**eMERGE Network**

Meeting Attendee List

March 30-31st, 2015; Bethesda, MD

CCHMC/BCH Armand Antommaria

CCHMC/BCH Beth Cobb

CCHMC/BCH John Harley

CCHMC/BCH Ingrid Holm

CCHMC/BCH Todd Lingren

CCHMC/BCH Melanie Myers

CCHMC/BCH Bahram Namjou

CCHMC/BCH Cassandra Perry

CCHMC/BCH Cindy Prows

CCHMC/BCH Wendy Wolf

CHOP Berta Castillo

CHOP John Connolly

CHOP Hakon Hakonarson

CHOP/UPenn Brendan Keating

CHOP Michael March

CHOP Frank Mentch

CHOP Patrick Sleiman

Geisinger Kenneth Borthwick

Geisinger David Carey

Geisinger Henry Kirchner

Geisinger Joseph Leader

Geisinger David Ledbetter

Geisinger/U of Maryland Casey Overby

Geisinger Diane Smelser

Geisinger Gerard Tromp

Geisinger Janet Williams

Geisinger Marc Williams

GH/UW David Carrell

GH/UW David Crosslin

GH/UW Stephanie Fullerton

GH/UW Andrea Hartzler

GH/UW Gail Jarvik

GH/UW Eric Larson

Marsh/Essentia/PSU Murray Brilliant

Marsh/Essentia/PSU Scott Hebbring

Marsh/Essentia/PSU Terrie Kitchner

Marsh/Essentia/PSU Cathy McCarty

Marsh/Essentia/PSU Peggy Peissig

Marsh/Essentia/PSU/CC Sarah Pendergrass

Marsh/Essentia/PSU/CC Marylyn Ritchie

Marsh/Essentia/PSU/CC Shefali Setia

Marsh/Essentia/PSU/CC John Wallace

Mayo Mariza de Andrade

Mayo Chris Chute

Mayo Robert Freimuth

Mayo Iftikhar Kullo

Mayo Jyoti Pathak

Mayo Richard Sharp

Mt. Sinai Noura Abul-Husn

Mt. Sinai Erwin Bottinger

Mt. Sinai Stephen Ellis

Mt. Sinai Genevieve Galarneau

Mt. Sinai Carol Horowitz

Mt. Sinai Eimear Kenny

Mt. Sinai Ana Mejia

Mt. Sinai Girish Nadkarni

Mt. Sinai Aniwaa Owusu Obeng

Mt. Sinai Michelle Ramos

Mt. Sinai/Columbia Chunhua Weng

Northwestern Rex Chisholm

Northwestern Geoff Hayes

Northwestern Laura Rasmussen-Torvik

Northwestern Luke Rasmussen

Northwestern Maureen Smith

Northwestern Justin Starren

NHGRI Rongling Li

NHGRI Teri Manolio

NHGRI Jackie Odgis

NHGRI Ken Wiley

Vanderbilt/Louisville/CC Kyle Brothers

Vanderbilt Ellen Clayton

Vanderbilt Nancy Cox

Vanderbilt/CC Josh Denny

Vanderbilt Todd Edwards

Vanderbilt Josh Peterson

Vanderbilt Dan Roden

Vanderbilt/CC Sarah Stallings

Vanderbilt Pedro Teixeira

CC Melissa Basford

CC Adam Hardebeck

CC Paul Harris

CC/Vanderbilt Bradley Malin

CC/Vanderbilt Nate Mercaldo

CC/Vanderbilt Martha Shrubsole

Network Invitees and Guests

CIDR Jane Romm

USAF Ruth Brenner

USAF Ronald Miller

USAF Catherine Witkop

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| **eMERGE Network** ***Summary of the eMERGE Steering Committee Meeting*** March 30-31st, 2015; Bethesda, MD |
| The eMERGE Steering Committee Meeting was held on March 30-31, 2015 in Bethesda, MD. Highlights from the Steering Committee Meeting are below.  Presentation slides are [available here](https://emerge.mc.vanderbilt.edu/?page_id=1046) (login required).  *Goals for the meeting:*   * Scientific presentations and discussions * Workgroup achievement and timeline * Network projects update   + PGx   + CERC Survey * Products dissemination update * NIH precision medicine workshop (Feb. 11-12, 2015) discussion |
| **Day 1: Full Session (Opening Remarks, Science Presentations)** |
| * Welcome, Opening Remarks, General Updates – *Rongling Li (NHGRI)*   + The Steering Committee was encouraged to refine plans and timelines for the final 4 months of Phase II, and to consider effective methods of completing outstanding workgroup issues in relation to Phase II goals.   + The Steering Committee was also encouraged to refine plans for disseminating eMERGE II network-wide lessons learned and best practices to the greater scientific community.   + The Genomic Medicine 8 Meeting (June 8-9, 2015) was announced. * Announcements, Opening Remarks – *Rex Chisholm (Northwestern)*   + The workgroups were urged to hone in and finalize timelines to complete project goals.   + Members were directed to the new eMERGE website and asked to provide feedback.   Scientific Presentations (selected from site submissions)   * Preliminary Results of the MIGENES Clinical Trial: an eMERGE Genomic Medicine Pilot Study – *Iftikhar Kullo (Mayo)*   + A review of the Myocardial Infarction Genes Study (MIGENES) at Mayo was provided. The study investigated the question of whether knowledge of genetic risk alters clinical outcomes. The trial measured changes in LDL levels for individuals who were told 10-year risk of Coronary Heart Disease (CHD) and Genetic Risk Score (GRS) using a graphical tool to demonstrate their risk compared to individuals told their Framingham CHD Risk Score and shown their risk graphically. They hypothesized that disclosure of a GRS for CHD would result in lower LDL-C levels than the Framingham Score alone. 