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| **eMERGE Network: External Collaborator Manuscript Concept Sheet** |
| **Reference Number** *(to be assigned by CC)* | NT423 |
| **Submission Date** | 3/19/2021 |
| **Project Title** | Survival Analysis GWAS with Age at Onset of Erectile Dysfunction |
| **Tentative Lead Investigator** *(first author)* | Ian Byrell Stanaway |
| **Tentative Lead Investigator Email Address**  | bard@uw.edu |
| **Tentative Senior Author** *(last author)* | Anne E. Justice (Geisinger) |
| **eMERGE Site Sponsor & Contact** | Gail Jarvik (gjarvik@medicine.washington.edu) |
| **All Other Authors**  | Hunter Wessells, David Russell Crosslin, Gail P. Jarvik, Elisabeth Rosenthal, David Carrell, Eric Larson, Lester Kirchner, Alexander J. Skokan, Navya S. Josyula, Melody Palmer, J Hotaling, S VandenEeden, Philip S. Tsao (MVP), Themistocles L. Assimes (MVP)other interested eMERGE co-authors |
| **Sites Participating** | All eMERGE Sites |
| **Background / Significance** | We will query genetic variants and EMR codes from the electronic MEdical Record and GEnomics (eMERGE) Network imputed data GWAS participants [1] and perform survival analysis GWAS with Erectile Dysfunction. Recent previous studies have found common variants adjacent to the SIM1 gene in a regulatory region associated with erectile dysfunction in two independent analyses [2,3]. It is likely that other loci will also be associated with erectile dysfunction. We will also be working with the Geisinger MyCode, UK Biobank and Million Veteran Program (MVP) to have a combined cohort size of ~900k male subject participants for meta-analysis and replication.References1. **Stanaway**, et al., 2019 "The eMERGE Genotype Set of 83,717 Subjects Imputed to ~40 Million Variants Genome Wide and Association with the Herpes Zoster Medical Record Phenotype.", Genetic Epidemiology, 2019
2. Jorgenson E, Matharu N, Palmer MR, Yin J, Shan J, Hoffmann TJ, Thai KK, Zhou X, Hotaling JM, **Jarvik GP**, Ahituv N, **Wessells H**, Van Den Eeden SK. Genetic variation in the SIM1 locus is associated with erectile dysfunction. Proc Natl Acad Sci U S A. 2018 Oct 23;115(43):11018-11023.
3. Bovijn J, Jackson L, Censin J, Chen CY, Laisk T, Laber S, Ferreira T, Pulit SL, Glastonbury CA, Smoller JW, Harrison JW, Ruth KS, Beaumont RN, Jones SE, Tyrrell J, Wood AR, Weedon MN, Mägi R, Neale B, Lindgren CM, Murray A, Holmes MV. GWAS Identifies Risk Locus for Erectile Dysfunction and Implicates Hypothalamic Neurobiology and Diabetes in Etiology. Am J Hum Genet. 2019 Jan 3;104(1):157-163. doi: 10.1016/j.ajhg.2018.11.004. Epub 2018 Dec 21.
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| **Outline of Project** | 1. Select Phenotype data for inclusions and exclusions.2. Perform GWAS while adjusting for site, principal components and clinical covariates.3. Replicate and meta-analyze between Geisinger MyCode, UK Biobank, MVP4. Write the paper. |
| **Desired Data - Common Variables\*** *(Available from the CC)* | [x] Demographics [x] ICD9/10 codes[x] CPT codes[x] Phecodes[x] BMI | [ ] Common Variable Labs[ ] Common Variable Meds☐ Geocoding 2015 ACS variables[ ] Other: Case/Control status  |
| **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** | [x] 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 [x] No |
| **Planned Statistical Analyses** | 1. Extract EMR phenotype and covariates definitions from cohorts.2. Compare prevalence and assess phenotype accuracy between cohorts.3. GWAS4. Replication and Meta-analysis |
| **Ethical Considerations** | None |
| **Available Funding or Resources** |  |
| **Target Journal** | Nature Genetics |
| **Milestones***(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | 1. Coordination of data between eMERGE, Geisinger, UKB and MVP (Present-2022)
2. Begin writing paper and refine analyses based on co-author input (2022)
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**\*Common Variables available across all datasets:**

* Demographics: sex, year of birth, decade of birth, race, ethnicity
* Codes: (repeated values & age at event): ICD, CPT, Phecodes
* BMI: (repeated value & age at event) height, weight, BMI
* Labs: (lab name, repeated lab value & age at event) Serum total cholesterol, LDL, HDL, Triglycerides, Glucose fasting/non-fasting/unknown, & White Blood Cell count
* Medications: (medication name, repeated, & age at event) Cerivastatin sodium, Rosuvastatin, Simvastatin, Fluvastatin, Pravastatin, Lovastatin, Atorvastatin, & Pitavastatin
* Other: Case/Control status on Phase I and Phase II phenotype: only on GWAS dataset participants