Compute for Personalized Medicine

Executive Summary

In 1990, the U.S. launched an audacious scientific endeavor with the potential to change the practice of medicine when the National Institutes of Health and the Department of Energy joined with the international community in a quest to sequence all 3 billion letters, or base pairs, in the human genome, which is the complete set of DNA in the human body. This concerted, public effort was the Human Genome Project (HGP). By 2000, scientists broke the code and paved the way for an explosion of investment in genetic and genomic testing, generating 116,000 U.S. jobs and USD 16.5 billion in national economic output. These developments are being repeated in Oslo, Beijing, and around the world.

Stemming from the human genome sequencing is a new field referred to as personalized medicine, where providers and patients use diagnostic tools to identify specific molecular characteristics to help assess which medical treatments and procedures are best for the patient. By combining an individual’s medical history and circumstances with this information, providers can develop customized treatment and prevention plans for patients who will benefit, sparing side effects and expense for those who will not. For example, tests that read the DNA structure of the most common form of leukemia in children have helped boost the 10-year survival rate from 4 percent in the 1960s to more than 80 percent today.1 Using the guidance from genetic tests, in the future physicians will more be increasingly able to prescribe the right drug, at the right time, in the right dosage.

Driving to the USD 1,000 Human Genome for Care Customization

The HGP, which took 15 years and nearly USD 3 billion to complete in 2001, can now be accomplished in about a day for less than USD 10,000 (Figure 1). Soon, that cost will likely drop below USD 1,000. Illumina, whose HiSeq® DNA sequencing systems produce the bulk of human genome sequence reads, offers its sequencing services in bulk for as little as USD 4,000.

The cost of next-generation sequencing methods is expected to make whole-genome sequencing both affordable and essential in giving a multi-faceted view of the patient’s health, the biological basis of cancer, infectious diseases, inherited diseases, and drug response. Technology advances will make it possible for the sequencing of individual genomes to become the standard and routine level of analysis for DNA variation.

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Changing Policy to Capture the Opportunity

Now that technology has moved us toward a new environment where understanding the genome is leading to unforeseen breakthroughs in identifying new strains of complex diseases and offering treatments individualized for patients, we need to rethink the laws and regulations governing genetic information.

1. Share the Data

More than 90 percent of U.S. physicians are using electronic health records (EHRs) according to a May 2013 Accenture report. This is incredible progress and a critical basis for becoming the data engine to provide a comprehensive data summary of a patient’s health and well-being. However, we only see the tip of the iceberg until we have the genetic information built into the patient information document and can ensure that the records are available to the patient’s care team. Then, through analytics of big data, targeted and individualized medicine will replace today’s trial and error efforts. That is where policy can help deliver the comprehensive record—by supporting the integration of whole-genome-sequenced data into health records (including clinical decision support tools) using the U.S. “meaningful use” requirements to activate widespread adoption by providers. This will not only allow physicians to have a full picture of a patient’s medical history, but it may also serve as an invaluable platform for research into the correlation of genomic markers with clinical data. The EHRs give much-needed context to the genomic information. Clinical decision support tools integrated with medical records are essential to allow physicians easy access to new patient-appropriate diagnostic tests, as well as to automated resources for the interpretation of test results.

Challenges include:

- Creating and ensuring the interoperability of technical standards for managing and sharing sequenced data in research and clinical samples.
- Developing the technology platform with open standards to enable secure storage, with a computational architecture and application programming interface (API) supporting apps and services. These standards need to provide global interoperability, scalability, stability, and resiliency, serving as building blocks for further innovation and contributions to a global community of data for disease cures and treatments.
- Dealing with the new dynamics of data—where to store, access, and make use of millions of variants for each individual. Do we really want or need to keep them all? How do we access the information we need in real time?

Making genomic data and tools interoperable in a secure and trusted way will generate a powerful network effect: the more data exchange on common platforms, the more value it will have to patients, researchers, and healthcare professionals.

2. Show Me the Evidence

With the adoption of electronic health records comes enormous potential for the value of the data held in millions of patient records—data that could help researchers determine whether a new drug can better treat high blood pressure than a less costly generic, or what the rate of increase is in the diagnosis of Alzheimer’s. Today, the use of this information is regulated by a series of consent requirements constructed for a very different kind of research. In clinical trial research, when comparing groups of patients taking new drugs to those who take placebos, discreet consent is necessary. But how do we
use today’s population data, now document-
ed through EHRs, to closely examine how
treatment outcomes vary among genetic
groups? And what is appropriate for broad
consent, for now and the future, when look-
ing at de-identified data to use in research
for new treatments?

Today, it is not possible to predict which
changes in DNA sequence lead to clinical con-
sequences. When held against a large reposi-
tory of such data, robust patterns and
relationships can be identified which will
require millions of samples from real patients,
their treatments, and conditions. Researchers
are hungry for the ability to access data on a
much wider basis than registries offer today.
Yet, growing concerns regarding the ability to
keep the data private need to be addressed.