207 participants were enrolled in the study.   + After providing study method details, it was concluded that disclosing a Genetic Risk Score did lead to lower LDL-C in the near term compared to patients that only knew their Framingham Risk Score. After the 3 month milestone, the decrease in LDL-C differed between study subgroups due to greater decrement in high GRS patients. Disclosure of a GRS for CHD did not change patient lifestyle, as measured by LDL cholesterol, but was associated with earlier initiation of statin medication.   + The study results suggest that there is potential clinical utility in incorporating genetic risk assessment for CHD. * [CERC](http://emerge.mc.vanderbilt.edu/qf/private/Appendicitis-Harley.pdf) Survey Update – *Ingrid Holm (BCH) & Maureen Smith (Northwestern)*   + The pilot CERC survey was circulated to 150 participants per eMERGE site in December. The survey had an 11% response rate. The response rate for the full survey should exceed this due in part to more propitious mailing timing and using two rounds of reminder postcards. Hispanic, Asian, and low education groups were oversampled which resulted in greater representation for those groups than is traditionally seen in surveys. Additionally, analysis of questions with multiple sub-parts suggested that a low percentage of people answered formulaically, choosing the same answer for every question (a “straight-line” response).   + Distribution of the first wave of surveys begins – 4/3/15   + The group is disseminating information based on the survey project:     - Systematic literature reviews – 3 papers (Nanibaa’ Garrison – lead)     - Methods (Ingrid and Maureen – leads)     - Cognitive interviews (Melanie Meyers – lead)     - IRB issues (Jen McCormick – lead)     - Poster presentation at ACMG (Ingrid)   + Analysis extends beyond end of grant period (no-cost extensions to February 2016 at all sites)   **ACTION ITEM: The workgroup will make the CERC survey available on the eMERGE website.**   * Returning Children’s CYP2D6 Research Results to Parents – *Cindy Prows & Melanie Myers (CCHMC)*   + The presentation provided an overview of CCHMC/BCH’s study to use return of CYP2D6 research results to explore parents’ response to and use of their children’s research results and better understand the factors that influence their decisions about learning incidental findings.   + The study found that:     - Parents feel they and their child’s physician can use the child’s CYP2D6 research result to provide care for child     - Parents report that they are likely to share their child’s CYP2D6 research result with their child’s physician   + Next steps of the project include comparing return of actual vs. hypothetical results, as well as further surveying of parents and physicians. * eMERGE PGx Plenary Session – *Workgroup Leads*   + The PGx project was discussed in depth, including a review of timelines and project progress. The project is currently on pace to be completed in June.   + Three network PGx phenotypes (MACE on Clopidogrel in adults and Methylphenidate and Intractable Epilepsy in children) are in progress and are expected to be completed by the end of Phase II.   + HapMap files have been received for the Network Variant Paper, and the CC is working with the Genomics workgroup to compare/evaluate different pipelines and filters.     - Calling pipeline and filtering parameters are available on SPHINX’s public site for those interested.   + UW’s PGRNSeq Multisample files are now available on the UW Aspera server     - 5,249 BAMs from the CC were realigned and recalled by UW, and IDs have been converted to eMERGE IDs.   + PGx Publications:     - PGx Lipid Analysis: annotation has started for the 4,069 samples recently provided by the network     - Network Variant Paper: analysis is complete, and authors are expected to provide feedback in time for the proposed submission date of April 23rd. The paper is being targeted for the *American Journal of Human Genetics.