eMERGE Network
electronic medical records & genomics

External Scientific Panel

Background Materials

Steering Committee Meeting

October 7-8, 2013 Bethesda, MD

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
National Human Genome
Research Institute
31 Center Drive MSC 2152
Building 31, Room 4B09
Bethesda, MD 20982-2152

September 23, 2013

Dear eMERGE External Scientific Panel members,

We very much appreciate all of your efforts and expertise that you have devoted to the eMERGE Network in the past, and we look forward to your continued input in eMERGE II, especially at the joint eMERGE II Steering Committee and External Scientific Panel meeting on October 7-8, 2013 at the Hyatt Regency Bethesda, One Bethesda Metro Center (7400 Wisconsin Ave), Bethesda, MD 20814.

We are happy to let you know that eMERGE investigators have made significant progress in the past year. It is worthy of note that the Network has established the pediatric workgroup to focus on the issues specifically related to pediatric participants. Sequencing of pharmacogenetic genes is underway and going smoothly.

To ensure a productive meeting, the eMERGE Coordinating Center (CC) has prepared these booklets in collaboration with the eMERGE investigators. We would like to ask that you review these materials prior to the meeting.

Within these booklets you will find the following important materials:

- Agenda for eMERGE Steering Committee (10/7/2013) and External Scientific Panel meeting (10/8/2013) – ***Note: You are welcome to attend the Steering Committee meeting, as well.***
- Network documents:
  - eMERGE Network Overview
  - eMERGE Workgroup Updates
  - eMERGE Tools Development
  - Cross Cutting Collaborative eMERGE Network Projects
  - Additional eMERGE Workgroup Initiatives
  - ESP Recommendations
  - Background Information

Please note that these same materials will also be made available to you on the eMERGE ESP website. If you have any questions or would like more information, please do not hesitate to contact us or the CC program staff (contact information is in this booklet).

We welcome your input to make this Network as successful as possible, and we look forward to seeing you in October.

Sincerely,

Rongling Li, MD, PhD, MPH
Project Scientist, eMERGE
Office of Population Genomics
NHGRI, NIH
lir2@mail.nih.gov

Coordinating Center Contact Information

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INSTRUCTIONS FOR EXPENSE REIMBURSEMENT

The eMERGE Coordinating Center will reimburse your travel-related expenses. This includes flight, hotel (including internet access), taxi fare, meals, etc. However, because we are federally funded, we cannot reimburse expenses for alcohol.

Vanderbilt's travel reimbursement policy requires your **original receipts**. We will not be able to return your receipts, so we recommend that you make and keep a copy for your records. Since the Coordinating Center (not Vanderbilt's Finance Dept.) will be reimbursing you, there is no Travel Expense Report form to fill out as described in the accompanying pdf. All we require is that your original receipts include the information below.

All receipts should show:

- Date
- Amount of payment
- Method of payment (i.e. cardholder's name and card number's last four digits)
- Your name (if this isn't already on the receipt, just sign the back)
- Item or description of service (if not already on the receipt, write on the back or attach the receipt to a sheet of paper that has a description)

Put all your receipts in one envelope, and mail to the address below. **Please include your Social Security Number and preferred mailing address** (the one to which your check should be sent) in your materials; this is required to complete the reimbursement forms**.**

Lauren Melancon
2525 West End Ave.
6th floor
Nashville, TN USA 37203

Special instructions for reimbursement

(In other words, if these details aren't on the receipts, you *may* be asked to submit more information, including a copy of the credit card statement showing these charges.)

If possible, **hotel** receipts should include the daily breakdown of charges.

The **flight** receipts should include the itinerary; if you paid online, the airlines may have emailed your receipt as a payment confirmation with itinerary. In this case, the email confirmation may be an acceptable original receipt if it includes your credit card information (cardholder's name and card number's last four digits).

If a **group meal** is included for full reimbursement, a list of attendees must accompany it. If the person is only paying for their portion of the bill, please indicate that on the receipt, and write the reimbursable amount beside the total on the receipt.

We recommend mailing us your receipts within 10 days after the event. Checks will generally be mailed within two weeks after their arrival at Vanderbilt. Please contact Lauren Melancon at lauren.magnifico@vanderbilt.edu or (615) 343-2284 if you have any questions.

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For access to more detailed information – please go to http://emerge.mc.vanderbilt.edu/emerge-network-steering-committee-meeting-esp . If you have any trouble logging in to the website please contact Lauren Melancon at the CC directly for access.

eMERGE Network Steering Committee Meeting
October 7-8, 2013

Agenda

Monday, October 7th

Arrival:	Hyatt Regency One Bethesda Metro Center, Bethesda, MD 20814
Meeting:	**Cabinet/Judiciary Room**
7:30-8:30am	***Networking breakfast– Meeting Room Foyer***

Full Session

8:30-8:40am	Welcome, opening remarks, general updates – Rongling Li
8:40-8:50am	Announcements, opening remarks – Rex Chisholm

Full Session

8:50-10:20am	eMERGE PGx Workgroup Session (plenary)
10:20-10:40am	***Networking Break***
10:40-11:00am	Genetic Variants Influencing Cardiorespiratory Fitness: an eMERGE Network Project - Mayo – Hayan Jouni
11:00-11:10am	CERC Survey Workgroup Session: Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network Project Update – Ingrid Holm
11:10-11:30am	Scalable Phenotyping: Use Case of Autism - CCHMC/BCH – Todd Lingren (CCHMC) and Guergana Savova (BCH)
11:30-11:50am	Genetic Variation associated with the Susceptibility to Herpes Zoster in the eMERGE Network - GroupHealth/University of Washington – David Crosslin
11:50-12:20pm	***Working Lunch***
12:20-1:20pm	Guest Speaker: Les Biesecker – ACMG Guidelines

Workgroup Discussions

Workgroup Breakout Session 1

1:20-2:50pm Workgroup Breakout Session (3 workgroups)

- Return of Results – Potomac Room
- Phenotyping - Cabinet/Judiciary Room
- Pediatrics – Susquehanna Room

2:50-3:10pm ***Networking Break***

Full Session

3:10-3:30 Replication of gene-gene Interaction Models Associated with Cataracts in the eMERGE Network - Marshfield/Essentia/Penn State – Marylyn Ritchie

3:30-3:50 Null (Loss of Function) Variants Project – Dana Crawford & Gerard Tromp

Workgroup Breakout Session 2

3:50-5:20pm Workgroup Breakout Sessions (3 workgroups)

- CERC – Potomac Room
- EHR Integration – Susquehanna Room
- Genomics – Cabinet/Judiciary Room

5:20pm Adjourn

Tuesday, October 8th – Meeting with the ESP

Meeting: **Cabinet/Judiciary Room**

7:00-8:00am ***Networking breakfast– Meeting Room Foyer***

7:30-8:00am Executive Session with ESP – Chairman's Boardroom

Full Session

8:00-8:15am Opening Remarks – Teri Manolio & Rongling Li, NHGRI

8:15-8:25am Comments from ESP Chair - Howard McLeod

8:25-8:45am eMERGE Network Overview: priorities and goals; review of Progress of Prior ESP Recommendations & Best Practices Topics – Rex Chisholm, Chair

