Published in final edited form as:
JAMA. 2013 April 10; 309(14): 1467–1468. doi:10.1001/jama.2013.1414.

Genomic Medicine, Health Information Technology, and Patient Care

Dr. Christopher G. Chute, MD, DrPH and
Mayo Clinic, Rochester, Minnesota

Dr. Isaac S. Kohane, MD, PhD
Harvard Medical School, Boston, Massachusetts

Celebrating the tenth anniversary of completing the draft human genome sequence in 2011, authors from the National Human Genome Research Institute of the US National Institutes of Health outlined the influence of genomic understanding across 5 domains: structure, the biology of the genome, the biology of disease, medicine, and improvements in health care.[1] The authors assert that this is the era of enhanced genomic understanding of medicine, which is expected to usher in improvements in health care effectiveness by the end of this decade. It is thus fitting to explore how health information technology will contribute to or hamper the promise of genomic medicine.

A fundamental premise of the rapidly emerging Learning Healthcare System (LHS) model[2] is that medical knowledge can be systematically rendered into executable decision logic to support the clinical care process. The underlying engineering of the LHS requires that knowledge is containable in a knowledge base, linkable to patient data in electronic records, and leveraged to inform clinicians and patients about data-driven clinical implications and treatment options. In the context of the LHS, the domains of genomics do not materially differ from actionable knowledge about, for example, low potassium levels. However, the implications of data volume, complexity, and in some circumstances ethical and legal issues add new dimensions to the implementation of genomic information into patient care.[3]

In 2013, a practical question is “Which genomic findings known today are reliably and consistently useful in patient care?” Despite the proliferation of genome-wide association studies, the number of persuasive genomic associations with disease risk, excepting rare mendelian conditions, remains small. However, pharmacogenomics, which focuses on the genomic influence on drug metabolism, has emerged as an important and practical application of genomics.[4] The genomic characterization of tumors or patient germ line has already become standard practice in the chemotherapy of many cancers. Nevertheless, evaluating the literature, marshaling evidence, and determining whether one genomic measure or another should become accepted practice has been left as an exercise for virtually every hospital and medical practice in the country. Given the accelerating pace of genomic discovery, this is neither efficient nor scalable. Any expectation that a clinician can

Corresponding Author: Christopher G. Chute, MD, DrPH, Health Sciences Research, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (chute@mayo.edu).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Role of the Sponsors: The funders had no role in the preparation, review, or approval of the manuscript.

Additional Contributions: We thank Robert R. Freimuth, PhD (Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota), for his insightful discussions of genomic identifiers. Dr Freimuth received no compensation for his contributions.

or should “know” the vast permutation of emerging genomic influences on disease risk, treatment, or prognosis, as well as the interactions of these influences with drugs or other diseases or, most confusingly, their co-occurrence with other genomic or environmental factors, is unrealistic.

The state of the art for academic medical centers in 2013 is determining a small number of relatively high-profile genomic variants from some or all of their patients likely to imminently require specific drug treatments (based on predictors in their clinical records) and integrating these findings into the electronic health records (EHRs) of those patients. Then, if a drug such as warfarin, clopidogrel, mercaptopurine, or codeine is ordered and a clinically significant drug-gene interaction is known, an alert to the physician or pharmacist is made, and in some settings an alternative recommended drug order is automatically generated. Although these demonstrations deliver in a small way on the promise of individualized medicine, they are unlikely to scale to the full promise of genomic medicine across the entire health care ecosystem. This has led to an academic and commercial race[5] toward the definition of comprehensive, continually updated, clinical- and population-context–sensitive reference knowledge bases that are routinely used and often integrated into clinical process automation.

Three criteria must be met to enable health care to address the scope and complexity of the genomic medicine challenge with clinical process automation linked to authoritative genome-scale annotation knowledge bases: (1) the emergence of a coherent, consistent, and uniform naming convention for genomic variants; (2) an authenticated, well-annotated, curated, and freely accessible knowledge base of genomic associations, risks, and warnings in machine-readable form; and (3) modular, standards-based decision-support rules that can be integrated into any EHR environment with associated, easily readable documentation and guidance. Two additional factors are necessary, but virtually achieved through the advent of Meaningful Use 2014 requirements from the US Office of the National Coordinator for Health Information Technology (ONC): standards-based naming for diseases and findings, which is achievable through the required adoption of SNOMED CT (Systematized Nomenclature of Medicine Clinical Terms); and standards-based naming from drugs and pharmaceuticals, for which the National Library of Medicine’s RxNORM (normalized drug names) suffices in the United States.

