eMERGE Network Steering Committee
June 23-24, 2014
Seattle, WA

Attendance

Network Members in Attendance

CCHMC/BCH	Armand Antommaria	Northwestern	Rex Chisholm
CCHMC/BCH	Ariel Chandler	Northwestern	Geoff Hayes
CCHMC/BCH	Beth Cobb	Northwestern	Jen Pacheco
CCHMC/BCH	John Harley	Northwestern	Laura Rasmussen-Torvik
CCHMC/BCH	Ingrid Holm	Northwestern	Maureen Smith
CCHMC/BCH	Todd Lingren	Northwestern	Justin Starren
CCHMC/BCH	Melanie Myers	Northwestern	Cathy Wicklund
CCHMC/BCH	Bahram Namjou		
CCHMC/BCH	Yizhao Ni	NIH	Rongling Li
CCHMC/BCH	Cindy Prows	NIH	Teri Manolio
		NIH	Jackie Odgis
CHOP	Berta Almoguera Casstillo		
CHOP	John Connolly	Vanderbilt	Kyle Brothers
CHOP	Hakon Hakonarson	Vanderbilt	Ellen Clayton
CHOP	Brendan Keating	Vanderbilt-CC	Josh Denny
CHOP	Frank Mentch	Vanderbilt	Todd Edwards
CHOP	Patrick Sleiman	Vanderbilt-CC	Brad Malin
CHOP	Lyam Vazquez	Vanderbilt-CC	Nate Mercaldo
		Vanderbilt-CC	Jonathan Scholdcrout
Geisinger	David Carey	Vanderbilt	Dan Roden
Geisinger	Helena Kuivaniemi	Vanderbilt	Laura Wiley
Geisinger	Gerard Tromp		
Geisinger	Janet Williams		
Geisinger	Marc Williams	CC	Melissa Basford
		CC	Paul Harris
GH/U WA	Laura Amendola	CC	Brandy Mapes
GH/U WA	David Carrell	CC	Lauren Melancon
GH/U WA	Paul Crane		
GH/U WA	David Crosslin	Affiliate Members	
GH/U WA	David Cronkite	Air Force	Ron Miller
GH/U WA	Jane Grafton		
GH/U WA	Ragan Hart	Network Invitees and Guests	
GH/U WA	Andrea Hartzler		
GH/U WA	Gail Jarvik	UCSF	Neil Risch
GH/U WA	Eric Larson	University College London	Harry Hemingway
GH/U WA	Evetter Ludman		
GH/U WA	James Ralston		
GH/U WA	Joseph Salama		
GH/U WA	Aaron Scroll		
Marsh/Essentia/PSU	Murray Brilliant		
Marsh/Essentia/PSU	Molly Hall		
Marsh/Essentia/PSU	Scott Hebbring		
Marsh/Essentia/PSU	Terrie Kitchner		
Marsh/Essentia/PSU	Cathy McCarty		
Marsh/Essentia/PSU	Peggy Peissig		
Marsh/Essentia/PSU	Shefali Setia		
Mayo	Chris Chute		
Mayo	Iftikhar Kullo		
Mayo	Jen McCormick		
Mayo	Jyoti Pathak		
Mayo	Richard Sharp		
Mt. Sinai/Columbia	Steve Ellis		
Mt. Sinai/Columbia	Zhe He		
Mt. Sinai/Columbia	Carol Horowitz		
Mt. Sinai/Columbia	Girish Nadkarni		
Mt. Sinai/Columbia	Aniwaa Owusu Obeng		
Mt. Sinai/Columbia	Saskia Sanderson		

The eMERGE Steering Committee meeting was held on June 23-24, 2014 in Seattle, WA. In order to make sure the Network remains productive as we move into our final year please find highlights from the Steering Committee meeting below.

Click here to view the slides from the Steering Committee meeting.

Highlights from the meeting include:

- Concept Clearance has been approved by NHGRI Advisory Council for eMERGE III. Three RFAs are being prepared and will be published in summer 2014 – these RFAs will reflect the eMERGE III goal of continuing genomic medicine discovery and implementation research using large biorepositories linked to EMRs.
- Goals for the meeting included:
  - Refresh and refine plans for final year of eMERGE II
  - Refine timelines for completing eMERGE II goals
  - Update plans for dissemination of the network-wide lessons learned and best practices to the scientific community

1. **ACTION ITEM: The Steering Committee was encouraged to determine a roadmap of projects to be completed in the last year of eMERGE Phase II. These items can be detailed in the next few weeks and progress tracked by the workgroups.**

- CHOP developed an algorithm for distinguishing mild, moderate, and severe asthma based on medications that they were encouraged to publish. A project timeline was requested. (action?)

