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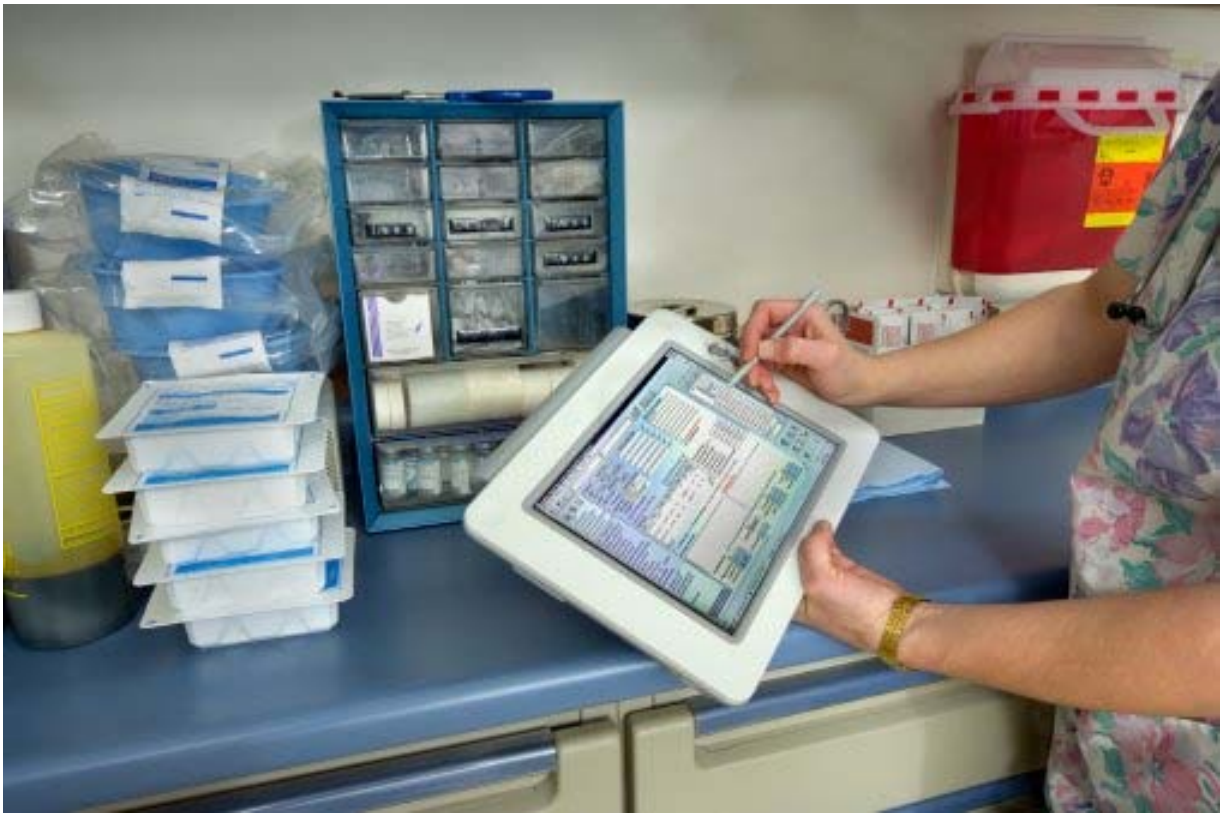

Lester Lefkowitz - Nurse holding electronic unichart entering patient record, close-up

Enabling Personalized Medicine through Health Information Technology

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EXECUTIVE SUMMARY

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With federal officials pursuing the goal of a personal human genome map under $1,000 in five years (White House, 2010), it is possible to envision a future where treatments are tailored to individuals' genetic structures, prescriptions are analyzed in advance for likely effectiveness, and researchers study clinical data in real-time to learn what works. Implementation of these regimens creates a situation where treatments are better targeted, health systems save money by identifying therapies not likely to be effective for particular people, and researchers have a better understanding of comparative effectiveness (President's Council of Advisors on Science and Technology, 2010).

