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| **eMERGE Network: Manuscript Concept Sheet** | | |
| **Reference Number**  *(to be assigned by CC)* | NT451 | |
| **Submission Date** | 6/27/22 | |
| **Project Title** | Designing the Genome Informed Risk Assessment Report: The eMERGE Consortium Experience | |
| **Tentative Lead Investigator** *(first author)* | Margaret Harr1 | |
| **Tentative Lead Investigator Email Address** | [harrm@chop.edu](mailto:harrm@chop.edu) | |
| **Tentative Senior Author**  *(last author)* | Karlson, Elizabeth2 | |
| **eMERGE Site Sponsor & Contact** | The Children’s Hospital of Philadelphia | |
| **All Other Authors** | Members of the GIRA Design workgroup interested in joining the writing team | |
| **Sites Participating** | 1 CHOP  2 BWH  Others… | |
| **Background / Significance** | The success of the eMERGE program relies in large part on the generation of the Genome Informed Risk Assessment (GIRA). The GIRA represents a novel risk communication tool which combines polygenic risk scores (PRS), family history, clinical, and monogenic risk factors for several medical conditions. It is designed to communicate risk results as well as clinical management recommendations to both study participants and their healthcare providers. The size, scope, and, particularly, novelty of such a document necessitated development of a GIRA design subgroup to create a comprehensive, yet accessible research report which meets the needs of the network’s key stakeholders (participants, parents, primary care and specialty care providers, study staff, and principal investigators). This paper will summarize the GIRA design subgroup’s approach to report design, the unique challenges associated with presenting the complex study procedures and results, and the methods utilized to optimize the design to meet the needs of the various stakeholder.. | |
| **Outline of Project** | First, the paper will introduce the goals of the Genome Informed Risk Assessment (GIRA), its intended use, and key components (summary of risk, clinical care recommendations, outline of individual phenotype risks, educational content, FAQs, and the research study methods and limitations).  Second, the paper will discuss the challenges of creating the complex result document including: 1) defining an audience, 2) language and graphics used for presentation of risk, 3) readability, and 4) balancing comprehensive content vs efficient delivery. This overlaps with work led by the PRS, genotyping, ELSI, Education, Clinical Decision Support, and other groups.  Finally, the paper will review the methods utilized to address these challenges including 1) learning from network ELSI projects, 2) interviews with physicians and potential participants, 3) focus groups, 4) community advisory groups, 4)reading level analysis, and 5) ultimate review by network co-chairs, PIs, NIH representatives.  Ultimately this paper aims to shed light on the process of creating a complex study result document, the challenges encountered and solutions utilized by a largescale and novel clinical trial of this kind, and aims to summarize lessons-learned for similarly ambitious programs. | |
| **Desired Data - Common Variables\***  *(Available from the CC)* | Demographics  ICD9/10 codes  CPT codes  Phecodes  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)*  Description of local sites’ ELSI sub-projects which helped to influence GIRA design.  Summary from VUMC review studio.  Data from local sites’ focus groups on GIRA review. | |
| **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** | none | |
| **Ethical Considerations** |  | |
| **Available Funding or Resources** |  | |
| **Target Journal** | Genetics in Medicine | |
| **Milestones**  *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)* | July 31, 2022: Provisional layout  September 1, 2022: Subgroups submit section content  November 30 2022: Draft 1 circulated among writing group  December 31, 2022: Manuscript submitted for review | |

**\*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