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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT343 | |
| **Submission Date** | 05/03/2019 | |
| **Project Title** | Associations Between Sex-Specific Renal Function Polygenic Risk Scores and the Clinical Phenome by Sex | |
| **Tentative Lead Investigator** *(first author)* | Jacklyn N. Hellwege | |
| **Tentative Senior Author**  *(last author)* | Digna Velez Edwards | |
| **All Other Authors** | Todd Edwards, Nancy Cox, Dan Roden, Josh Denny | |
| **Sites Participating** | Open to all sites  Current participants:  Vanderbilt | |
| **Background / Significance** | Chronic kidney disease (CKD) is defined by estimated glomerular filtration rate (eGFR) lower than 60 ml/min/1.73 m2, is a global health concern, and is associated with premature death. CKD has a prevalence of 15% in the US, which is higher in women than men (16.5% vs 13.0%), though mortality rates are higher in men than women (120.2 vs 102.6 per 1000 patient-years). The eGFR equation contains variables for both race and sex due to differences in muscle mass across men and women of white and black race. Identifying genetic loci associated with eGFR differentially across men and women by race will allow us to further disentangle body composition differences from kidney function. | |
| **Outline of Project** | We will construct sex and race-specific polygenic risk scores (PRS) for eGFR using stratified GWAS results from BioVU, and validated in an external data set. We will perform PheWAS of these PRS stratified by race and sex in the eMERGE data, adjusted for age, body mass index, and principal components of ancestry. We will also use meta-analysis to calculate estimates of effects and significance across races and sexes. We will summarize the results of the association tests, with secondary analysis of Phecode groupings, as well as network analysis of results. | |
| **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)*** |  | |
| **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** | PheWAS | |
| **Ethical Considerations** | None | |
| **Target Journal** | Depends on results, likely a genetics journal such as Human Molecular Genetics or a general journal such as elife, Nature Communications, or Scientific Reports | |
| **Milestones**  *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | Gather data from coordinating center: 5/2019  Conduct statistical analyses: 6-10/2019  Write manuscript: 10-12/2019  Circulate and submit manuscript: 1/2020 | |