8:45-9:05am Site Specific Genomic Medicine Implementation Project – 10 min report, 10 min discussion – Mayo – Iftikhar Kullo

9:05-9:25am Site Specific Genomic Medicine Implementation Project – 10 min report, 10 min discussion – Children's Hospital of Philadelphia (CHOP) – Hakon Hakonarson

Workgroup Presentations– 20 minutes for report, 10 minutes for discussion

9:25-9:55am CERC Survey Workgroup Session: Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network Project Update – Ingrid Holm

9:55-10:10am Networking Break

10:10-10:40am Genomics – Dana Crawford & David Crosslin

10:40-11:10am Phenotyping – Josh Denny & Peggy Peissig

11:10-11:40am	Pediatrics – Hakon Hakonarson & John Harley
11:40-12:10pm	eMERGE PGx – Josh Denny, Laura Rasmussen-Torvik, & Dan Roden
12:10-12:25pm	***Working Lunch***
12:25 – 12:55pm	Return of Results – Gail Jarvik & Iftikhar Kullo
12:55-1:25pm	EHR Integration – Justin Starren & Marc Williams
1:25-1:55pm	Consent, Education, Regulation and Consultation – Ingrid Holm
1:55-2:15pm	Break
2:15-2:45pm	Input-Feedback from ESP, General Discussion
2:45-3:00pm	Closing Remarks

End Full Session

3:00pm	Adjourn
3:00-3:30pm	Executive Session with ESP - Chairman's Boardroom

Note: The Joint CSER/eMERGE Meeting will be held in TBD room beginning at 5:30PM.

Electronic Medical Records and Genomics (eMERGE) Network
OVERVIEW

eMERGE is a national consortium organized by NHGRI to develop, disseminate, and apply approaches to research. It combines DNA biorepositories with electronic medical record (EMR) systems for large-scale, high-throughput genetic research with the ultimate goal of returning genomic testing results to patients in a clinical care setting.

The Network is currently exploring more than a dozen phenotypes (with 13 additional electronic algorithms having already been published). Various models of returning clinical results have been implemented or planned for pilot at sites across the Network. Themes of bioinformatics, genomic medicine, privacy and community engagement are of particular relevance to eMERGE.

Site	Principal Investigator(s)
Children's Hospital of Pennsylvania (CHOP)	Hakon Hakonarson, MD, PhD
Cincinnati Children's Hopsital Medical Center/Boston's Children's Hospital (CCHMC/BCH)	John Harley, MD, PhD – CCHMC, & Issac Kohane, MD, PhD – BCH
Geisinger Health System	David Carey PhD & Marc Williams, MD
Group Health Cooperative & University of Washington (GHC/UW)	Eric Larson, MD, MPH – GHC & Gail Jarvik, MD, PhD – UW
Essentia Institute of Rural Health & Marshfield Clinic (Marshfield/Essentia/PSU)	Catherine McCarty, PhD, MPH – Essentia & Murray Brilliant, PhD – Marshfield Clinic
Mayo Clinic	Christopher Chute, MD, DrPh, & Iftikhar Kullo, MD
Mount Sinai School of Medicine	Erwin Bottinger, MD
Northwestern University	Rex Chisholm, PhD & Maureen Smith, MS
Vanderbilt University	Dan Roden, MD
Coordinating Center	Jonathan Haines, PhD

eMERGE Network Workgroups

Consent, Education, Regulation, & Consultation – Co-Chairs: Ingrid Holm (CCHMC/BCH) & Maureen Smith (NU)
The CERC Workgroup explores ethical, legal, educational and social issues as related to the eMERGE projects. To achieve this goal, the group plans to work as a full workgroup along with develop specialized subgroups to explore specific focus areas including Consent Forms and Physician and Patient Education.

EHR Integration – Co-Chairs: Justin Starren (NU) & Marc Williams (Geisinger)
The EHR Integration workgroup plans to develop eMERGE II consensus and concepts for EMR integration of genomic information and delivery of clinical genomic decision support utilizing EMR. The workgroup will work to delineate common and distinct approaches and challenges for EMR integration, share best practices, address challenges and approaches for utilization of whole genome/exome sequence-associated information, establish a dialog with EMR vendors and support the use and evaluation of CDS tools.

Genomics – Co-Chairs: Dana Crawford (VU) & David Crosslin (Group Health/UW)
The Genomics Workgroup handles all GWAS data QC and analysis. The Workgroup determined the genotyping technologies for the Network: the Illumina 660W for Caucasians and the Illumina 1M for the QRS and T2D African American cohorts. The Workgroup also determined basic QC measures and processes for the network, as well as a format for sample identifiers. The Workgroup will produce published manuscripts for each site's primary phenotype, as well as manuscripts on the QC process and other GWAS topics.

Phenotyping – Co-Chairs: Josh Denny (VU) & Peggy Peissig (Marshfield/Essentia/PSU)
The Phenotyping Workgroup coordinates and executes network phenotypes and supports covariates for analysis. This will be executed through the development of best practices and a prioritization of phenotype algorithms. This group will also seek to advance the science of de-identification; transportable phenotyping methods, structure and standards; and portable components of algorithms and methods. The workgroup is actively looking to collaborate both within eMERGE and the larger scientific community through other consortia and through the creation of PheKB, a knowledge base for discovering phenotypes from electronic medical records.

Pediatrics – Co-Chairs: John Harley (CCHMC/BCH) & Hakon Hakonarson (CHOP)
The Pediatric Workgroup was formed to provide a forum to find solutions for the scientific, public policy, ethical, and legal issues confronting eMERGE that have a uniquely pediatric component. Examples include the vagaries of human subject consent in pediatrics, the complexities of the return of results to pediatrics patients and their guardians, and the phenotypes that are different from those found at adult institutions, including pediatric-specific diseases, growth and developmental milestones. Also, coordinating phenotypes and data collection will constitute a special opportunity for this workgroup. The Pediatric Workgroup will strive to minimize the duplication of the work being done by the other workgroups in eMERGE and endeavor to focus its attention on the pediatric component in instances where this will be helpful.