Yet despite these benefits, consumer and system-wide gains remain limited by an outmoded policy regime. Federal regulations were developed years before recent advances in gene sequencing, electronic health records, and information technology. With scientific innovation running far ahead of public policy, physicians, researchers, and patients are not receiving the full advantage of latest developments. Current policies should leverage new advances in genomics and personalized medicine in order to individualize diagnosis and treatment. Similarly, policies creating incentives for the adoption of health information technology should ensure that the invested infrastructure is one that supports new-care paradigms as opposed to automating yesterday's health care practices.

To determine what needs to be done, a number of key leaders from government, academia, non-profit organizations, and business were interviewed about ways to promote a better use of health information technology to enable personalized medicine. The interviews focused on policy and operational issues surrounding interoperability, standards, data sharing protocols, privacy, predictive modeling, and rapid learning feedback models.

This paper outlines the challenges of enabling personalized medicine, as well as the policy and operational changes that would facilitate connectivity, integration, reimbursement reform, and analysis of information. Our health system requires a seamless and rapid flow of digital information, including genomic, clinical outcome, and claims data. Research derived from clinical care must feed back into assessment in order to advance care quality for consumers. There currently are discrete data on diagnosis, treatment, medical claims, and health outcomes that exist in parts of the system, but it is hard to determine what works and how treatments differ across subgroups. Changes in reimbursement practices would better align incentives with effective health care practices.

Furthermore, we need privacy rules that strike the right balance between privacy and innovation. These rules should distinguish health research from clinical practice, and create mechanisms to connect data from multiple sources into databases for secondary research usage and population cohort analysis. More balanced rules would improve innovation. It is nearly impossible to evaluate treatment effectiveness without being able to aggregate data and compare results. Faster knowledge management would enable "rapid learning" models and

evidence-based decision-making on the part of physicians and public health officials.

As more information on treatment, lab tests, genomics, and financial costs get integrated into health care, it is hard to incorporate data from medical history, vital signs, genetic background, and lab testing into diagnosis and treatment. Predictive modeling represents a way for physicians to move towards systematic and evidence-based decision-making. While the first step toward enabling personalized medicine is ensuring clinicians have access to what is known about patient gene variants, computer models can go beyond this approach to predict what treatments are likely to be most effective given observed symptoms. Public policy should incorporate rapid learning and predictive modeling to gain the full benefits of personalized medicine.

If researchers and healthcare providers are not able to exchange information, it raises the cost of health care and makes it difficult to learn in real-time.

There are several ways in which personalized medicine can be enabled: (1) "meaningful use" requirements promulgated by the executive branch, (2) change driven by consumer demand for personalized medicine, (3) pilot and demonstrations projects supported by the Centers for Medicare and Medicaid Services (CMS) Innovation Center, and (4) academic-industry collaborations encouraged by the government through investment. The declining costs of DNA sequencing will drive consumer demand and generate growing demands for physicians to personalize medicine. In addition, CMS should deploy some of its $10 billion in pilot project resources through its new innovation center to encourage personalized medicine. Along with the National Institute of Health, the agency could fund new projects designed to demonstrate innovation in health care (Wechsler, 2009).

The Challenges of Enabling Personalized Medicine

There are a number of policy and operational challenges that interfere with the public's ability to gain the benefits of personalized medicine through health information technology (Pollack, 2010; Wade, 2010). These include issues such as interoperability, inconsistent coding and language standards, problems in data sharing, weak feedback loops, privacy concerns, and ineffective reimbursement policies.

Interoperability represents a major challenge because of the difficulty of integrating data from different sources. If researchers and healthcare providers are not able to exchange information, it raises the cost of health care and makes it difficult to learn in real-time. A considerable amount of medical information is collected, but too little of it is integrated or put into data bases that are usable for research or public health purposes.

