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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT330 | |
| **Submission Date** | February 15, 2019 | |
| **Project Title** | Approaches to the return of actionable adult-onset conditions in pediatric research: Lessons learned from eMERGE 3 | |
| **Tentative Lead Investigator** *(first author)* | Ingrid A. Holm, BCH | |
| **Tentative Senior Author**  *(last author)* | Cynthia A. Prows, CCHMC | |
| **All Other Authors** | Melanie F. Myers, CCHMC  Margaret Harr, CHOP  John Connolly, CHOP  Others TBD | |
| **Sites Participating** | Invite representatives from pediatric eMERGE sites and others involved in ELSI in pediatrics:   * Cincinnati Children’s Hospital * Children’s Hospital of Philadelphia * Others | |
| **Background / Significance** | The return of results for highly actionable adult onset conditions in pediatrics is controversial. Pediatric researchers conducting sequencing studies in which such results are generated need to make plans for how to deal with this potential information. The eMERGE Network provides a laboratory in which to generate evidence for recommendations regarding how to handle children’s results for adult onset disorders. Over 30,000 Network participants were sequenced with the eMERGESeq panel which included genes for several highly actionable adult onset conditions. The pediatric sites implemented different approaches that were responsive to ethical issues and published professional recommendations regarding the return of genomic results that inform risk for adult onset conditions. . | |
| **Outline of Project** | 1. Establish a core writing group comprised of representatives from the pediatric eMERGE sites. 2. Gather the protocols used by the 2 pediatric sites for handling results for highly actionable adult onset conditions in those <18 years, as well as the BCH BabySeq project. 3. Compare and contrast the approaches at the pediatric sites, and with the BCH BabySeq project, and discuss the ethical, legal, and social implications (ELSI) (e.g. future autonomy, best interests, family interests) and how they are addressed. 4. Develop recommendations and options to approach return of results for adult onset conditions for researchers who are conducting studies where these genes are sequenced. | |
| **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)*  None | |
| **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):  **NONE** | |
| **Does project pertain to an existing eMERGE Phenotype?** | Yes, if so please list  X No | |
| **Planned Statistical Analyses** | None, the project will be descriptive of practices across eMERGE sites. | |
| **Ethical Considerations** | Ethical considerations around the return of highly actionable adult onset conditions in children include future autonomy, best interests, and family interests and will be discussed | |
| **Target Journal** | Genetics in Medicine; Journal of Medical Genetics; or similar. | |
| **Milestones**  *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | Data collection phases of the project to be completed by April 30, 2019.  Manuscript submission to be completed by June 30, 2019. | |

**\*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