Return of Results – Co-Chairs: Gail Jarvik (Group Health/UW) & Iftikhar Kullo (Mayo)
The Return of Results Workgroup's charge is to define an initial set of variants that are potentially useful in clinical practice for purposes such as assessment of genetic risk for complex disorders or selection or dosing of drugs. This initial set will focus on common disease risk variants and pharmacogenetic variants for which we expect to have data. We will assess the levels of evidence supporting these variants and consider the cost and benefit of incorporating them into patient care. To do this we will interact with the larger eMERGE II community and external return of results projects, such as the pharmacogenetics research network and the NHGRI return of results consortium. This workgoup is also actively looking to assess ways to address the dynamic nature of genetic risk, i.e., potential change in risk, as additional susceptibility variants are identified.

eMERGE PGx – Co-Chairs: Josh Denny (VU), Laura Rasmussen-Torvik (NU), & Dan Roden (VU)
The purpose of the eMERGE-PGx project is to initiate a multi-site test of the concept that sequence information can be coupled to electronic medical records (EMRs) for use in healthcare. The sequencing platform PGRN-Seq, developed by the Pharmacogenomics Research Network (PGRN). The long-term goal of the eMERGE-PGx project is to begin to develop strategies for the optimal implementation of genetic sequence data into the clinical environment with the ultimate goal of improving patient care.

eMERGE Phenotypes, Genotypes. & Publications

Phenotype	Lead Site	Secondary Site	Implementation Date
Clostridium difficile	GroupHealth	Vanderbilt	September 2012
Abdominal aortic aneurysm	Geisinger	Mayo	September 2012
Venous Thromboembolism	Mayo	Vanderbilt	September 2012
Ocular Hypertension	Marshfield	Geisinger	November 2012
Diverticulosis	Northwestern	Vanderbilt	November 2012
Glaucoma	Marshfield	Geisinger	January 2013
Herpes Zoster	GroupHealth	Vanderbilt	February 2013
ACE-Inhibitor Induced Cough	Vanderbilt	Northwestern	March 2013
Cardio Respiratory Fitness	Mayo	Geisinger	April 2013
Extreme Obesity	Geisinger	Marshfield	May 2013
Asthma	CHOP	Marshfield	June 2013
Child Obesity	CCHMC/BCH	CHOP	September 2013
Heart Failure	Mayo	GroupHealth	October 2013
Colon Polyps	Northwestern	Marshfield	October 2013
Autism	CCHMC	BCH	October 2013
Statins for MACE	Vanderbilt	Marshfield	October 2013
Lipids	CHOP		October 2013
Age-related Macular Degeneration	Marshfield	Northwestern	October 2013
Upcoming Phenotypes: Diabetic Hypertensive CKD, Rapid Renal Decline in Diabetic HTN Nephropathy, CAAD as quantitative measure, MRSA, Upper GI/PUD, Remission of diabetes after ROUX-EN_Y, Pulmonary HTN, appendicitis, epilepsy, atopic dermatitis, ADHD, GERD			

Network Manuscripts	
Developed	19
Published	16
Site Specific Manuscripts	
Published	18
Total Network Activity Last Quarter	**53**

BEAGLE Imputed Data (Adult Sites only)

	# Genotyped Samples	# BEAGLE Imputed SNPs
Merged eMERGE-I 1M	2,634	
Merged eMERGE-I 660	16,029	
Adult sites (unmerged)	*19,625*	
Adult Site Total	**38,288**	**15,212,466**

Impute2 Imputed Data (Adult and Pediatric)	
	# Genotyped Samples
Merged eMERGE-I 1M	2,634
Merged eMERGE-I 660	16,029
Geisinger	3,111
Group Health	731
Marshfield	500
Mayo	3121
Mt. Sinai	6,290
NU	2,951
Vanderbilt	3,461
BCH	1,038
CCHMC	4,322
CHOP	6,850
Total - All Impute2 Imputed Samples	**51,038**

WORKGROUP OVERVIEW CHART: CERC & EHR Integration

Workgroup	Charter	Aims & Projects	Collaborations	Recent Highlights 2013 (April – November)
Consent, Education, Regulation & Consultation (CERC) Chairpersons: Maureen Smith, MS, CGC (NU) Ingrid Holm, MD, MPH (CCHMC/BCH)	The CERC Workgroup explores ethical, legal, educational and social issues as related to the eMERGE projects. To achieve this goal, the group plans to work as a full workgroup along with develop specialized subgroups to explore specific focus areas including Consent Forms and Physician and Patient Education.	Assessing Physician and Patient Responses to Incidental Findings from PGRNSeq MyResults.org: Centralized Repository of Patient Education Resources: A public eMERGE Website Clinical Integration Projects in Diverse Healthcare Settings Developing Consents for Returning Pharmacogenomics Results: The eMERGE Experience Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network Patient and Physician Education Materials for PGx Seeking Informed Consent for the Inclusion of Samples from Children and Adolescents in Biorepositories: Practical Approaches and Model Language	**Internal** EHRI WG –Infobutton Project; Genetics in Medicine Special Issue PGx WG –Assessing Physician and Patient Responses to Incidental Findings from Return of Results WG –Assessing Physician and Patient Responses to Incidental Findings from PGRNSeq, Site Specific Impact of ACMG Guidelines Pediatric WG – Seeking Informed Consent for the Inclusion of Samples from Children and Adolescents in Biorepositories: Practical Approaches and Model Language **External** Clinical and Translational Science Awards (CTSA) Consortium - Biobanking Workgroup – Membership Overlap Clinical Sequencing Exploratory Research (CSER) Consortium – Membership Overlap, Developing a Joint Project with the RoR Informed Consent and Governance WG Return of Results (RoR) Consortium – Membership Overlap	June: Leadership change –Andrew Faucett, MS (Geisinger) outgoing co-chair, Ingrid Holm, MD, MPH (CCHMC/BCH) incoming co-chair August : Submitted Network-wide project proposal, Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network, in response to ANPRM themed NHGRI Supplement invitation October : MyResults.org: eMERGE Patient Education website launched (Project led by John Connolly, CHOP)
EHR Integration Chairpersons: Justin Starren, MD, PhD (NU) Marc Williams, MD (Geisinger)	The EHR Integration workgroup plans to develop eMERGE II consensus and concepts for EMR integration of genomic information and delivery of clinical genomic decision support utilizing EMR. The workgroup will work to delineate common and distinct approaches and challenges for EMR integration, share best practices, address challenges and approaches for utilization of whole genome/exome sequence-associated information, establish a dialog with EMR vendors and support the use and evaluation of CDS tools.	Primary Aims: • EHR implementation guidance and tracking • Clinical Decision Support integration guidance and tracking across sites Additional Projects: • Genetics in Medicine Special Issue • Infobutton Project	**Internal** CERC WG –Genetics in Medicine Special Issue; Infobutton Project PGx WG –Infobutton Project **External** Clinical Decision Support Consortium (CDSC) Clinical Sequencing Exploratory Research (CSER) Consortium – Genetics in Medicine Special Issue IGNITE - Membership Overlap Health Level Seven (HL7) – Standards Implementation (use cases?)	May : Began tracking site-specific EHR implementation milestones month by month. October : eMERGE Network's Genetics in Medicine Special Issue, led by the EHRI workgroup, in print November: Several sites will be presenting on eMERGE/EHRI specific topics and a the Network will present Genetics in Medicine Special Issue topics during a President's Pick Session at AMIA 2013.