As our understanding of diseases becomes ever more stratified by their genomic signatures, even larger data sets will be needed to establish treatment protocols. Patient data across geography and health care plans will need to be queried simultaneously. This can only be achieved through large, federated pools

of information that includes patient genomic data and their health histories.

Legitimate concerns over privacy and confidentiality complicate secondary use of health care information. Even when data are aggregated and depersonalized, it is hard for researchers to gain access to information that helps them spot trends or gain insights into public health trends.

Regulatory processes will be strained by genomic discoveries. There will be no way to conduct conventional clinical studies for every genetic signature as a unique diagnostic test. One solution would be a statistical strength standard that must be demonstrated before genetics can be applied to medical decision-making. Statistical strength could be determined through mining of federated data pools. This mechanism could alleviate capacity constrains and costs associated with clinical studies and speed innovation to the marketplace.

There also are problems in terms of reimbursement policies. Many programs are not well aligned with laudatory goals such as preventive medicine or positive health outcomes. *This mismatch makes it difficult to judge quality or build incentives for healthy outcomes.* We need to reward providers for good behavior and reduce incentives for wasteful or unnecessary treatment.

Three Revolutions and How They Affect Health Care

The Medical Delivery Revolution: New Actors and New Relationships

Health care is shifting from a hierarchical delivery system to one that features greater transparency, collaboration, and patient involvement. For much of the 20th century, medicine was dominated by physicians with considerable professional autonomy, hospitals, the pharmaceutical industry, insurance companies, and government agencies that focused on the elderly, veterans, and the poor (Starr, 1984).

Now we are seeing a more empowered relationship between primary care doctors and their patients, and the emergence of customer-driven medicine that has expanded the range of non-traditional health care providers and placed more information-gathering responsibility on patients and their care-givers, such as children with elderly parents. Businesses such as CVS and Wal-Mart have developed in-store treatment centers (Jones and Japsen, 2010). Out-patient facilities have proliferated at a rapid rate. Patients can order drugs through Internet sites. Rather than rely only on doctors, consumers can get health information from the Internet, social networking sites, fellow patients, and chat rooms (Miller, 2010).

Remote monitoring devices and mobile health applications allow people to monitor their own weight, blood pressure, pulse, and sugar levels, and send results electronically to health care providers. Patients can store their medical records online and have access regardless of where they are in the United States or around the world. Some get personalized feedback via email and reminders when

they gain weight, have an uptick on their cholesterol levels, don't take their medicine, or have high blood pressure (West, October, 2009).

Scans and imaging have improved to a high level of resolution. Imaging tests, especially computed tomography or CT scans, can measure tissue down to one-third of a millimeter in size. This development allows health care providers to describe physical anomalies with tremendous precision and monitor patient responses to various therapies. Imaging enhances medical personalization and tailors treatment to someone's individual circumstances.

Policymakers hope to extend the utilization of electronic health records... [and] increase the usage of health information technology from 10 to 90 percent of health care providers so that they have adopted electronic health records in meaningful ways by 2015.

The Digital Revolution and Ways to Convert Data into Knowledge

Concurrent with major changes in medical care delivery has been an explosion of digital resources for patients as well as physicians. Websites such as WebMD.com, MedlinePlus.gov, MerckSource.com, HealthFinder.gov, and MayoClinic.com answer questions and provide links to discussion groups about particular illnesses. In states such as Massachusetts, California, New York, and Michigan, consumers can visit health department sites and compare quality performance data on provider care programs. Nationally, the U.S. government has a website, www.hospitalcompare.hhs.gov, that evaluates 2,500 hospitals on mortality rates, room cleanliness, call button responses, and how patients judge their quality of care (West, 2009).

Social networking sites represent another way to share information among chronic condition sufferers. For example, a network developed by the company PatientsLikeMe has 23,000 patients who have signed up to share information regarding five different illnesses: mood disorders, Parkinson's, multiple sclerosis, HIV/AIDS, and Lou Gehrig's disease. Particularly for rare illnesses where it is hard to generate the patient numbers required for clinical trial, site organizers say "patients have been a tremendously underutilized resource." While large clinical trials with randomized assignment clearly need to remain central to drug assessment, digital technology that helps providers and researchers identify worrisome trends represents an additional way to gain useful feedback.

