Confronting real time ethical, legal, and social issues in the Electronic Medical Records and Genomics (eMERGE) Consortium

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Increasingly, genomic research is being conducted through large, multi-site consortia. For example, the Electronic Medical Records and Genomics (eMERGE) Consortium was funded by the National Human Genome Research Institute to evaluate the scientific feasibility and potential value of performing genome wide association studies (GWAS) using information from electronic medical records together with hundreds of thousands of single nucleotide polymorphisms from samples obtained in the course of existing cohort studies, biorepositories, or from residual tissue or blood samples. This experiment, if successful, will enable a vast amount of research, especially because more and more medical information is stored electronically and as the cost of genotyping and sequencing decreases. However, the ability to use existing clinical information and samples for GWAS, while exciting, raises a number of ethical, legal, social, and policy issues.

Examples of some of the issues raised by this type of research include the following: What sort of consent, if any, is required for such research? When might it be necessary to obtain new consent for the use of previously collected samples? Recognizing the value and the cost of obtaining such rich clinical and genetic variation data, and the desirability of combining datasets to permit more robust analysis, the National Institutes of Health (NIH) has strongly encouraged GWAS funded by the NIH, including the eMERGE data, be placed in a central repository called the database of Genotypes and Phenotypes (dbGaP) for use by other qualified investigators.[1] To what extent should patients and research participants be able to opt out of having their data shared with the broader research community through government-sponsored databases such as dbGaP? When diverse data sources are combined and then shared beyond the originating institutions, the abilities of investigators or biorepository managers to protect participants' interests, including privacy, necessarily change. Given this shift, do the obligations of those who originally collected samples change, and if so, how? Should investigators' obligations differ depending on whether data and samples come from patients seeking routine care or from participants in a pre-existing research project? When, if ever, should research results, either aggregate or individual, be returned to participants? What about incidental findings? And what role should communities play in long-term oversight and governance of these projects?

To address these, and related concerns, each eMERGE site was required to bring together genetic researchers and ethical, legal, and social implications (ELSI) investigators to address the ethical and social challenges of such research. Building an ethics component into large scientific studies provides an opportunity for transdisciplinary ELSI research that is immediately responsive to the emerging issues raised by scientific innovation, an approach that is becoming more common in genomics research.[2–4] The eMERGE Consortium provides a particularly rich landscape in which to pursue such research. The five partner institutions are examining data from a variety of populations that differ in their demographic characteristics, the ways they were recruited, and in the depth and stability of their relationships with the particular research team and institution (Table 1). Each eMERGE site includes investigators who bring particular disciplinary perspectives and approaches to studying the implications of using information from electronic medical records for GWAS (Table 1). (Additional information about each member site and its research can be found at www.gwas.net).

To maximize what can be learned from the diverse eMERGE research settings, ELSI investigators are not only conducting transdisciplinary research at their own institutions but have also joined together in a Consent and Community Consultation (C&CC) Working Group to share strategies and results and to collaborate on ethical issues and policy related to the conduct of GWAS. To facilitate this work, a number of prominent investigators from non-eMERGE institutions were invited to join the C&CC Working Group. Their names and affiliations are listed at the end of this article. The larger group quickly organized a number of smaller groups to focus on key, cross-cutting topics. The current groups, their leadership, and their goals follow are detailed below.

Community engagement (Barbara Koenig, Joel Wu, and Amy Lemke)

Communities have been involved to greater and lesser degrees in the governance, planning, and oversight of genetics and

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Table 1 eMERGE sites and ELSI activities

Institution	Circumstances under which patient/participant collection being used for this project was created	Stability of relationship between institution & participants	ELSI projects	eMERGE-specific ELSI methods	ELSI investigators' disciplines
Group Health Cooperative/University of Washington	ACT Study (cohort investigation of Alzheimer Disease and related diseases of aging)	Long-term health care provider for patients who are also participants	Implement a consensus process with key stakeholders to develop recommendations concerning consent, data sharing, and return of research results to subjects. Stakeholders include ACT subjects, GHC patients, GHC leadership, and ACT investigators. The consensus process will be informed by targeted focus group data collection from ACT subjects and GHC enrollees	Focus groups with ACT participants and general Group Health members; consensus development on research policy	Bioethics, communication, psychology, genetics, medicine, public health
Marshfield Clinic	Personalized Medicine Research Project—specifically collected information, plasma, serum, and DNA samples from residents of specified areas	Long-term health care provider for patients who are also participants	(1) Community consultation regarding consent for dbGaP; (2) Return of genetic results to research subjects position paper; and (3) Development and evaluation of computer-based consent process	Informed consent; community oversight[12]; focus groups; ethics and security advisory board	Genetic epidemiology, public health, bioethics
Mayo Clinic	Two populations (1) The Mayo Clinic Biobank—a general collection of blood and health information linked to the medical record; and (2) Clinical samples from ongoing cardiovascular genetics studies	Health care provider for participants (often with long-term relationship)	(1) Deliberative community engagement event to guide the development and operation of biobank; (2) Follow-up survey of the local community to assess acceptance of deliberative recommendations; (3) Development of an educational video describing the community engagement process; and (4) In-depth interviews of cardiovascular study participants followed by creation and evaluation of a biobank informed consent process based on the empirical findings	Deliberative community engagement; observation of consent process paired with in-depth interviews; surveys; community advisory board	Anthropology, law, religious ethics, bioethics, nursing, public health
Northwestern University	NUgene—specifically created DNA repository of patients at an urban medical center	Because of the presence of other providers in the area, patients may not have long-term relationships	A three-phase community consultation designed to gather stakeholder views of the consent process for genome-wide technologies and data sharing for GWAS, including the NIH GWAS Policy, although (1) focus groups of NUgene participants and the public; (2) survey of IRB professionals; and (3) consensus meetings with key professional stakeholders	Informed consent; focus groups[15]; IRB survey; consensus process; community advisory group	Genetic counseling, public health, community health sciences, genetics