WORKGROUP OVERVIEW CHART: eMERGE PGx & Genomics

Workgroup	Charter	Aims & Projects	Collaborations	Recent Highlights 2013 (April – November)
eMERGE PGx Chairpersons: Dan Roden, MD (VU) Josh Denny, MD, MS (VU) Laura Rasmussen-Torvik, PhD, MPH (NU)	The purpose of the eMERGE-PGx project is to initiate a multi-site test of the concept that sequence information can be coupled to electronic medical records (EMRs) for use in healthcare. The sequencing platform PGRN-Seq, developed by the Pharmacogenomics Research Network (PGRN). The long-term goal of the eMERGE-PGx project is to begin to develop strategies for the optimal implementation of genetic sequence data into the clinical environment with the ultimate goal of improving patient care.	Primary Aims: • Establish consented cohorts of subjects likely to benefit from phamacogenomics information within 1-3 years – 9,000 Network wide • Implement PRGN-Seq platform across all sites' cohorts • Integrate validated genotypes into the EMR with clinical decision support • Assess uptake, acceptance and clinical impact – PGx Process Outcomes Metrics • SPHINX (Sequence, Phenotype, and pHarmacogenomics INtegration eXchange)- Development of a repository of variants of unknown significance with EMR derived phenotype data	**Internal** CERC WG – Centralized Repository for Patient Education Resources: a public eMERGE website – my results.org; Assessing Physician and Patient Responses to Incidental Findings from PGRNSeq EHRI WG –Infobutton Project Phenotyping WG – SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange), PGx Outcomes Genomics WG – SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange Return of Results WG: Site Specific RoR plans for PGRN Seq **External** Center for Inherited Disease Research, Johns Hopkins University – CLIA-compliant validation genotyping CIDR - Sequencing Pharmacogenomics Research Network (PGRN) – PGRNSeq Platform, open exchange of tools & knowledge	May: Participant recruitment and enrollment began June: End of year deliverables finalized for PGx outcomes metrics, sequencing, and variant repository 9038 total participants / samples expected by project's end Recruitment and sample collection to date: • 3622 Participants Recruited • 1100 DNA Samples Sequenced • 300 Sequences Called • >100 Participants with Results in their clinical record
Genomics Chairpersons: Dana Crawford, PhD (VU) David Crosslin, PhD (GroupHealth/UW) Marylyn Ritchie (QC), PhD (CC)	The Genomics Workgroup handles all GWAS data QC and analysis. The Workgroup determined the genotyping technologies for the Network: the Illumina 660W for Caucasians and the Illumina 1M for the QRS and T2D African American cohorts. The Workgroup also determined basic QC measures and processes for the network, as well as a format for sample identifiers. The Workgroup will produce published manuscripts for each site's primary phenotype, as well as manuscripts on the QC process and other GWAS topics.	Primary Aims: • 36 genomics analyses on different network phenotype cohorts (Resistant Hypertension, C.Diff Colitis, Glaucoma) • Genotyping data QC and imputation Additional Projects: • AAA-Meta Analysis • Exome Chip • Frontiers in Genetics Special Issue • Gene-Gene Interactions • Genetic Risk Scores • Log R and B Allele • Null (Loss of Function) Variants	**Internal** PGx WG: Development of SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange Phenotyping WG: Null (Loss of Function) Variants, SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange, Resistant Hypertension Return of Results WG: Chromosomal Abnormalities, Frontiers in Genetics Special Issue, Genetic Risk Scores Site Collaboration – Exome Chip **External** Welcome Trust – AAA-Meta Analysis	June: Completed re-analyzing the Resistant Hypertension data and developed a new plan to move forward July : Began investigation of Null (Loss of Function) Variants August: Imputation on BEAGLE and IMPUTE2 complete. Sets released: xx samples September: SPHINX (PGx Variant Repository) will be piloted

WORKGROUP OVERVIEW CHART: Phenotyping & Pediatrics

Workgroup	Charter	Developing Projects	Collaborations	Recent Highlights 2013 (April – November)
Phenotyping Chairpersons: Peggy Peissig, MBA , PhD (MC/EIRH/PSU) Josh Denny, MD, MS (VU)	The Phenotyping Workgroup coordinates and executes network phenotypes and supports covariates for analysis. This will be executed through the development of best practices and a prioritization of phenotype algorithms. This group will also seek to advance the science of de-identification; transportable phenotyping methods, structure and standards; and portable components of algorithms and methods. The workgroup is actively looking to collaborate both within eMERGE and the larger scientific community through other consortia and through the creation of PheKB, a knowledge base for discovering phenotypes from electronic medical records.	Primary Aims: • Develop and implement 36 electronic phenotype algorithms across the Network Additional Projects: • PheKB (www.phekb.org) - a public knowledgebase for sharing and co-developing electronic phenotypes • eMERGE RecordCounter – a Network tool to aid in hypothesis generation and assessing feasibility • Portable NLP Phenotype Standardization – to enhance sharing of electronic algorithms • Methods for Extracting and Sharing Medication Data (RxNorm) using standardized formats • Data Standardization for internal and external sharing of phenotype data	**Internal** Genomics WG: Null (Loss of Function) Variants, SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange Resistant Hypertension PGx WG: SPHINX (Sequence, Phenotype. & pHarmacogeneomics Integration eXchange, PGx Outcomes	• 12 Completed Phenotypes: C Diff, AAA, VTE, Ocular HTN, Diverticulosis, Glaucoma, Zoster, ACE-I Cough, CRF, DILI, Extreme Obesity, Asthma • PheKB has 233 active users representing 24 institutions. Overall, there are 20 publicly available phenotypes and 44 phenotypes shared privately amongst authors/collaborative groups • eMERGE RecordCounter has over 52,000 records representing genotyped samples available for counts based on search criteria including demographic data, ICD9 data, and CPT data. • Demonstrated the portable NPL Phenotype Standardization on 3 eMERGE phenotypes • Developing Data dictionary/Data validation and standardization tool to be implemented into PheKB.org
Pediatrics Chairpersons: John Harley, MD, PhD (CCHMC/BCH) Hakon Hakonarson, MD, PhD (CHOP)	The Pediatric Workgroup was formed to provide a forum to find solutions for the scientific, public policy, ethical, and legal issues confronting eMERGE that have a uniquely pediatric component. Examples include the vagaries of human subject consent in pediatrics, the complexities of the return of results to pediatrics patients and their guardians, and the phenotypes that are different from those found at adult institutions. Also, coordinating phenotypes and data collection will constitute a special opportunity for this workgroup. The Pediatric Workgroup will strive to minimize the duplication of the work being done by the other workgroups in eMERGE and endeavor to focus its attention on the pediatric component in instances where this will be helpful	• Common Survey Instrument	**Internal** CERC WG: Seeking Informed Consent for the Inclusion of Samples from Children and Adolescents in Biorepositories: Practical Approaches and Model Language PGx WG: Process Outcomes Metrics Phenotyping WG: Pediatric Phenotype Development & Implementation	June: Workgroup formed July: First workgroup meeting held

