APPENDIX 1: Internal Manuscript Concept Sheet

eMERGE Network: Manuscript Concept Sheet	
Reference Number *(to be assigned by CC)*	NT481
Submission Date	06.27.2023
Project Title	Design of an improved sex- and gender-related data model and usage principles for genetics research
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Sites Participating	VUMC (primary), MCG, NW, UW
Background / Significance	It is critical to collect gender identity data to ensure affirming and equitable genetics care for transgender, gender diverse, and sex diverse (TGSD) patients. Further, a person's phenotypic sex (expression of primary, secondary, and endocrinological sex characteristics), chromosomal sex, and organ/tissue inventory can directly impact crucial aspects of testing and care recommendations. However, TGSD individuals can experience psychosocial and clinical harms if gender/sex data collection and related care are not culturally competent and accurate. Realistic fears about such harms could deter TGSD individuals from participating in clinical research, and enrolled TGSD participants may experience harms from participation if data models and study processes do not appropriately account for these variables. Automated processes are increasingly used to streamline care and reduce health system burden, yet these processes increase the risk of misgendering participants or providing clinically inappropriate recommendations if these data are not accurate. The Electronic Medical Records and Genomics (eMERGE) Network is collecting sex/gender data at two points with different question/response options, and also has access to electronic health record data, offering an opportunity to evaluate the impact of a large electronic health record (EHR)-integrated genomics research study on TGSD individuals. The Network is evaluating the influence of a novel EHR-integrated integrated genome-informed risk assessment (GIRA) report on clinical care in 25,000 patients across 10 sites. The GIRA relies on data in the sex field to automate inclusion of recommendations on the report for certain conditions,

	and as a result has the potential to negatively impact TGSD participants. Further, the family history-based risk assessment, which supplies a component of risk information included in the GIRA, utilizes a separate sex field with a different question/response structure, creating the potential for misaligned data elements. In a supplement application to the Vanderbilt Genome-Electronic Records (VGER) Project, which supports the Vanderbilt University Medical Center site of the eMERGE Network, we poposed to use in-depth semi-structured qualitative interviews to investigate the impact of the eMERGE data collection, data usage, and processes on the validity of the GIRA for TGSD individuals and on potential psychosocial and clinical harms from the study on this population. We will use information gleaned in these interviews to develop a best practice guide for genomics research involving TGSD populations and propose a model for data collection that can support such research while remaining culturally competent and accurate. This model will be included in the FHIR specification for the GIRA. This supplement directly supports the overall project goals to validate and improve upon the GIRA. This concept sheet will support the development and usage principles for an updated sex- and gender-related data model designed for trans-inclusive collection of data elements required for genetic risk assessment, along with the associated FHIR specification
Outline of Project	This concept sheet will cover Aim 2 proposed in the eMERGE supplement. Aim 2. Develop recommendations for data collection, data usage, automated processes, and EHR integration for genomics research involving TGSD populations. 2a. Propose a model for sex and gender data collection in genomics research to maximize data quality and validity and integrate that model into the FHIR (Fast Healthcare Interoperability Resources) specification for the GIRA 2b. Create a best practice guide to minimize individual- and group-level harms to TGSD populations for sex and gender data usage, automated processes, and EHR integration in genomics research.
Desired Data - Common Variables* *(Available from the CC)*	X 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)*

	legal sex, assigned sex at birth, and gender identity as recorded in the EHR, if this data is present in EHR.
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 XOther (not listed above): GIRA risk results (component-by-component) which may be relevant to or changed by information found in interview. No full genomic data sets are required; data from the sibling project related to qualitative work
Does project pertain to an existing eMERGE Phenotype?	☐Yes, if so please list XNo
Planned Statistical Analyses	N/A
Ethical Considerations	Transgender participants are particularly vulnerable; not all data will be shared with all authors, only summary data generated from the qualitative aspects of the project.
Target Journal	JAMIA
Milestones *(This section should include the key dates for completion of project, including approval, project duration, draft completion, and submission.)*	Project begin: following interview completion in Aim 1 (~January 2024) Full draft: May 2024 Submission: Summer 2024

******** *This section should include the timeline for completion of project, including: approval, project duration, first and second draft of the paper and submission.*

APPENDIX 4: Acknowledgement Text

eMERGE Network (Phase IV)

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