(*Continued*)

Table 1 *Continued*

Institution	Circumstances under which patient/participant collection being used for this project was created	Stability of relationship between institution & participants	ELSI projects	eMERGE-specific ELSI methods	ELSI investigators' disciplines
Vanderbilt University	BioVU—combining residual blood samples with a synthetic derivative of the medical record of patients seeking medical care at Vanderbilt; given chance to opt out of blood collection	Because of the presence of other providers in the area, patients may not have long-term relationships	Assess the ethical, scientific, and societal advantages and disadvantages of the BioVU model, and determine best practices for oversight, community involvement, and communication as the resource grows	Focus groups; surveys; interviews; community oversight; external ethics advisory board	Law, ethics, privacy analysis, business

ACT Study, Adult Changes in Thought Study; GHC, Group Health Cooperative.

genomics research for many years,[5–10] including prominently in the International HapMap Project.[4,11] The different eMERGE sites are using a broad range of community engagement approaches, ranging from surveys and focus groups to assess a priori values and concerns, to engagements based on deliberative democracy theories, to studies of population attitudes toward various issues in EMR-linked biobanks, and finally, to creating mechanisms for community involvement in biobank design and oversight based on empirical research findings fully integrated into normative analysis.[12]

Data sharing (Amy McGuire)

Although data sharing has always been part of the scientific ethos, it has been particularly important in genomics research.[13,14] eMERGE investigators are working together to establish agreed on best practices for sharing genotype data linked to clinical information in the electronic health record, both interinstitutionally within the consortium and also more broadly with other investigators through dbGaP. They are also examining research participants' attitudes about these policies, what concerns they have, and what protections they desire.[15]

Identifiability of DNA and electronic medical record data (Brad Malin)[16–21]

Brad Malin has been developing empirical measures of the risk of reidentification within eMERGE, particularly with regard to clinical information. He is also examining the risk of reidentification when individuals within institutions compare clinical records with research datasets as well as the efficacy of data use agreements and data access tracking in preventing reidentification and misuse of information. The Working Group will develop policy recommendations in light of these measures.

Informed consent (Laura Beskow)

Drawing on examples of existing consent language, including some that has been the subject of empirical research[22–24] and best practice guidelines,[25] this group drafted model language to describe the major issues posed by GWAS and related genomic studies, which can be found at http://www.genome.gov/27526660. Model language addresses the purpose of the biobank; procedures for the collection of biospecimens and data; duration of storage; data sharing; recontact; risks and benefits; privacy protections; costs and payments; commercialization; participants' access to individual and aggregate research results; and the ability to withdraw. The group also developed optional wording so that the language can be customized depending on the underlying policies and procedures for a particular study.

Institutional review boards (Maureen Smith)

Institutional review boards (IRBs) around the country are struggling to comply with NIH requirements that the procedures used in initial data collection and interaction with human participants have been reviewed by an IRB or privacy board and an institutional official from the submitting institution has provided verification that the NIH submission criteria has been met.[26,27] The eMERGE IRB group, working with investigators at NHGRI Centers of Excellence in ELSI Research at Case Western Reserve University and the University of Washington, surveyed IRB professionals to learn about their practices and challenges in genomic research review.[28] This broader group of investigators will develop best practices for the review of GWAS and obtaining certification for data sharing as well as educational materials of IRBs.

Return of results (Malia Fullerton and Wylie Burke)

This group is bringing together literature review[29–42] with empirical studies of participants' preferences, and the experience of scientists and clinicians participating in other GWAS consortia, such as GENEVA,[43] to identify relevant principles and develop a framework for considering the return individual results in different research settings. In addition, a Return of Results oversight group, headed by Gail Jarvik, is deciding how best to handle specific results generated from Consortium research that may be clinically relevant, including sex chromosome anomalies discovered by the routine quality control processes common to the analysis of GWAS data.

The C&CC Working Group, working with eMERGE scientists and actively engaging across institutions, is aiding translational research by considering an array of vital conceptual concerns while simultaneously meeting practical challenges. It is our hope that eMERGE will make significant contributions to the national discussion about longstanding ethical, legal, social, and policy issues posed by the unprecedented new uses of clinical and genetic information, recognizing that if ethically and socially acceptable research practices are not adopted, opportunities to apply the tools of genomics to human health and disease will be hindered.

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