Through these and other digital resources, doctors and patients have much more information at their disposal (Christensen, Grossman, and Hwang, 2008). They know more about their own histories, can link to additional sources of information, and can interact electronically with health care providers. This level of information strengthens patients' access to information and helps them ask more informed questions about their medical conditions.

As part of the 2009 American Recovery and Reinvestment Act, Congress authorized $44 billion in public funding of physician and hospital adoption of electronic health records. Policymakers hope to extend the utilization of electronic health records by providing grants to hospitals and physicians meeting "meaningful use" standards. Their goal is to increase the usage of health information technology from 10 to 90 percent of health care providers so that they

have adopted electronic health records in meaningful ways by 2015. The new investment creates the opportunity to adopt information systems that accelerate personalized medicine as opposed to merely automating systems designed years ago.

Genomics and the Impact on Medical Care

Scientists have made extensive progress over the last two decades in understanding human genetics and the role of proteins and chemicals in gene behavior (Goodman, 2009). In 1989, the National Institutes of Health launched the Human Genome Project in an effort to identify the basic building blocks for human beings. By 2003, investigators had sequenced the genome and identified three billion discrete "chemical units."

Since that time, scientists have worked to establish links between gene structures, human illnesses, treatment effectiveness, and adverse effects (Institute of Medicine, 2010b). Integrating genetic sequencing data into electronic health records potentially cuts health care costs through more effective targeting of treatments and more accurate diagnoses. This type of connectivity speeds research feedback into clinical care, and gets more timely information to patients, physicians, and medical researchers.

Advances in DNA sequencing have made it possible to develop greater understanding regarding the role of genetic structures in disease susceptibility and treatment efficacy (Wade, 2010). Scientists have identified genes that raise the odds of getting illnesses such as breast cancer, or increase the likelihood of adverse reactions or bleeding.

For example, they have found that those carrying certain mutations in the BRCA1 or BRCA2 genes have a higher risk of breast cancer and those expressing the HER2 protein are at greater risk of reoccurrence. Combined with detailed family histories and diagnostic tests, doctors can pinpoint who is most susceptible to breast cancer and therefore needs to be monitored most carefully. Physicians have documented that you can't just treat patients based on population averages, but need to be aware of subgroup and individual differences.

Investigators have made progress in determining who is most likely to benefit from possible treatments and who is likely to be harmed. In oncology, for example, pathologists measure estrogen receptor expression to determine eligibility for tamoxifen hormone therapy among those suffering from breast cancer. Effectiveness has been found to be contingent on a cytochrome enzyme P450 2D6 needed to metabolize the drug, although the results have not always been consistent across studies (Goodman, 2009). Genetic tests for HLA-B*1502, a particular variant of human leukocyte antigen (HLA), are already available and can predict increased susceptibility to dangerous or even fatal skin reactions such as Stevens Johnson syndrome and toxic epidermal necrolysis resulting from carbamazepine therapy used in the treatment of seizures. This allele occurs almost

exclusively in patients with ancestry across broad areas of Asia.

There has been mixed evidence regarding a link between the genotype CYP450 and treatments using selective serotonin reuptake inhibitors (SSRI) antidepressants. Some patients suffering from metastatic colorectal cancer whose tumors have a gene mutation called KRAS have not responded well to treatments using panitumumab or cetuximab (Downing, 2009).

