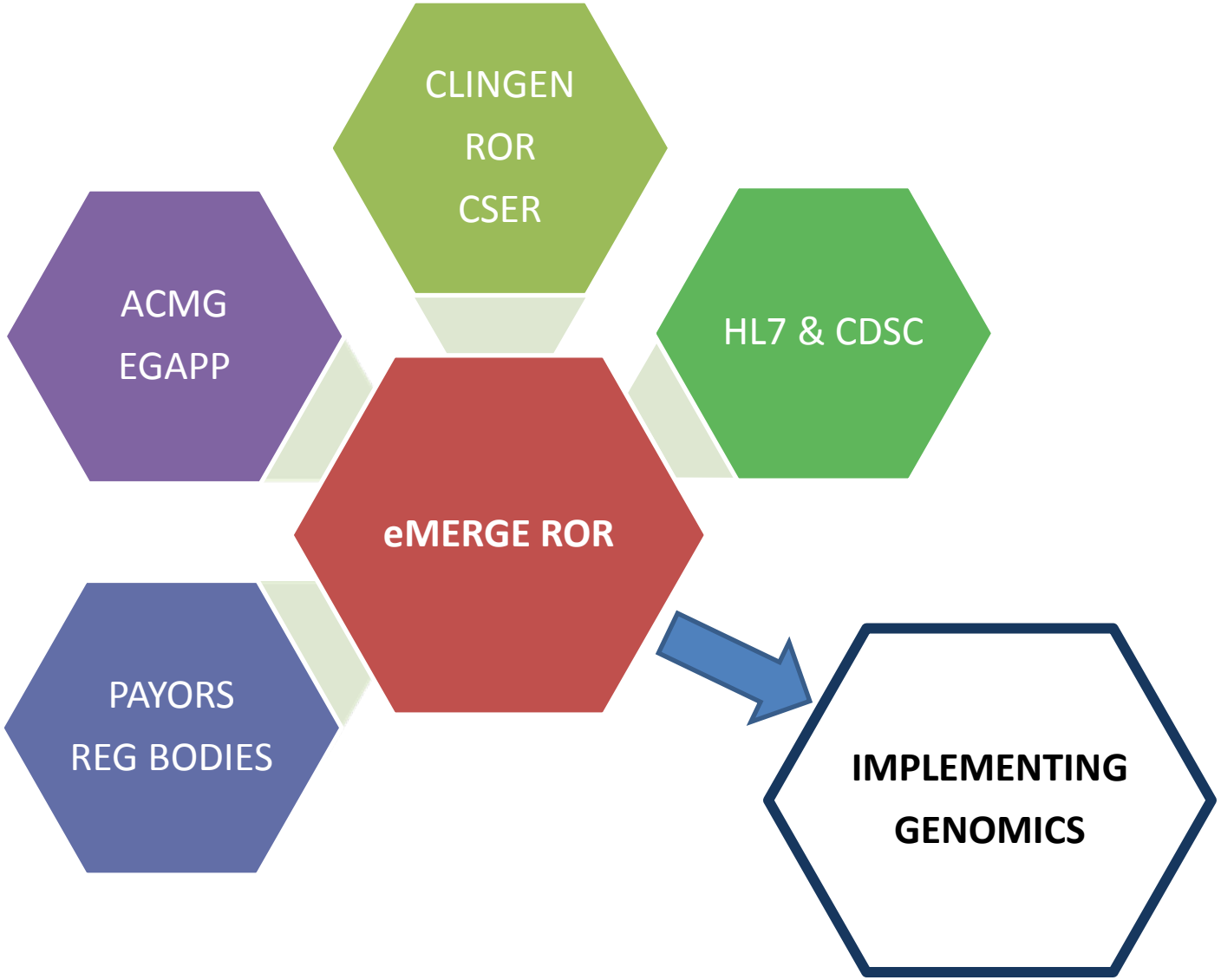
Consent

- Participant **privacy** and potential vulnerability to adverse social consequences
- Consent to include genomic **data in the EHR**
- **Recontact** to ascertain preferences and reconsent
- **Electronic ascertainment of preferences** over time

Stakeholders

- **Participants**, parents/guardians in pediatric projects, legally authorized representatives for adult incompetents, deceased
- **Family members**
- **Care providers**
- **Laboratorians**
- **Investigators**
- **Biorepository scientists**

eMERGE ROR interactions



Summary

- eMERGE is uniquely positioned to address these knowledge gaps and challenges
  - Linkage to EHR with deep and diverse phenotypes
  - Diversity of clinical settings and EHRs
  - Diversity of genomic information
  - Best practices for implementation
  - n=50,000 including pediatric patients