

At the Interface between Medical Informatics and Personalized Medicine: The eMERGE Network Experience

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An important goal of the human genome project was the promise that detailed information about variation in an individual's genome would inform healthcare providers and patients about their disease susceptibility and predict response to therapy. Often described as Personalized Medicine, the use of genomic information promises to improve the quality of healthcare. Medical informatics will play an important role in the successful implementation of Personalized Medicine. Without medical informatics support and Electronic Medical Records it would be extremely difficult to provide the clinical decision support that is critical to enable healthcare providers to effectively use genomic information. In addition, there is great need to discover new associations between genetic variations and disease susceptibility or therapeutic outcomes that can ultimately be applied to clinical care.

One approach to discovering these novel associations between genetic variation and therapeutic outcomes has been through linking genomic information to information from Electronic Health Records (EHR) in a discovery mode. The eMERGE (Electronic Medical Records and GENomics), is a network of nine academic medical centers with a DNA biobank linked to EHR [1,2]. The eMERGE consortium is funded by the National Human Genome Research Institute at the National Institutes of Health and includes investiga-

tors from Children's Hospital of Pennsylvania, Cincinnati Children's Medical Center with Boston Children's Hospital, Geisinger Health System, Group Health Cooperative with University of Washington, Marshfield Clinic, Mayo Clinic, Mount Sinai School of Medicine, Northwestern University, and Vanderbilt University.

The network's goals are to discover new associations between genetic variation and disease susceptibility, quantitative traits and therapeutic outcomes, including response to drug therapy and adverse events. The consortium has developed a large number of phenotyping algorithms that utilize data captured during routine clinical care to define cases and controls for genomics research [3]. The phenotype algorithms developed by eMERGE are collected and freely available from www.phekb.org.

As a proof of principle, the eMERGE network developed a type 2 diabetes case and control algorithm, identified cases and controls from their cohorts, then used a genome wide association study to identify genetic variation associated with diabetes. This study identified a similar set of genetic variants that had previously been identified using cohorts specifically built for diabetes studies, effectively demonstrating the validity of using routine clinical data for genomics research [4]. In addition it demonstrated that data from multiple clinical sites and different EHR systems could effectively be combined across sites.

One advantage of this disease agnostic approach for developing cohorts is that the collections of participants include a wide range of diseases, phenotypes and therapeutic responses. Since individuals often exhibit multiple diseases and phenotypes, and individuals selected as a case for one

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study might effectively serve as controls for a different study, the eMERGE approach is a very efficient way to deploy expensive genotyping that can be reused for multiple studies.

To demonstrate this, the eMERGE network developed a phenotyping algorithm to identify cases and controls for a genomic study of hypothyroidism. This study used only participants in the eMERGE network sites who had been genotyped for studies ranging from dementia, QRS duration, peripheral artery disease and other conditions. By re-analyzing the data from this genotyped collection, the eMERGE investigators identified a novel genetic association between FOXE1 variants and hypothyroidism [5], suggesting this may be a broadly useful approach.

Finally, the eMERGE consortium is undertaking genomic medicine clinical implementation projects. One of these projects, in collaboration with the Pharmacogenomics Research Network, is using deep sequencing of a collection of 84 genes known to be important in drug metabolism and response. This project will discover new associations between genetic variants and drug response. In addition, for drug-gene variant pairs where a clinical guideline has been developed, eMERGE sites are developing methods for storing genotypes in the EHR, and producing both clinical decision support tools for physicians and practitioners and patient education materials. The eMERGE consortium is studying both process measures and if using pharmacogenomic data improves clinical outcomes.

The experience of the eMERGE network provides a framework for how to deploy medical informatics in support of implement personalized medicine. A key element of medical informatics that will be needed is the development and implementation of decision support logic and tools to sup-

port genomics based alerts. Finally additional training for medical informatics professionals in genomics and genomic medicine needs to be developed and deployed.

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