Analysis has demonstrated that many patients are not able to benefit from particular drug therapies. Iressa and Tarceva are drugs for treatment of non-small cell lung cancer, but they are effective only in tumors that express the epidermal growth factor receptor gene. Other medications are ineffective for 70 percent for Alzheimer sufferers, 50 percent for those with arthritis, 43 percent who are diabetic, 40 percent who suffer from asthma, and 38 percent who take SSRI antidepressants (Spear, Heath-Chiozzi, and Huff, 2001; Goodman, 2009). Since people metabolize medicine in so many different ways depending on their particular combination of genes, the resulting enzymes, and their current health status, it is vital for a safer and more effective healthcare system to have an understanding of genomic information to reduce adverse events and determine optimal therapy (U.S. Department of Health and Human Services, 2008).

The capture and storage of genomic information will redefine health informatics data flows.

Policy Challenges and Recommendations

While technology, patient engagement, and scientific advancement are changing health care practices, genomic information in particular has the potential to transform medical practices and outcomes in fundamental respects. Genomics is being introduced in several ways. One is through patient empowerment, making genetic information available directly to them so they can address genetic factors directly with their physician (Pollack, 2011). Another model that is unfolding through public and private sector initiatives is to employ genomic information through medical practice and weaving that material into patient care throughout their lifetime.

The capture and storage of genomic information will redefine health informatics data flows. The result will be improved decision rules and streaming of information directly into medical decision-making. This will make health care delivery more efficient. Therapies can be given more precisely to those patients most likely to benefit and not offered to those patients who would be harmed by the treatment. While there needs to be additional research on these questions, there is reason to believe that the net cost of care per patient could be reduced.

Realizing the use of genomic information in health care has the potential to generate important benefits for patients, physicians, and public health officials. In order to take advantage of these developments, though, it is vital to connect genomic and other personalized information to electronic health records, and to integrate established statistical correlations between genetics and drug effectiveness. Diagnostic and treating physicians need this information to

coordinate patient care effectively. As researchers learn more, genetic information and susceptibility to drugs and side effects should be at the fingertips of doctors in the same way that family history, vital signs, and medical tests are. Timely information would help caregivers incorporate what works and doesn't work into their clinical decisions.

Better Data-Sharing Networks

One of the biggest barriers to gaining efficiencies in our current system is interoperability problems in connecting different information systems (President's Council of Advisors on Science and Technology, 2010). The United States has a health care system that is quite fragmented owing to the existence of 650,000 doctors and 5,800 hospitals. The clinical records of patients do not travel with them electronically, and most of the computing systems do not enable data flow. Many have different systems for compiling billing, lab tests, medical records, prescriptions, treatment, and appointments, which makes it very difficult for providers to exchange information outside of electronic converters. And to make matters worse, the information captured in some of these systems relies on different semantics that make cross correlation nearly impossible.

There currently are discrete data sets that exist in parts of the system, but they are not integrated. It is hard to determine what works and how to assess costs and benefits. Technology has been used to improve the accounting and administrative aspects of health care, but not its knowledge management. We need information systems that help us analyze the overall contours of health care.

In the medical area, the creation of national drug codes (NDC) created reimbursement efficiencies. Establishing a 10-digit code for each medication helped to make drug administration safer and more economical. It facilitated the tracking of pharmacological information, and produced benefits both for consumers and businesses.

Health information technology and electronic health records can serve the same type of integrative role. It is possible to track claim receipts in real time. When combined with information on medical tests and clinical outcomes, this material will shorten evaluation cycles and enhance our ability to control costs in ways that do not weaken quality. Treatment guidelines in electronic health records would help physicians understand their treatment options.

The goal of data-sharing networks is to develop a so called "virtuous cycle" for health care where improvements build on one another. Electronic health records with proper coding and the use of that data could inform clinical care and help evaluate substantive value. Treatment information should be linked to outcomes, with reimbursements based on the end-result. A balance between costs and benefits would help people make informed decisions. Right now, there is much greater concern about the costs and burdens of integration than its possible benefits to patients, physicians, researchers, and public health administrators.