- **ACTION ITEMS: CHOP will compose a timeline for their asthma project that will be presented on a future Phenotyping call.**

- The eMERGE PGx project was discussed in depth, including a review of timelines and project progress. All sites are making progress and the group is hopeful that all work will be completed by the end of Phase II. Specific projects (Rare Variants in SCN5A and KCNH2 and arrhythmia traits in the EMR; Rare variants in LDLR, HMGCR, NAT2, ABCA1, and APOA1 with plasma lipid levels) were presented and discussed along with a platform update from PGRN. PGRNseq v2.0 is in process and any sites interested in nominating specific variants or general input should contact Adam Gordon to get involved in the selection process. This updated platform will not be available prior to the end of eMERGE II. The eMERGE PGx group is seeking research ideas for phenotypes to be explored in the eMERGE PGx cohort; suggestions should be sent to the phenotyping workgroup for further exploration and scoring for biological significance and difficulty. (action?)

- **ACTION ITEM: Any sites interested in nominating specific variants or general input for the PGRNSeq 2.0 platform should contact Adam Gordon to get involved in the selection process.**

- Guest speaker, Neil Risch, PhD of Kaiser Permanente's Northern California Division of Research and UCSF, presented to the group. Neil presented on the project, Genetic Epidemiology Research on Aging in an EMR-based Cohort of 100,000, which is a study supported by the Research Program on Genes, Environment, and Health (RPGEH) and the GERA cohort research grant.
- Sites were reminded to review and adhere to the publication policy of the Network.
- The CERC Survey Workgroup is diligently working to move the project along and to completion prior to the end of the funding period.

- **ACTION ITEM: NHGRI asked sites to prepare a budget list for their CERC Survey projects allowing NHGRI to review funding and confirm all sites would have enough funding to complete their assigned tasks after the grant has expired.** *After further discussion this action item has been retracted by NHGRI.*

- ESP Recommendations from the spring 2014 ESP call were reviewed. Steering Committee members were asked to consider the recommendations and offer feedback/suggestions on how they can be addressed Network-wide. Suggestions included:
  - The Network should look for other points of impact in addition to publications. EHRI is currently working to compose a list of activities and consortia the EHRI workgroup members are involved with in addition to eMERGE and then evaluate what impact eMERGE has had on these external groups.
  - All workgroups were encouraged to engage with pediatric projects and include discussion and engagement with all sites, even those that do not have pediatric samples.

- **ACTION ITEM: Workgroups should discuss how they can integrate pediatric goals into their projects**

  - The Network has been working hard on implementation, specifically on the InfoButton Project. Along with this project it was mentioned that the EHRI group is committed to developing translatable educational materials according to infobutton standards that are widely available.

- **ACTION ITEM: Workgroups should all discuss how their workgroup is contributing to the translational aspect of eMERGE.**

- The Steering Committee discussed the National implementation of ICD10 codes across the Network sitesand the impact of that effort on electronic phenotyping. As leaders in the field of electronic phenotyping, could eMERGE provide guidance in this area? All sites plan to execute this implementation in different ways and not all sites plan to double code, using ICD 9 and ICD 10 codes simultaneously. Generally, it was thought that

incorporating ICD10 codes into current and future Phase II algorithms was not a fruitful endeavor since the required implementation date is not until after the Phase II funding period has ended and it remains to be seen exactly how practitioners will use the codes in actual clinical billing. However, the group thought additional discussion and the possible creation of a future Network-wide plan to utilizing ICD10 codes within Network algorithms should be discussed on a future Phenotyping workgroup call.

ACTION ITEM: Assess and discuss ICD 10 implementation and response on a future Phenotyping call.

- In addition to the presentations and discussions mentioned above the following sites and workgroups presented updates:
  - Site Update:
    - CCHMC/BCH
    - Northwestern
  - Workgroup Update:
    - Pediatric Workgroup
    - Phenotyping Workgroup
    - Genomics Workgroup
    - CERC Workgroup
    - EHRI Workgroup
    - Return of Results Workgroup
- Remaining Phase II Workgroup Timelines were presented and discussed in some detail, these items are listed below by workgroupattached. These may need to be prioritized and will be tracked closely by the Coordinating Center for the Steering Committee (action item, could replace item 1 below). Updates on progress of these high priority tasks will be a key focus of future meetings and calls.

Workgroup Timelines and Ongoing Projects

- CERC
  - Developing Consents for Returning Pharmacogenomics Results: The eMERGE Experience (Smith et al.)
  - Joint eMERGE/CSER Manuscript: Re-consent of Minors at the age of Majority (Brothers et al.)
  - Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network (Survey Project)
    - Current status: draft survey complete; cognitive interview preparation underway; population data collection in process
- EHRI
  - Genomics CDS Implementation Across All Sites
    - Current status: 3 go-live since last meeting; 7 sites with PGx CDS live
  - Joint eMERGE/CSER manuscript
    - Current status: data collection almost complete
  - Assessing Opinions about Information Resources for Genomic Medicine
    - Current status: manuscript concept sheet to be submitted soon