WORKGROUP OVERVIEW CHART: Return of Results

Workgroup	Charter	Developing Projects	Collaborations	Recent Highlights 2013 (April – November)
Return of Results Chairpersons: Iftikhar Kullo, MD (Mayo) Gail Jarvik, MD, PhD (GroupHealth/UW)	The Return of Results Workgroup's charge is to define an initial set of variants that are potentially useful in clinical practice for purposes such as assessment of genetic risk for complex disorders or selection or dosing of drugs. This initial set will focus on common disease risk variants and pharmacogenetic variants for which we expect to have data. We will assess the levels of evidence supporting these variants and consider the cost and benefit of incorporating them into patient care. To do this we will interact with the larger eMERGE II community and external return of results projects, such as the pharmacogenetics research network and the NHGRI return of results consortium. This Workgoup is also actively looking to assess ways to address the dynamic nature of genetic risk, i.e., potential change in risk, as additional susceptibility variants are identified.	• Hemochromatosis (HFE)	**Internal** CERC WG: Assessing Physician & Patient Responses to Incidental Findings from PGRNSeq, Site Specific Impact of ACMG Recommendations, Seeking Informed Consent for the Inclusion of Samples from Children and Adolescents in Biorepositories: Practical Approaches and Model Language Genomics WG: Frontiers in Genetics Special Issue; Genetic Risk Scores, Chromosomal Abnormalities PGx WG: Site Specific RoR Plans for PGRNSeq **External** Clinical Sequencing Exploratory Research (CSER) Consortium – Membership overlap Return of Results (RoR) Consortium – Membership overlap	June: Assessed site specific impact of the ACMG Guidelines in terms of PGx related incidental findings July: Assisted with composing the Joint eMERGE/CSER Return of Results Session for the October join meeting

eMERGE Tools Development

	Released Tools Available to Public
Phenotyping	**eleMAP (Mayo/CC)** *113 users representing 70 institutions* **PheKB (CC)** *233 users representing; 24 institutions; 2,936 unique visitors to the website since release*
Genotyping	**PennCNV (CHOP)** *Widely-used: 577 Citations to date* **NGS data Analysis Pipeline (CHOP)** *Over 1,700 subjects whole exome sequencing with over 100 different rare medical disorders, resolved over 30 rare disorders; sequencing an average of 50 exomes per week at 70x coverage, with an average turn-around time of four to six weeks from sample-processing to variant identification* **Biofilter, BioBin (Penn State/ Marshfield)** *Provides methods for prioritizing and analyzing variants singly or in groups, over 50 downloads since June, 2013* **PLATO, ATHENA (Penn State/ Marshfield)** *Provides platforms for QC and integrating multiple methods of analysis, over 50 downloads since June, 2013* **Synthesis-View PheWas-View, Phenogram (Penn State/ Marshfield)** *Provides visualization tools for genome and phenome-wide data, over 900 unique visitors*
Consent	**eMERGE Model Consent Language (eMERGE Network)** *Freely available on NIH website*
CDS	**ANNOVAR (CHOP)** *Widely used: 394 citations to date* **MyResearch, integration between Registrar and MyChart (NU)** *502 patients registered as of end of August*
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eMERGE Tools Development

	In Development	Beta Testing	Early (Limited) Release
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Cross Cutting Collaborative Network Projects

Projects	Status	CERC	eMERGE PGx	Genomics	Phenotyping	EHRI	RoR	Pediatrics
PGx Outcomes	Seven Outcome Domains defined. Definitions being finalized. First Results Due October 2013							
SPHINX (Sequence, Phenotype, and pHarmacogenomics Integration eXchange)	Early stage specifications and design							
Genomics in Medicine Special Issue	Complete (Oct. 2013)							
Infobuttons	Configuring and content creation in process.							
Chromosomal Abnormalities	In Process.							
Centralized Repository of Patient Education Resources: A public eMERGE Website - myresults.org	Early stage release (Oct. 2013)							
Null (Loss of Function) Variants	Study design defined. Initial variant annotation with SNPeff complete.							
Frontiers in Genetics Special issue	Manuscripts defined. Completed manuscripts due to Frontiers by Oct. 15.							
Resistant Hypertension	Study redesigned. Re-analysis of data in process.							
Genetic Risk Scores	Publication in process focused on lipids. T2D and cancer planned.							
Assessing Physician and Patient Responses to Incidental Findings from PGRNSeq	Project plan proposed, study design TBD.							
Seeking Informed Consent for the Inclusion of Samples from Children and Adolescents in Biorepositories: Practical Approaches and Model Language	Data review underway, manuscript draft in process.							

Additional Workgroup Initiatives

Projects	Status	CERC	eMERGE PGx	Genomics	Phenotyping	EHRI	RoR	Pediatrics
Methods for Extracting and Sharing Medication Data using standardized formats	Initial instutional review in process							
eMERGE RecordCounter	Released (January, 2013)							
PheKB	Released (February, 2012)							
Portable NLP Phenotype Standardization	Initial demonstration in process							
Data Standardization for internal and external sharing of phenotype data	Early stage development and testing							
Hemacromatosis	Chart abstractions in process.							
Log R and B Allele	Phase I 660 data complete, September, 2013. Project is ongoing.							
Gene-Gene Interactions	Cataracts complete (August 2013) & Lipids are in process.							
AAA-Meta Analysis	Sites are submitting data.							
Exome Chip	Recruiting additional sites and examining associations.							
Imputed Data	Released (August 2013)							
Developing Consents for Returning Pharmacogenomics Results: The eMERGE Experience	Manuscript concept sheet under PI review.							
Clinical Integration Projects in Diverse Healthcare Settings	Project deliverables defined.							
Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network	Project deliverables defined, study design and methodology in process							
Common Patient Survey Instrument	In discussion with pediatric teams; comparison of current RoR methods between sites.							