The first requirement—that for a uniform naming convention for genomic variants—has many contenders. The Human Genome Variation Society and its associated nomenclatures have been among the most successful, in that insertions, deletions, substitutions, and multiple changes in an allele are accommodated through a logical grammar for variant description. However, for clinical application these systems either conflate or sidestep naming, annotation, description, interpretation, and alignment among versions of the genome.[6] The National Center for Biotechnology Information is exploring taking on the ambitious task of curating the various contributions from academic and commercial efforts to its ClinVar database.[7] If the ClinVar or similar consortial approach succeeds, then attaching a uniform, arbitrary identifier to each observed variant and combinations of variants at each locus could function as a practical clinical identifier for genomic variants and considerably accelerate the nomenclature standardization process.

Second, once reliable and clinically useful identifiers are uniformly established for observed genomic variants, a database of their frequency, provenance, and clinical implications must be systematically established. Despite the abundance of fragmented, proprietary, and product-specific resources, no comprehensive, publically accessible, integrated repository has emerged. Nevertheless, examples of well-curated, authoritative, public efforts such as the Clinical Pharmacogenetics Implementation Consortium (CPIC),[8] which is part of the

National Institute of General Medical Sciences–sponsored Pharmacogenomics Research Network, provide a model. Unlike ClinVar, the CPIC guidelines are rendered as text, which does not support direct implementation of automated decision support without building an executable algorithm. A National Institutes of Health (NIH)–wide and NIH-sponsored effort, which extends the scope of ClinVar and includes a highly structured, standards-based body of content that can inform clinical decision making, would create a necessary information commons and satisfy this second requirement.

Third, notwithstanding these standardization efforts, the real world of implemented clinical decision support within EHR systems is also fragmented, splintered by proprietary clinical decision support data structures, interfaces, and rule sets. The ONC has established Health eDecisions,[9] which supports clinical decision knowledge and implementation. The expectation of this process is that after a future specification of meaningful use regulations, the clinical and health information technology standards community will be able to write clinical decision support logic, expressed in the Health eDecisions syntax, that will be implementable by any EHR system meeting Health eDecisions specifications, thereby addressing the third requirement. It is not a great leap to envision that the second requirement—a curated database of clinically significant genomic associations—would then be expressed in the ONC-specified syntax.

Clinical organizations would then be able focus on the simpler question of whether they choose to adopt extant clinical decision support rules on genomic variation for supporting individualized medicine and whether these would be recommendations or order overrides. With this approach, the prediction of Green and Guyer[1] that incorporation of genomics in patient care may indeed become a practical reality before the end of the decade seems feasible and likely for many leading health care organizations.

Acknowledgments

Funding/Support: Dr Chute and Dr Kohane participate in the National Human Genome Research Institute–funded eMERGE projects (and the National Institute of General Medical Sciences co-sponsored pharmacogenomics integration projects) in partnership with the Pharmacogenomics Research Network.

References

1. Green ED, Guyer MS. National Human Genome Research Institute. Charting a course for genomic medicine from base pairs to bedside. Nature. 2011; 470 (7333):204–213. [PubMed: 21307933]
2. McGinnis JM. Evidence-based medicine—engineering the Learning Health-care System. Stud Health Technol Inform. 2010; 153:145–157. [PubMed: 20543243]
3. Biesecker LG, Burke W, Kohane I, Plon SE, Zimmern R. Next-generation sequencing in the clinic: are we ready? Nat Rev Genet. 2012; 13(11):818–824. [PubMed: 23076269]
4. Wang L, McLeod HL, Weinshilboum RM. Genomics and drug response. N Engl J Med. 2011; 364(12):1144–1153. [PubMed: 21428770]
5. Poh, A. Next-Gen Sequencing Software: The Present and the Future. BioIT World; Sep 28. 2010 http://www.bio-itworld.com/BioIT_Article.aspx?id=101665 [Accessed February 7, 2013]
6. Oetting WS. Exome and genome analysis as a tool for disease identification and treatment: the 2011 Human Genome Variation Society scientific meeting. Hum Mutat. 2012; 33(3):586–590. [PubMed: 22213110]
7. ClinVar website. Jan 19. 2013 http://www.ncbi.nlm.nih.gov/clinvar/
8. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. Clin Pharmacol Ther. 2011; 89(3):464–467. [PubMed: 21270786]

9. Office of the National Coordinator. [Accessed February 7, 2013] Health eDecisions Homepage. Standards and Interoperability (S & I) Framework website. 2012. http://wiki.siframework.org/Health+eDecisions+Homepage