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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT382 | |
| **Submission Date** | 3/10/20 | |
| **Project Title** | Preeclampsia: Genome-Wide Association Study and Polygenic Risk Scores | |
| **Tentative Lead Investigator** *(first author)* | Elizabeth Jasper | |
| **Tentative Senior Author**  *(last author)* | Todd Edwards and Digna R Velez Edwards | |
| **All Other Authors** | Sarah Jones, Jacklyn Hellwege | |
| **Sites Participating** | Open to all sites  Current participants:  Vanderbilt | |
| **Background / Significance** | Preeclampsia, a pregnancy complication characterized by hypertension after 20 gestational weeks, is a major cause of maternal and neonatal morbidity and mortality. The exact biologic mechanism leading to preeclampsia is unclear. However, genetic susceptibility is evident, with those with a family history of preeclampsia being two to five times more like to develop the condition. We propose using eMERGE data to conduct a genome-wide association study (GWAS) to further identify genetic variants association with preeclampsia. Results of the GWAS will be independently validated within the BioVU population at Vanderbilt University Medical Center. As preeclampsia is classified as a blood pressure disorder, we also propose applying existing polygenic risk score (PRS) models for blood pressure traits (systolic blood pressure, diastolic blood pressure, and pulse pressure) to women of reproductive age in eMERGE to determine if these models can accurately estimate an individual’s risk for preeclampsia. We will also develop a PRS of preeclampsia and test for its association with adult hypertension and blood pressure traits. | |
| **Outline of Project** | GWAS analysis will be conducted in women of reproductive age in eMERGE. A similar cohort from BioVU will serve as a replication cohort. Existing PRS models for blood pressure will also be applied to reproductive age women within eMERGE. | |
| **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** | GWAS, PRS | |
| **Ethical Considerations** | None | |
| **Target Journal** | Human Reproduction or Obstetrics and Gynecology | |
| **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: 3/2020  Conduct statistical analyses: 3-7/2020  Write manuscript: 7-8/2020  Circulate and submit manuscript: 9/2020 | |