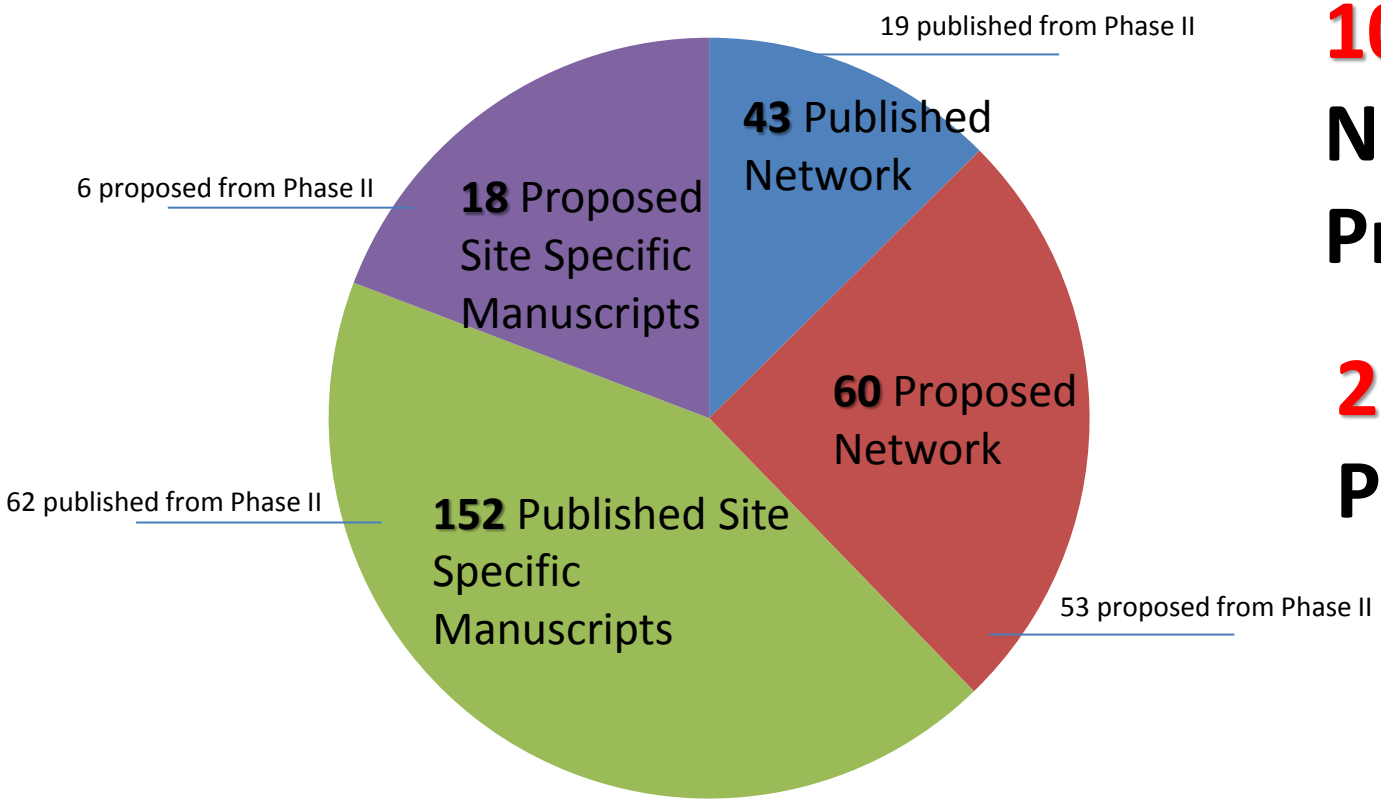
eMERGE Expert Scientific Panel Recommendations

October 2013

On-going

Recommendation: Pursue Network projects and communicate externally.

