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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT340 | |
| **Submission Date** | 4/19/2019 | |
| **Project Title** | Sequencing Centers and eMERGE Site Interactions related to Return of Genomic Results in Phase III of the eMERGE Network | |
| **Tentative Lead Investigator** *(first author)* | David Kochan | |
| **Tentative Senior Author**  *(last author)* | Iftikhar Kullo | |
| **All Other Authors** | Ingrid A. Holm, Richard Sharp, Richard Gibbs, Heidi Rehm, Eric Venner, Hana Zouk, other eMERGE investigators | |
| **Sites Participating** | Mayo, other interested sites & sequencing centers | |
| **Background / Significance** | Several population-scale genetic sequencing projects are underway. Genomic medicine implementation efforts across eMERGE Network sites as part of eMERGE Phase III have identified several challenges related to the application of sequencing at-scale. Such situations include variable interpretation of genotype-phenotype discordance, gender mismatches, cases of potential genetic mosaicism, and reclassification of sequencing results. We aim to enumerate such challenges as they occurred among eMERGE sites, and to describe the approaches and rationale used by research teams and the sequencing centers to identify and resolve these prior to RoR. Our proposed work will be distinct from that outlined in concept sheets NT337 and NT171, focusing on aspects related to ROR. | |
| **Outline of Project** | Semi structured interviews with Sequencing Centers and eMERGE investigators regarding the challenges related to variant interpretation, gender mismatches, mosaicism, and revised reports. Documentation of these situations will be aggregated into a research manuscript detailing the challenges encountered and how SCs and investigators approached/resolved situations prior to the RoR process. | |
| **Desired Data - Common Variables\***  *(Available from the CC)* | Demographics  ICD9/10 codes  CPT codes  Phecodes  BMI | Common Variable Labs  Common Variable Meds  Other: Case/Control status on Phase I and Phase II phenotypes |
| **Other Desired Data *(Available from participating sites)*** | *Please specifically list out any data elements that participating sites would collect or extract from clinical or other sources for this project (i.e. not common variables above)* | |
| **Desired Genetic Data** | eMERGE I-III Merged set (HRC imputed, GWAS)  eMERGE PGx/PGRNseq data set  eMERGEseq data set (Phase III)  eMERGE Whole Genome sequencing data set  eMERGE Exome chip data set  eMERGE Whole Exome sequencing data set  Other (not listed above): | |
| **Does project pertain to an existing eMERGE Phenotype?** | Yes, if so please list  No | |
| **Planned Statistical Analyses** | Data will be aggregated from eMERGE sites in the form of semi-structured interviews. Data collection and analysis will be guided by typical qualitative inductive approaches. | |
| **Ethical Considerations** | None | |
| **Target Journal** | Genetics in Medicine? | |
| **Milestones**  *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | * April: Introduce concept sheet * May 13-17: Gather experiences from sites regarding interactions with sequencing centers, sequencing issues to develop an interview guide. * May 20-31: Schedule semi-structured interviews with sites interested in participating. * June 14: Complete interviews * June 28: Distribute manuscript draft * July 12: Submit for publication | |