Harvard University Professor Latanya Sweeney
published findings in April 2013 showing that
her team re-identified the names of more
than 40 percent of a sample of anonymous
participants in a recent DNA study, highlight-
ing the risk that many see to sharing their
DNA sequence. 2

To enable greater sharing of patient data for
research, privacy and security risks must be
kept manageable. De-identification is a key
safeguard, but not a panacea. As the Harvard
example shows, there is residual risk with de-
identified data that can enable re-identifica-
tion and breach, especially with new types of
data, such as DNA, that we are just starting to
understand. Furthermore, many types of
research require some fields, such as the
patient's age or zip code, that would normally
be eliminated during de-identification. To keep
privacy and security risk manageable, enable
much broader sharing of data, and support
research that requires more than fully de-
identified data, the best practice of a multi-
layered approach to security should be used.

De-identification is combined with other safe-
guards, including encryption, tokenization, and
access controls, which must be usable, perfor-
mant, and robust to effectively mitigate risk
and avoid compelling end users to do
workarounds when security gets in the way.

3. Current Laws Governing Patient
Data Privacy

The Health Insurance Portability and
Accountability Act of 1996 (HIPAA) has many
privacy provisions designed to safeguard medical
information and restrict access to it, yet it serves
as an important reminder of how policy can have
unintended consequences. Since becoming law,
HIPAA has had a chilling effect on scientific
investigation. For example, retrospective, chart-
based research is difficult to conduct due to reg-
ulatory hurdles, and response rates in follow-up
investigations are very low given the challenges
of securing HIPAA-based requirements for
patient permission.

Another important privacy and safety provision
is the Common Rule, which protects patients in
federally funded clinical trials. It requires
researchers to obtain informed consent and
puts in place other provisions to protect
patients in those trials, explicitly safeguarding
vulnerable populations such as pregnant
women, children, and prisoners. The principles
of the Common Rule are also transferred to
non-federally-funded research through other
regulatory guidelines. Thus, the overall system
of clinical trials is coordinated to ensure privacy
and safety, and these rules extend to studies
involving genomic information.

How does the U.S. balance the need for patient
data that will accelerate research and provide
individualized treatments with common and
rare diseases against the interest in keeping
patient health information private?

Scientists argue for widespread and easy
access by researchers to vast collection of data,
but must adhere to the research participants’
conditions of access. When and how will partici-
pants be allowed to access their own data? We
need policies that allow the return of individual
research results from genomic studies to
patients ethically and efficiently.

Since DNA cannot be effectively de-identified,
how do we design informed consent while bal-
ancing with considerations of patient privacy in
the context of that fact? How do we give
patients the tools to decide who will see and
use their data to contribute to public
research/public health or give patient discounts
on health coverage and early access to clinical
trials and new treatment?

As data sharing increases in scope, research
participants will no longer be asked to consent
to a single study, but rather to make their
data available to a large number of researchers,
likely from different countries. Public trust in
the procedures used to store and access data
will be essential.
Today’s privacy and consent requirements need a twenty-first-century review of the data that will allow efficient, secure access for legitimate research on health data while appropriately protecting the confidentiality of individual patients. Patients should be empowered to have a right to share their data as well as to protect the data they choose. This will require new protocols where individuals can dictate access to their information for medical or research purposes. Privacy is ensured by limiting data access to authorized users and auditing all use.

The penalties for lack of controls need to be specified, much like the breach notification regulations in the U.S. HITECH Act, where institutions are required to alert patients of regulations in the U.S. HITECH Act, where specified, much like the breach notification The penalties for lack of controls need to be specified, much like the breach notification regulations in the U.S. HITECH Act, where institutions are required to alert patients of any suspected misuse of data.

4. Show Me the Money

Insurers, including Medicare, are funding genomic testing for specific chronic diseases—like cancer, HIV, and heart disease—in patients and their families. This has significantly increased both predictive and preventative options. However, the limits on reimbursement place both the patient and the healthcare system at risk. As Congress considers cost-saving policies that will transform healthcare delivery, genomic mapping will need to be one of the chief considerations to enable our healthcare practices to target and accelerate care. Genetic mapping will provide the research that will lead to savings from eliminating unnecessary tests and drugs and inappropriate diagnoses.

Today’s static system of codes prevents the Centers for Medicare and Medicaid Services (CMS) from differentiating single tests for disease rather than creating a dynamic testing system based on the value of the test. CMS payment needs to be realigned with the complexity of the test and the risk associated with the disease. Additionally, CMS should set standards for the evidence that the agency and other payers will require to validate the benefits of the tests on a value-based coverage and reimbursement approach for these products. Because reimbursement for high-value products must be driven by true clinical benefit for the covered population, criteria for demonstrating both clinical utility and validity must be developed and standardized. These criteria can then be used to guide both product development and reimbursement decisions.