eMERGE Publications through October 2013



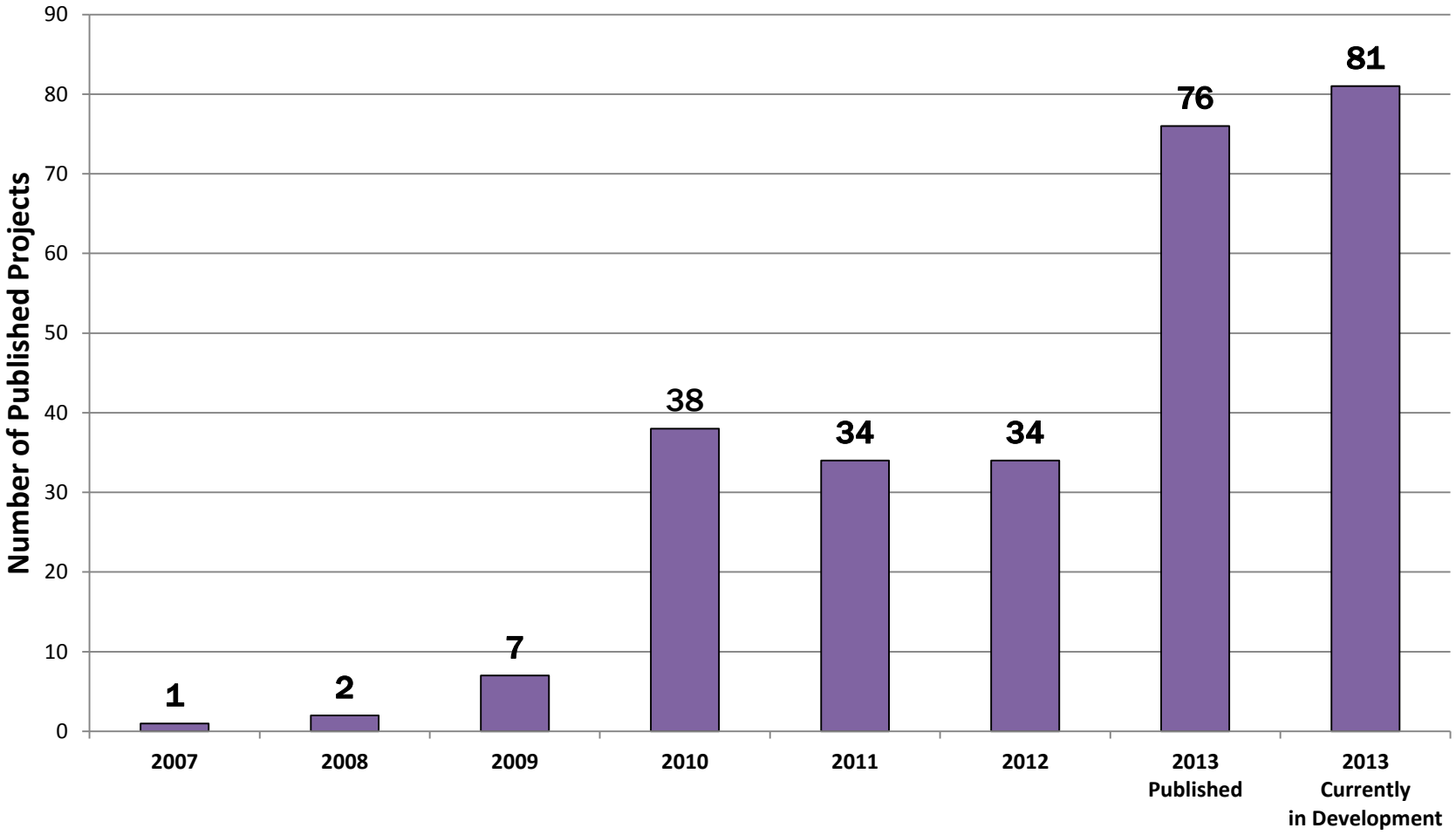
103 Total Network Projects

273 Total Projects

eMERGE

External Communication

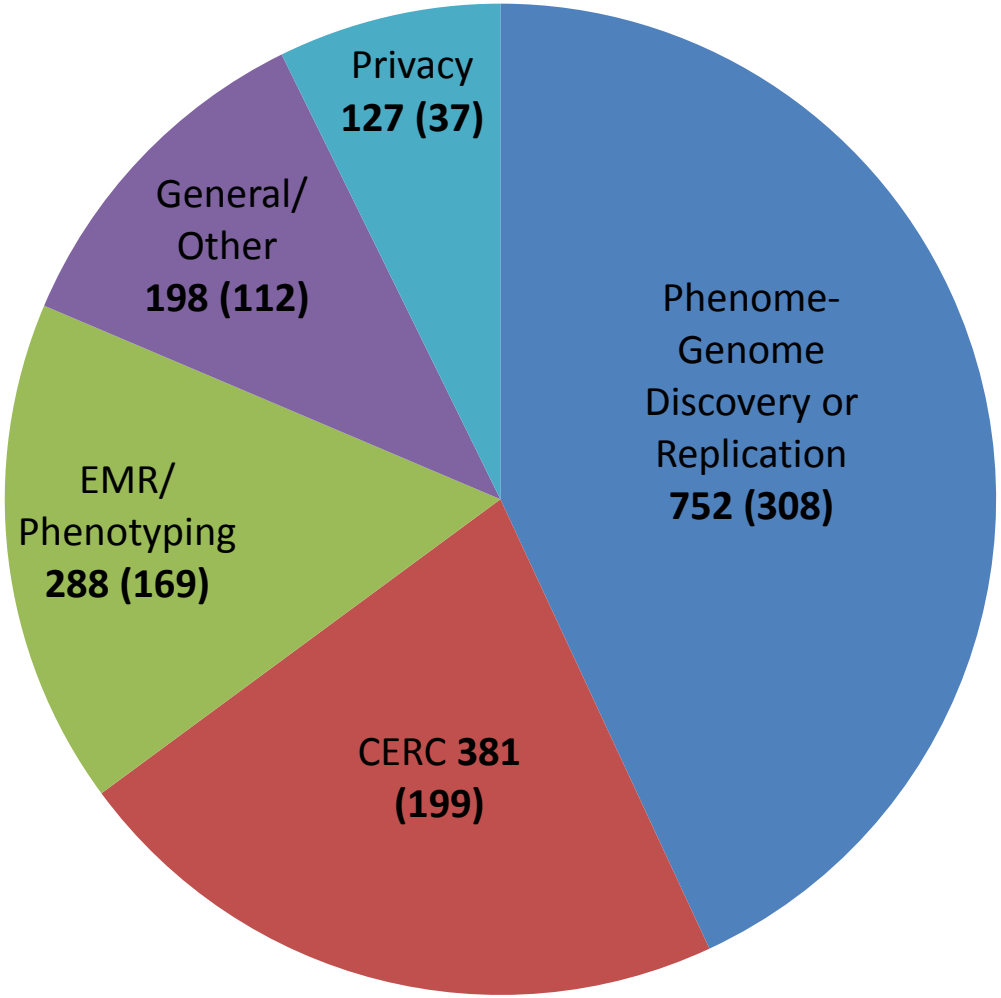
eMERGE Projects Published by Year through Oct 2013



eMERGE

Citation Analysis

eMERGE Publications: Number of Times Cited through October 2013



Total Number of Times Cited

- 2007-October 2013: **1,746**
  - Phase II Publications Only: **261**
- April –October 2013: **825**
  - Phase II Publications Only: **213**

*** Chart totals in parenthesis reflect number of times cited between April -October 2013.**

eMERGE

Special Journal Issues

Genetics In Medicine Special Issue - Lead: Marc Williams and Joseph Kannry

- Published **October 2013**: Features nine articles specific to EHR implementation and integration experiences of the eMERGE Network.
- AMIA 2013 President's Pick Session presentation scheduled for November 2013.

Frontiers in Genetics Special Issue - Lead – Marylyn Ritchie

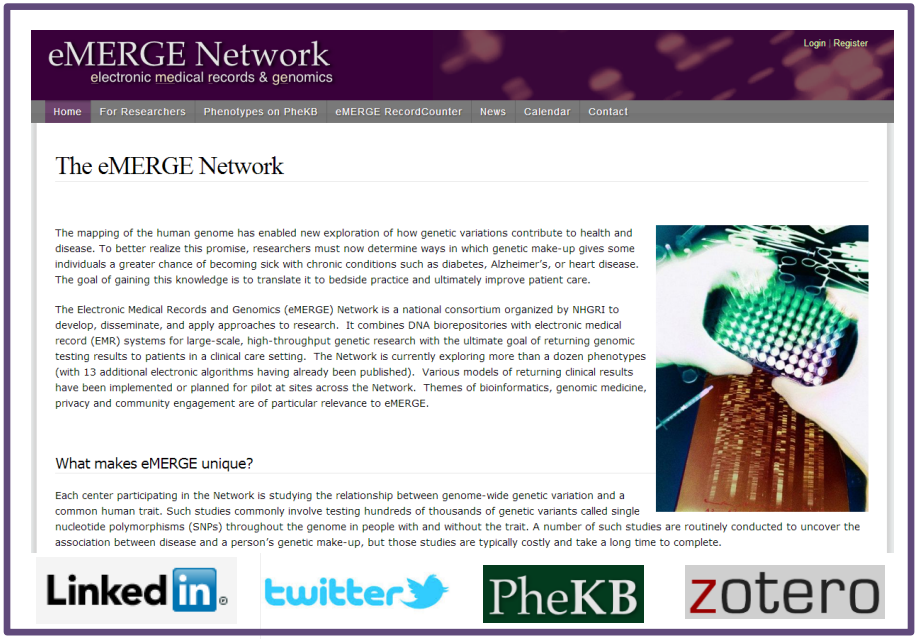
- Article/Topics: In Development
  - Imputation and QC for Combining Genome-wide Datasets
  - Evaluation of Population Stratification in Large Biobanks Linked to EHR
  - State of Returning Genomics Research Results
  - EMR-linked GWAS Study: Investigation of Variation Landscape of Loci for Body Mass Index in Children
  - PheWAS in EHR datasets
  - Using Publicly Available Controls for GWAS Studies
  - Review of eMERGE Progress in Genomics – First 6 Years
  - Replication of Metabolic Phenotypes from EHR Data Using the CardioMetabochip
  - Analysis Pipeline for the Epistasis Search – Statistical Versus Biological Filtering
  - Genetic Risk Prediction
  - The Struggle to Find Reliable Results in Exome Sequencing Data
  - EMR-Linked CNV: Meta Analysis of Copy Number Variants Across the eMERGE Network
  - EMR-linked LoF: Assessing the Functional Consequence of Loss of Function Variants Using the Electronic Medical Record
  - EMR-linked Framework for Assessing Drug-Genome Interactions
- Target Publication Date: Fall 2013

Recommendations:

-- Share eMERGE science and products

GWAS.org

- The eMERGE website provides a one-stop shop for updates and additional information on eMERGE science as well as tools for sharing
  - PheKB.org – phenotype knowledge base
  - Record Counter – subject counts for hypothesis generation and feasibility assessment
  - *Coming Soon*
    - Myresults.org – patient education
    - SPHINX – **S**equence, **P**henotype, and p**H**armacogenomics **I**ntegration e**X**change
  - GWAS.org receives over **700 unique visits** per month.



eMERGE

Recommendations:

