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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT407 | |
| **Submission Date** | October 6, 2020 | |
| **Project Title** | Outcomes of returning medically actionable results in pediatric research  (Using existing eMERGE III data) | |
| **Tentative Lead Investigator** *(first author)* | Amy Blumling, CCHMC | |
| **Tentative Senior Author**  *(last author)* | Melanie Myers, CCHMC | |
| **All Other Authors** | Cynthia A. Prows, CCHMC  John Connolly, CHOP  Hakon Hakonarson, CHOP  John Harley, CCHMC  Margaret Harr, CHOP  Ingrid A. Holm, BCH  Michelle McGowan, CCHMC  Others: TBD | |
| **Sites Participating** | Representatives from pediatric eMERGE sites and others returning pediatric research results in eMERGE III   * Cincinnati Children’s Hospital * Children’s Hospital of Philadelphia | |
| **Background / Significance** | It is important but difficult to include pediatric cohorts in large genomic research networks and consortia. Identifying disease risk and implementing available surveillance and disease prevention strategies during childhood provides an opportunity to study the effectiveness of such interventions on future health. Actionable genomic results were returned at all 10 eMERGE sites and outcome measures relevant primarily to adult health were collected. It has therefore proven difficult to combine survey items and clinical outcome measures for adult and pediatric participants. Consequently, the eMERGE network manuscripts to date focused on medical and psychosocial outcomes associated with return of medically actionable results to adults. Even between the two pediatric sites (CCHMC and CHOP) significant differences existed. For example, CCHMC returned negative and positive results to adolescent/parent dyads, whereas CHOP returned children’s positive results to parents. Like CHOP, CCHMC returned children’s positive results to a different cohort of parents whose children’s samples had been previously stored in a biorepository and parents had given permission for recontact about actionable results identified in future studies.  We will describe CCHMC and CHOP cohorts and results returned with a focus on outcomes following return of positive (P/LP) results for disease risk. We will limit analyses to electronic health record outcomes data entered in eMERGE Outcomes forms when positive results were returned. We will supplement descriptive quantitative results with case exemplars. | |
| **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 returning results, as well as the planned follow-up to briefly summarize 3. Summarize e3 outcomes data for pediatric participants 4. Provide case exemplars | |
| **Desired Data - Common Variables\***  *(Available from the CC)* | Demographics  ICD9/10 codes  CPT codes  Phecodes  BMI | Common Variable Labs  Common Variable Meds  Other: Freeze 3 outcomes data |
| **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** | Descriptive analysis(es) (practices and outcomes) and case exemplars | |
| **Ethical Considerations** | Ethical considerations around the return of genomic research results in pediatrics | |
| **Target Journal** | Pediatrics; 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 November 1, 2020.  First draft of manuscript to be completed by December 2020.  Manuscript submission to be completed by January 2021. | |

**\*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