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- o Infobutton Implementation
  - ▪ Current status: implementation underway; concept in development; gathering requirements for a content authoring & management system; OpenInfobutton configuration complete at NU.
  - ▪ Next steps: develop end user evaluation metrics; implement OpenInfobutton at other interested sites
- o Sharing Genomic Medicine Content
  - ▪ Next steps: working with sites to gather requirements for a software system to facilitate sharing
- Genomics
  - o Frontiers in Genetics Special Issue
    - ▪ Current status: 12 papers published, 5 under review, 1 submission pending
  - o Null Variant Homozygosity in eMERGE Phase I
  - o GWAS for Phase II Phenotypes
- Pediatrics
  - o PheWAS Analysis into Pediatric Data
    - ▪ Next steps: complete screening of all GWS GWAS SNPs from NHGRI GWAS catalog and from gene network and pathway papers of interest from drug target/pgx or therapeutic standpoint; replicate findings of interest at CCHMC/BCH and other sites as needed; reciprocal PheWAS analysis between the pediatric sites for optimized publications
- PGx
  - o Channel Gene Variants and Arrhythmia Traits
  - o Lipid Regulation Gene Variants and Lipid Traits
  - o Return of results issues
- Phenotyping
  - o Phase II Phenotype Implementation
    - ▪ Current status: 17 completed; 10 in-process; 2 additional planned
  - o Modular Phenotyping (Peissing et al.)
  - o PGx Phenotypes
    - ▪ Current status: proposals for PGx discovery projects include: malignant hyperthermia (CCHMC), lipids (GHC/Mayo), cardiac variants (VU)
    - ▪ Next steps: propose 1-2 Network phenotypes; repeat PheWAS with larger sample size
  - o Portable Applications for Implementing Multi-site Clinical NLP Algorithms (Carrell et al.)
  - o PheKB.org: An Online Collaboration Tool for Phenotype Algorithm Development and Sharing (Kirby et al)
  - o From Feasibility to Implementation (Pacheco et al)
- Return of Results
  - o Hemochromatosis (HFE) Penetrance analyses & manuscript
    - ▪ Current status: most data compiled; waiting for one more site
  - 1. Annotation and classification of "highly penetrant" PGx genes

Recently Completed Project Projects

- CERC

- o MyResults.org (designed by John Connolly)
  - o Practical Guidance on Informed Consent for Pediatric Participants in a Biorepository (Brothers et al.) *Accepted in Mayo Clinic Proceedings.*
- EHRI
  - o A Template for Authoring and Adapting Genomic Medicine Content in the eMERGE Infobutton Project. *Accepted in AMIA*
- PGx
  - o Association of Rare Variants in LDLR, HMGCR, NAT2, ABCA1, and APOA1 with Plasma Lipid Levels: Initial Results from the eMERGE PGx Project. (Kullo et al.) *Submitted to ASHG*
  - o Design and Anticipated Outcomes of the eMERGE PGx Project: A Multi-center Pilot for Pre-emptive Pharmacogeniomics in Electronic Health Record Systems. (Rasmussen-Torvik et al). *Accepted in CPT.*
- Phenotyping
  - o PheKB Validation Script Implementation (designed by Luke Rasmussen)
  - o Development and Validation of an Electronic Phenotyping Algorithm for Chronic Kidney Disease (Nadkarni et al.) *Accepted in AMIA*
- Return of Results
  - o Return of Genomic Results in the Genomic Medicine Projects of the eMERGE Network. (Kullo et al) Front Genet. 2014 Mar 26;5:50. PMID: 24723935; PMCID: PMC3972474
  - o Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices In Between. (Jarvik et al) Am J Hum Genet. 2014 May 7; PMID: 24814192

ACTION ITEMS:

1.2. The Steering Committee was encouraged to determine a roadmap of projectss to be completed in the last year of eMERGE Phase II. These items can be detailed in the next few weeks and progress tracked by the workgroups.

2.3. NHGRI asked sites to prepare a budget list for their CERC Survey projects allowing NHGRI to review funding and confirm all sites would have enough funding to complete their assigned tasks after the grant has expired**.** *After further discussion this action item has been retracted by NHGRI.*

3.4. Workgroups should all discuss how their workgroup is contributing to the translational aspect of eMERGE.

4.5. Phenotyping ideas for the PGx cohort should be submitted to the Phenotyping Workgroup

5.6. Workgroups should discuss how they can integrate pediatric goals into their projects

6. Assess and discuss ICD 10 implementation and response on a future Phenotyping call.Assess and discuss ICD 10 implementation and response for further discussion

7. Any sites interested in nominating specific variants or general input for the PGRNSeq 2.0 platform should contact Adam Gordon to get involved in the selection process.

8. CHOP will compose a timeline for their asthma project that will be presented on a future Phenotyping call.

Remaining Phase II Workgroup Timelines As Per Discussion as the June 23-24 Steering Committee Meeting

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- **Remaining Phase II In-Process Projects**
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