-- Share eMERGE science and products

-- Measure and assess impact

	Released Tools Available to Public
Phenotyping	**eleMAP (Mayo/CC)** *113 users representing 70 institutions* **PheKB (CC)** *233 users representing; 24 institutions; 2,936 unique visitors to the website since release*
Genomics	**PennCNV (CHOP)** *Widely-used: 577 Citations to date* **NGS data Analysis Pipeline (CHOP)** *Over 1,700 subjects whole exome sequencing with over 100 different rare medical disorders, resolved over 30 rare disorders; sequencing an average of 50 exomes per week at 70x coverage, with an average turn-around time of four to six weeks from sample-processing to variant identification* **ANNOVAR (CHOP)** *Widely used: 394 citations to date* **Biofilter, BioBin (Penn State/Marshfield)** *Provides methods for prioritizing and analyzing variants singly or in groups* **PLATO, ATHENA (Penn State/Marshfield, Vanderbilt)** *Provides platforms for QC and integrating multiple methods of analysis* **Synthesis-View, PheWAS-View, Phenogram (Penn State/Marshfield, Vanderbilt)** *Provides visualization tools for genome and phenome-wide data*
CERC	**eMERGE Model Consent Language (eMERGE Network)** *Freely available on NIH website*
CDS	**MyResearch, integration between Registrar and MyChart (NU)** *502 patients registered as of end of August*
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Recommendations:

-- Measure and assess impact

-- Track Developmental Stages of Tools

	In Development	Beta Testing	Early (Limited) Release
Phenotyping		**PheWAS R Package (VU)** **Web-based Ophthalmology Data Collection (Marshfield/ESS/PSU)** *Evaluation in progress at one institution*	**Phewas 1.0 (VU)** *3944 downloads from website*
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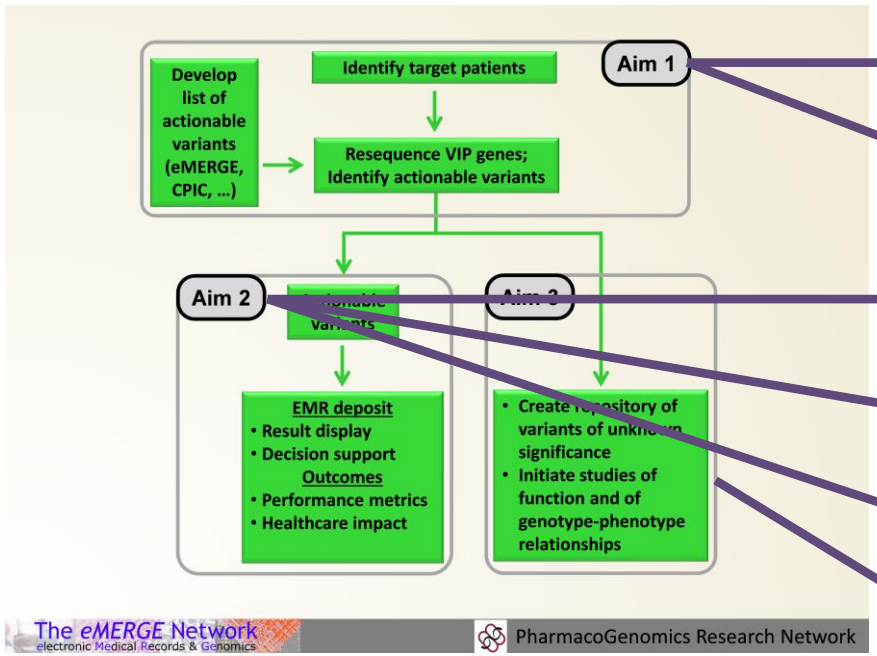
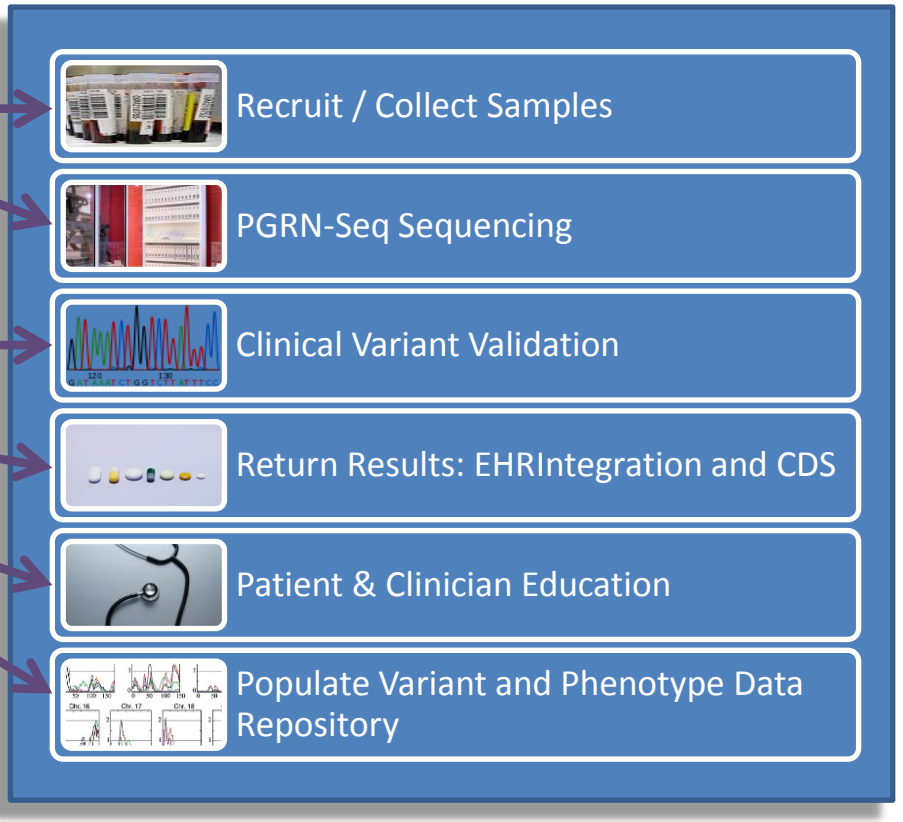
Recommendation:

-- Refine Project Goals for eMERGE PGx

- Project Aims organized into 6 primary goals
- Site-specific approaches to these goals being tracked at the Coordinating Center





eMERGE

Recommendation:

-- eMERGE PGx to Measure Implementation Process vs Clinical Outcomes

The Process Metrics plan incorporates this recommendation:

Organized outcomes into 7 Outcomes Domains:

- Recruitment
- PGRN-Seq Sequencing
- Validation Genotyping
- EMR Integration and CDS
- Returned Results
- Clinician Education
- Patient Education

For each domain, we are collecting :

- Descriptive measures; some comparative implementation descriptions being considered
- Quantitative QC and tracking metrics

Clinical outcomes measures are at the sites' discretion and capacity

Recommendation:

-- Use Common Instruments/Measures among Genomic Medicine Projects

Use of Existing Methods

- Incorporation of published methods/measures for studying usability of implementations (EHRI)

Use/Creation of Common Resources

- Use of common Clinical Decision Support information resources (Infobutton project, EHRI/CERC)
- Provider education (CERC/PGx)
- Patient/Provider Surveys (Pediatrics)