*     - Cardiac Phenotypes and SCN5A-KCNH2: a final draft is being circulated April 3rd, and submission is being prepared for *New England Journal of Medicine*   + dbGaP Submission     - Phenotype files and VCFs are ready to be submitted in early April 2015. The final submission to dbGaP will take place on July 1, 2015.   + SPHINX     - The CC is investigating risks associated with adding phenotypic data to SPHINX. Currently, an end-user license agreement (EULA) has been added to the public site, and enhanced access control methods are being considered. Brad Malin’s privacy presentation given on Day 2 (below), will expand on a robust discussion of various ideas proposed during the presentation.     - The SC identified a need to submit variants from SPHINX to ClinVar, and to also add SPHINX as an ‘expert submitter’ in ClinVar. Variants should be added soon, while annotations can be added later.   **ACTION ITEM: The PGx workgroup will further investigate the process of submitting to ClinVar.**   * + PGx Process Outcomes     - Timelines for metric templates were reviewed. Publications are being planned for ROR & CLIA-PGRNseq Concordance, Provider Education, and CDS Process/Metrics. The leadership group placed priority on the CDS metrics.   + CDS Outcomes Metrics     - Most project milestones have been reached, only ‘receiving data from sites’ and ‘data cleaning/analysis’ are remaining. Sites need to submit their site scenario data set by April 6th.     - The CDS metrics publication was identified as the priority to have completed by the end of Phase II.     - Variation between sites’ data collection methods/results was identified as an important aspect for further study. * Results from GWAS Using Imputed Data from All Sites – *Patrick Sleiman & Berta Castillo (CHOP)*   + Phenotypes and algorithm validation and accruals were overviewed for Asthma, Atopic Dermatitis, ADHD, and GERD. [Please see the presentation slides for more detailed information.](https://emerge.mc.vanderbilt.edu/wp-content/uploads/2015/04/CHOP_eMERGE_presentation2_March2015.pdf) * CDS Repository: Proposal and Design from the EHRI Workgroup and Coordinating Center *– Luke Rasmussen (Northwestern) & Josh Peterson (VU)*   + The presentation showcased the development of a lightweight repository to use as a platform to publically disseminate unstructured CDS artifacts in an effort to promote genomic CDS design & innovation while also developing a community of experts and interested users. The repository will initially focus on genomic medicine but will be designed agnostically to support all decision support domains.   + The initial version of the Clinical Decision Support Knowledgebase (CDSKb) is under development, with plans for contributors to review the content at the end of May and a go live date in early June.   + The strength of the knowledgebase will be through broad participation. The project already includes collaborations with IGNITE, and the project team will approach other organizations involved in CDS to expand this collaborative effort.   **ACTION ITEM: Additional example artifacts for curation and inclusion in CDS KB may be sent to Luke Rasmussen (**[**luke.rasmussen@northwestern.edu**](mailto:luke.rasmussen@northwestern.edu)**).**   * [Use](http://emerge.mc.vanderbilt.edu/qf/private/Appendicitis-Harley.pdf) of Natural Language Processing for PheWAS Studies and Two Methods and Proof of Concept Studies – *Scott Hebbring (Marshfield), Pedro Teixeira, & Josh Denny (VU)*   + The presentation provided an overview of a text-based PheWAS study, hypothesizing that text data from physician notes embedded in an EMR system can be used to define a PheWAS phenome, currently defined from ICD-9 codes. EHR text is rich and potentially more accurate data source than ICD-9 codes, and NLP extracts concepts from unstructured text, possibly yielding more granular and accurate phenotypes than ICD-9-only based PheWAS codes.   + The two text filters considered are medically meaningful terms based on the UMLS dictionary and frequency. The best results may come when text data is combined with other relevant health information (e.g., prescription data, lab values…).   + Future Directions:  1. Collapse Concept Unique Identifiers (CUIs) into phenotypes by hierarchy 2. Cluster multiple sclerosis (MS) phenotypes   –by symptom-lesion location  –by MS-subtypes   1. Examine treatment differences within subtypes 2. Examine outcomes based on different treatments within clustered subsets  * [GWAS and PheWAS](http://emerge.mc.vanderbilt.edu/qf/private/Steel%20Syndrome-Kenny.pdf) of Diverticular Disease – *Jennifer Pacheco & Laura Rasmussen-Torvik (Northwestern)*   + This presentation discussed the GWAS & PheWAS study of diverticulosis in European and African American populations. GWAS results resulted in top hits in CAV1/CAV2 (7q31.2, rs76633992, p= 9.28E-08) for EA diverticulosis samples. In AA diverticulitis samples, the GWAS resulted in top hits in PRR16/LOC102467226 (5q23.2, rs62382461, p= 4.62E-08).   + The GWAS model initially used reduced case and control numbers. Investigators plan to try a simplified model to increase power and will test out a MANTRA meta-analysis.   + The group will refine their PheWAS cohort. They will look to see if the genes were expressed in the colon, since it did not appear immune and also consider a case only age at diagnosis analysis – segregating cases based on age. * NIH Precision Medicine Workshop – *Erwin Bottinger, Murray Brilliant, Rex Chisholm, Josh Denny, David Ledbetter, Dan Roden, & Marc Williams (Mount Sinai, Marshfield, Northwestern, VU, Geisinger)*   + eMERGE members who participated in the NIH’s workshop presented and commented on the meeting agenda and materials. The materials are posted on the [Precision Medicine website](http://www.nih.gov/precisionmedicine/workshop.htm). eMERGE was one of the most commonly cited models at the meeting.   + The FDA is actively exploring a framework to regulate genetic tests, though they are looking for more technology cases (and data) that integrate into the EHR.   + There was general discussion on developing a 1 million person cohort, including processes to be used (blend of bringing existing cohorts together and starting new ones), and questions to be answered (what problem is the cohort trying to solve).   + The development of mobile health technological (mHealth) capabilities, and their use in precision medicine (including what they would look like and what data will be tracked/gathered) will play a role in this initiative.   + As this 1 million cohort is being defined, it is TBD where the data will be stored (whether the cloud or elsewhere).   + There was general agreement that, due in large part to work from eMERGE, that EHR data are proven useful for phenotyping, but challenges remain. New tools and competencies brought in from the big data sciences - computer science, machine learning, & artificial intelligence − that eMERGE has not yet used or considered. Broadening the eMERGE perspective will allow for this transition. Another challenge is creating a data standard in such a large cohort, which inevitably will leave some functionality out. Interoperability between medical systems will also play a role in expanding data – how many different systems could be used?   + There was a discussion of centralized vs. federated data structures. Federated models allow for those who are responsible for the data to generate and interpret it locally while contributing to a broader cohort. Federated models require more coordination per study. Centralized models are very efficient once established, but are difficult to build and face considerable regulatory hurdles.   + A commitment to re-thinking how researchers think about patient engagement was mentioned and how eMERGE III could be a model for “participants as partners”.   + eMERGE Investigator, Joshua Denny, was named to the Precision Medicine advisory committee, which will meet in the coming months.   + Next steps: The Precision Medicine advisory committee will consult and collect information from cohort leaders, mobile health technology thought leaders, and potential participants. Governance and coordination will be addressed, especially dealing with inter-agency coordination mechanisms. Congress has been receptive on both sides of the aisle. A special issue on Precision Medicine Informatics (guest edited by Josh Denny, Elmer Berstam, and Lewis Frey) is expected in spring 2016. [Call for paper request](http://jamia.oxfordjournals.org/sites/default/files/JAMIA-Special-Issue-PrecisionMedicine%203.25.15_LOM_jd.pdf). |