Expanding genetic testing can appear to increase CMS funding unless a comprehensive cost analysis is considered, including misallocated treatments, missed diagnosis of early stage disease, and the total costs of trial and error medicine.

5. Clarify the Regulations

Is a new framework needed for regulation of clinical laboratory tests that generate genetic-based data? Regulation of in vitro diagnostics in the U.S. is split between two agencies:

- The Food and Drug Administration (FDA), operating under its authority to regulate medical devices
- CMS, operating under the authority of the Clinical Laboratory Improvement Amendments of 1988 (CLIA)

Are these regulatory systems equipped to deal with complex, high-value tests that draw on cutting-edge genomics technology to directly inform high-stakes clinical decisions? Of the two agencies with jurisdiction, CMS has responsibility for laboratory-developed tests (LDTs) through its regulation of the quality and safety standards for labs. The FDA regulates in vitro diagnostic products (IVDs) as medical devices and has stated its authority to regulate LDTs, but the agency has exercised its enforcement discretion and refrained from regulation. However, the FDA has stated its intention to apply risk-based oversight of LDTs as medical devices. Final guidance providing illustrative examples that distinguish products that will be subject to pre-market approval from those that will not is essential.

Regardless of the stakeholder position on the agency of record, it is time for policymakers to clarify agency jurisdiction, reducing the confusion that is slowing the growth of this critical industry to the detriment of patients.

6. Protect My Predictions

The U.S. has one of the world’s most far-reaching protections for genomic information. GINA, the Genomics Information Non-Discrimination Act, provides a national framework for enforceable protections to advance both medical research and public health. GINA creates federal rules to protect insured patients from discrimination by employers and insurers. It is a milestone and a best practice for the rest of the world.

To use patient-specific health information available through genomic mapping, we must remove the stigma associated with genomic testing and integrate it ubiquitously as yet another set of lab test results. If we want to extend affordable, personalized medicine and whole-genome sequencing to patients, we need to integrate the higher-value/lower-cost treatments as the new standard of care. As patients, we can take control and manage our diets, behavior, and exercise, but not be penalized for what we cannot control. An informed partnership among the patient, doctor, and payer should not penalize patients for test results but reward proactive and appropriate use of diagnostics, interventions, and improved outcomes to make data-based decisions.

How can the U.S. close the loopholes that were left in the Act, including nondiscrimination based on genetic information for mortgages, long-term care insurance, the disability and life insurance marketplaces, and coverage for our military men and women? We still have work to do.
7. Bring it Now

The future is here, the research is ongoing, and the challenge is to integrate the new data into advanced clinical decision support software connected to EHRs with the clinical training required to use the patient data and bring this science into daily clinical operations. Centers like Cleveland Clinic are holding summits for clinicians to earn CME credits while building upon the genetic data that is familiar—such as family history—and migrating to pharmacogenomics and more as clinicians begin to weave these additional sources of data into their workflows. At Mayo Clinic, the goal is to get every physician to use personalized medicine, starting with an alert system issued by the EMR. For example, when a physician prescribes abacavir, an AIDS drug that causes severe reactions in some people who have certain genetic variants, the EMR alert pops up and gives the name and pager of an expert in Mayo whom the prescriber can call for advice. The Clinical Decision Support tool, combined with genomics data, is changing medicine today.

Ongoing challenges include:

- How to change workflows and education requirements to convince doctors to adopt personalized medicine within their practices.
- In the absence of an open and interoperable solution, closed proprietary systems will by necessity be created. We need to move quickly before the walled gardens are erected.

Conclusion

Integrating personal health into clinical practice requires policy and practice changes which are today being led by academic medical institutions, technology corporations, and policymakers worldwide (Figure 2).

In 2008, The President’s Council on Science and Technology issued “Priorities for Personalized Medicine,” calling for “the Federal government, through the leadership of HHS, to join with the private sector to create a public/private sector ‘Personalized Medicine R&D Roadmap’ for coordinating discovery and translational research in personalized medicine.” The report focused on policy recommendations for technology, regulation, and reimbursement.

Five years later, many of the issues remain to be addressed and resolved. The roadmap is long overdue. As we enter the decade for next-generation sequencing, we need to get the policy right to ensure the benefits from this miraculous new science, providing individualized treatments for patients at a speed that will dwarf Moore’s law.

Learn more about Intel’s solutions for healthcare and life sciences here.
Compute for Personalized Medicine

2 Forbes, Harvard Professor Re-Identifies Anonymous Volunteers In DNA Study, April 25, 2013
4 Personalized Medicine Coalition, Personalized Medicine Regulation Pathways for Oversight of Diagnostics, 2012

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