| **Day 2: Full Session (ESP Commentary, Science Presentations)** |
| * Network Status update - *Rex Chisholm (Northwestern)*   + The Network is on schedule to complete 28 phenotypes by April 30th and 28 genetic analyses by the end of July. Phenotypes in progress include MACE on Clopidogrel (secondary validation in progress, expected to be released to network April 30), Methylphenidate (in review at lead site), and Intractable epilepsy (secondary validation in progress).   + There have been several web enhancements, including on InfoButton, which is expected to be integrated into MyResults.org June 30, 2015. Also, the Patient Education Metric template was approved with expected integration into REDCap in May 2015. The final version of the physician education form is complete and the data collection timeline is in development.   + The PGx plan and status were reviewed with the project nearing completion   + dbGap-related Dated:     - Imputed merged dataset primary submission to dbGaP completed in March.     - Site led, study based dbGaP data will be released on dbGaP July 31, 2015.     - PGx first dbGaP submission is set for dbGaP release April 30, 2015.     - The final round of submissions are scheduled to be released July 31, 2015. |
| Workgroup Presentations   * [CERC](http://emerge.mc.vanderbilt.edu/qf/private/CERC-%20Holm,%20Smith.pdf) – *Ingrid Holm (BCH) & Maureen Smith (Northwestern)*   + Projects     - Patient Perspectives on Broad Consent in Biobank Research in the eMERGE Network (Survey Project)       * Current status: The survey is being mailed in 2-3 days, with data analysis expected to start in September. Data analysis is expected to be complete by Feb. 2016 with subsequent paper submission.     - MyResults.org       * Current status: Web-tool includes information for patients on 7 drug/gene pairs, 1 condition, and numerous fact sheets and videos. It also includes a provider portal.   + Collaborations     - Infobutton Project (In collaboration with EHRI workgroup)       * Current status: An abstract has been submitted recently. Provider portal integration into Myresults.org is currently being developed.     - PGx Outcomes (In collaboration with RoR and PGx workgroups)       * Current status: review of outcomes is complete, templates are being created now.   + Publications: the workgroup has published two manuscripts and has one in progress. * [Pediatrics](http://emerge.mc.vanderbilt.edu/qf/private/Pediatrics-%20Hakonarson.pdf) – *Hakon Hakonarson (CHOP), John Harley (CCMCH), & Ingrid Holm (BCH)*   + Current projects     - The following algorithms have been developed and deployed within the Network: ADHD, Appendicitis, Asthma, Asthma (severe), Atopic Dermatitis, Autism, BMI, Bilirubin, Early Childhood Obesity, and GERD. The workgroup is currently developing the following algorithms: Methylphenidate in ADHD, Liver Function Tests, malignant hyperthermia, epilepsy drug response, atomoxetine in ADHD, migraine, and JIA.     - GWAS and PheWAS are being performed on early childhood obesity, autism, bilirubin, methlyphenidate in ADHD, epilepsy, JIA, Migraine, and atomoxetine in ADHD. A detailed report was given on the bilirubin GWAS findings, which confirmed the substantial contribution of the UGT1A1 gene on serum bilirubin in both pediatric and adult populations and the strong effect between genotype and phenotype. The effect is stronger in males than females, and stronger in adults than pediatrics. It also confirmed the known effects of other genes on serum bilirubin levels (SLCO1B1, ARHGEF7, TDRP) and that there is no gene-gene interaction between them and UGT1A1. GWAS results on appendicitis were preformed, with no significant GWAS association detected. The workgroup plans to genotype another 500 patients.     - The group has also been working on 4 GWAS datasets (all with genome-wide significant locus): Asthma, Atopic dermatitis, ADHD, and GERD. The algorithms have proven highly sensitive in terms of predictability, which has allowed for a new locus to be found on asthma, the possible clinical relevance of a GERD locus, and shown the genome wide significance of a locus for Atopic dermatitis, and ADHD.     - The workgroup also presented on a pilot childhood obesity (GECO) project that used an algorithm from eMERGE to identify a cohort, then targeted exome sequencing and functional studies to define the variant. This is a pilot project for the Genomics Research and Innovation Network (GRIN) which includes CHOP, CCHMC and BCH, but the case identification pipeline can be expanded to sites with biorepositories to identify cohorts, including Vanderbilt. * Privacy Update – *Brad Malin (VU)* **(Scientific Presentation)**   + Projects: A privacy competition was held for performing the fastest secure computation of genomic data in a commercial cloud in conjunction with I-NCBC, a challenge that looked at secure multi-party computing on the cloud.   + A privacy workshop is being planned at IEEE symposium of security and privacy in a couple of months and will consist of 9 research papers and 1 keynote speaker.   + An overview was provided of the new regulations mandating scientists de-identify genomic data so subjects cannot be readily ascertained, and the expectation of informed consent for future use and broad data sharing even if the data is de-identified. There was also discussion about the use of cloud computing, with a consensus that it is acceptable to use cloud computing as long as the cloud was used before uploading the data to NIH.   + The presentation discussed treating privacy as a risk analysis problem, and analyzing the risk of identification vs. the amount of information left to use after de-identification (The Stackleburg game). The suggestion was to use safe harbor as a threshold, but there are better options (lower info loss, lower risk for re-identification). Novel findings indicated situations where there would be no/little risk of an attack but researchers would be able to share a lot of data.   + Proposed next steps:     - Expand the risk analysis model to SPHINX and run an analysis in both the genotype and phenotype direction, considering rational and non-rational attackers.      * [Phenotyping](http://emerge.mc.vanderbilt.edu/qf/private/Phenotyping-%20Denny,%20Peissig.pdf) – *Josh Denny (VU) & Peggy Peissig (Marshfield)*   + Projects     - Current status: PheWAS in pediatrics was completed. 42 phenotypes completed overall and 9 in progress. 11 extra phenotypes were explored during the project. Also, updated rights management to facilitate access, and data validation/sharing have been released in PheKB.     - The group gave a detailed report on GWAS findings linking APOL1 and MSSM. Specifically, APOL1 (which occurs at a frequency between 13-16%), is strongly associated with increased blood pressure at younger ages, allowing it to explain a sizeable portion of the increased burden of high blood pressure and increased frequency of stroke in African Americans.     - Next Steps: A SPHINX data refresh, dbGaP submissions (due to CC by June 1st), completing the planned algorithms and data gathering for phenotypes in progress, finalize the manuscript on “modular” phenotypes, and begin geo-mapping cohorts for environmental variables. The workgroup is discussing the use and benefits/drawback of using a common data model and expect to explore more deeply in the future.   + Publications:     - At the 2015 TBI-CRI Summit the workgroup presented/participated in 2 panels, 2 workshops/tutorials, 6 papers, 4 presentations and 2 posters.       * eMERGE members were recipients of the distinguished paper award and the student paper award     - Several papers are underway, “[A Prototype for Executable and Portable Electronic Clinical Quality Measures Using KNIME Analytics Platform”](http://informatics.mayo.edu/phema/images/1/13/PhEMA_KnimePrototype_AMIAjoint_2015.pdf) received the AMIA CRI distinguished paper award.     - 6 other manuscripts in progress     - The Workgroup has a call for proposals in the special issue of JAMIA Precision Medicine Informatics Journal, due date August 31st. Josh Denny (Vanderbilt), will be a co-editor. * [Genomics](http://emerge.mc.vanderbilt.edu/qf/private/Genomics-%20Crosslin,%20Tromp.pdf) – *David Crosslin (UW) & Patrick Sleiman (CHOP)*   + Projects     - The group discussed harmonizing, filtering, and annotating data. There was agreement that end point data sequences should be realigned to the same reference using the same pipeline, but there is still discussion on whether to hard filter or use hard variant scores, so the data will be annotated as filtered but not removed so it will still be available. A combination of several types of available tools will be used to annotate and consensus will be taken.     - Quality control was also discussed, and “Genome in a bottle” can be used as a reference to evaluate the pipeline. The QC process for INDELS will be to call them using the same pipeline and researchers will make the call on quality. CNV data processes are maturing, decent software is available, and quality methods have been reported. Regardless if it is done centrally there is a potential for exomes to be pulled from PGx files.     - eMERGE will be sharing raw phenotype data with ENCODE colleagues. Upcoming calls (1st and 3rd Monday QC calls) will determine which phenotypes ENCODE is interested in and how they will use data. The FTP site at Penn State will be used to transfer data. The collaboration has begun with the sharing of WBC, RBC, and PheWAS data. Proposed process: ENCODE will complete a concept sheet and sites will opt in to participate and give access to data.     - The Null Variant sub-group reported that they had collected predicted null variants, divided the complete eMERGE dataset into discovery and replication for adults and pediatrics, and performed an ICD-9 code based PheWAS. They found that the adult PheWAS has many replicating genome-phenome associations, the pediatric has none.   + Publications:     - Led the Frontiers in Genetics Special Issue: “Genetic Research in Electronic Health Records Linked to DNA Biobanks       * 19 published articles over a variety of topics.       * Over 35k views as of 3/25/15     - A manuscript draft of the adult PheWAS studied by the Null Variant Subgroup is circulating the network next week   + Next steps: Wrap up PGRN QC and analyses and move forward with structural variation- association analyses. CHOP array data has been transferred to the CC to run association analyses. * [EHRI](http://emerge.mc.vanderbilt.edu/qf/private/EHRI-%20Williams.pdf) – Justin Starren (Northwestern) & Marc Williams (Geisinger)   + Projects     - The workgroup is currently developing a CDS repository, studying TPMT and abacavir, and collaborating with the PGx project outcomes workgroup to receive data on CDS triggering and usage. They also gave a detailed update on the status of the Infobutton project, in which formal evaluation of physician content is expected to be completed in May 2015, and capabilities will be updated into MyResults.org for targeted content by June 2015.       * Next steps: Casey Overby is seeking family practice, internal medicine, and neurology practitioners to participate in a stakeholder needs survey to inform further development. Members with suggestions should contact Justin, Marc or Luke.   + Publications/Panels/Presentations     - The workgroup has 5 manuscripts in progress, has participated in 3 panels, and has one presentation accepted at the 36th Annual Meeting & Scientific Sessions of the Society of Behavioral Medicine. * Development and Testing of Patient and Provider Facing Genomic Test Reports – Janet Williams & Marc Williams (Geisinger) **(Scientific Presentation)**   + The Genome Patient Provider Summary Project is using a recipient reported evaluation process to develop a dynamic report available to families/providers through the EHR that will increase overall knowledge about rare conditions and improve communication around the results of genomic tests for rare diseases. The technical aspect, the format of the report, and overall themes from focus groups (such as parent’s need for information and resourced regarding a child’s condition, and the provider’s desire to have access to both the provider and patient reports) were discussed.   + Next steps will include developing the enhanced version of the report, and completing a prospective randomized comparative effectiveness trial will be done to measure patient engagement, patient and provider satisfaction, communication, and adherence to recommendations. The Go-Live date is May 1, 2015, with results expected in 2016.   **ACTION ITEM: Members interested in being an alpha and/or beta testing site for the Genome Patient Provider Summary website should contact Janet Williams or Marc Williams.**   * [Return of Results](http://emerge.mc.vanderbilt.edu/qf/private/ROR-%20Jarvik,%20Kullo.pdf) – Gail Jarvik (UW) & Iftikhar Kullo (Mayo)   + Workgroup Projects:     - The group has analyzed several variants for complex disease risk and looked at the phenotypic correlates of variants of uncertain significance (arrhythmia and lipid levels) with a special consideration of pathogenicity, penetrance, and actionability. Findings include the identification of 7 SNPs associated with Macular Degeneration, 28 SNPs associated with coronary heart disease, an association between the ApoL1 SNP association and hypertensive renal disease in African Americans, and SNPs associated with HFE, FV, and FII.     - PGx: PREDICT has tested 14,715 people, is expanding and transitioning to a new platform to allow new DGIs plus expansion and refinement of existing DGIs. Also, CDS prototypes for carbamazepine and abacavir have been completed at GW-UW and IRB approval has been granted to perform small scale usability testing with select providers to guide iterative refinements.     - The primary results of WGS tests were returned to 10 families, and the secondary findings analysis has been completed. None were pathogenic, but one VUS that may be of relevance was found.     - CHOP has returned CYP2D6 results to parents and providers, and the TPMT CDS is complete. 190 individuals with autism have had results returned by CAG through the Center for Autism Research for CNVs, and the program returned results for 48 participants with novel discoveries of Mendelian disease genes following CLIA validation of causative variants.   + Network-wide projects     - The workgroup is engaged in actionable PGx variants for clopidogrel, warfarin, and simvastatin which have been placed in EHR with linkage to CDS.   + Publications     - Thirteen eMERGE ROR abstracts were presented at [ASHG](http://www.ashg.org/2014meeting/pdf/2014_ASHG_Meeting_Platform_Abstracts.pdf)     - One family WGS story was published in the Journal of Inherited Metabolic Disease     - GHC/UW is developing a manuscript on design opportunities for genome guided CDS     - Manuscript being prepared for NEJM on Variants of Unknown Significance for two phenotypes - Long QT and lipids     - Plan for network wide manuscript to describe eMERGE PGx RoR     - The hemochromatosis manuscript is out to writing group/sites     - An NEJM editorial on the new FDA regulations of lab testing next generation sequencing is in the third review     - Barbara Evans and Gail Jarvik responded to FDA call for comments. Attention was spent on the implication of the regulation in research settings. Members interested in receiving a copy should contact the CC or the respondents.   + Next steps     - Several analyses are planned to identify phenotypic associations, possible actionability and RoR.     - HFE: Return of results to begin in April 2015. Carbamazepine and Abacavir alert deployed as test cases. Also, further family members are being tested.     - Hemochromatosis: The workgroup is working to get length of time of diagnosis to illicit how/when individual was diagnosed.     - Have a collaborative role across the network with any groups that have issues with any variants pathogenicity annotation particularly for the ACMG or PGRNSeq variants.     - Running annotation pipeline across a multi sample from David Crosslin to get high penetrance data. Members interested in data should contact David.     - Continuing to follow FDA and impact regulation     - Continuing to collaborate with other networks   **ACTION ITEM: Members are encouraged to review and contribute instruments being used at their site for RoR.** |
| **Summary of Action Items:**   1. The CERC Survey will be made available on the eMERGE website. 2. The PGx workgroup will further investigate the process of submitting to ClinVar. 3. Additional example artifacts for curation and inclusion in CDS KB may be sent to Luke Rasmussen ([luke.rasmussen@northwestern.edu](mailto:luke.rasmussen@northwestern.edu)). 4. Members interested in being an alpha and/or beta testing site for the Genome Patient Provider Summary website should contact Janet Williams ([jwilliams3@geisinger.edu](mailto:jwilliams3@geisinger.edu)) or Marc Williams ([mswilliams1@geisinger.edu](mailto:mswilliams1@geisinger.edu)). 5. Members are encouraged to review and contribute instruments being used at their sites for RoR. |
| **Next Meeting: June 29-30th, 2015; New York, NY** |