An excellent example of a new kind of data exchange is the cancer Biomedical Informatics Grid, or caBIG. This network, launched in 2003 by the National Cancer Institute, connects more than 50 NCI-designated Cancer Centers, along with other academic and commercial organizations, making it the largest national biomedical information network in the United States. Capabilities compliant with caBIG interoperability specifications enable the collection, analysis, and exchange of a wide range of biomedical information through a well-integrated, standards-based infrastructure coupled with open-source and commercial software applications. These technologies create an integrated electronic system that enables clinical research, genomics, medical images, biospecimens, and patient outcomes data to flow easily but securely between and among authorized individuals, organizations, and institutions. These capabilities enable health care providers to leverage resources developed in research settings to identify molecularly sub-grouped patients, collect and view their patients' histories individually and in the aggregate, and collaborate across organizations to test research hypotheses and evaluate new treatments.

Current electronic health systems have a "Tower of Babel" feature that undermines connectivity.

Ending the Health Care "Tower of Babel": Improved Semantics and Data Coding

Current electronic health systems have a "Tower of Babel" feature that undermines connectivity. Researchers, clinicians, and industry employ inconsistent standards in how medical terms are defined and applied to health conditions. They don't classify diseases in the same way or describe symptoms with similar language. These semantic inconsistencies make it difficult to populate electronic records with data that are comparable.

In the world of specialty care, this problem becomes even more serious. Health providers from various specialties require different information and often record symptoms in dissimilar ways. Pathologists may have different informational protocols from oncologists or internal medicine physicians. As long as there are semantic inconsistencies, it is hard to take full advantage of digital record-keeping systems. The College of American Pathologists has worked with oncologists to develop cancer checklists which standardize reporting and help to close this gap.

Right now, the United States does not have adequate diagnostic coding protocols. Each of our 5,800 hospitals has its own nomenclature and fields of description. Many providers use different terms to describe the same symptoms. The data are overly aggregated and therefore hard to determine what actually is going on. For example, there now are 60 different types of leukemia, but the currently-used International Classification of Diseases (ICD) codes do not reflect the diversity of that disease. Physicians and administrators say they need greater granularity in the coding conventions. Since diagnostic tests represent up to 70 percent of physician's core decisions, according to informed experts, the best way to evaluate costs involves greater precision in coding lab tests. However, with the future implementation of ICD-10, additional granularity with regard to specific

diagnosis will be enhanced.

The same problem develops in regard to genomics. Although the CPT (Current Procedural Terminology) Editorial Panel of the American Medical Association is working to correct this issue, we currently do not have differentiated billing codes for various molecular or genetic conditions. Many health care systems don't distinguish gene tests for breast cancer versus other illnesses where genetic tests are employed. This makes it impossible to aggregate data or link genomic information to disease diagnosis and treatment. Validating genetic links to particular diseases will improve drug targeting and treatment.

There have been improvements on some of these dimensions. The Systematized Nomenclature of Medicine – Clinical Terms (Snomed CT) has developed a disease categorization nomenclature that is used in 15 countries. But many of its codes are not detailed enough for research purposes. There are disconnects between clinical and research communities that prevent each from building on the work of the other. Common points of reference are required that make use of new research as it develops. This includes more variegated descriptors, more detailed codes, and more specificity on the different types of cancers that are being identified. The system needs to be dynamic in nature so that it is regularly updated as researchers develop new knowledge about medical illness.

Professional networks are making progress on coding and language description. The role of the Clinical Data Interchange Standards Consortium has been helpful and its reliance on professional experts from several fields led to the development of widely-used standards. Clinical genomics guidelines for health care providers would be useful in order to provide an overall framework for integrating genetic information into electronic health records. There remains a need for greater specification of different types of genetic background.

Of course, standardized vocabularies work only when there is uniformity in what is being described. Medicine still is constrained by the imprecision of human language and vagueness of patient symptoms. True semantic uniformity may come best with machine-generated data, not perceptual data (Shirky, 2003).

More Balanced Privacy Rules

Privacy represents a major issue for the American public. According to survey data, many Americans are concerned over the confidentiality of online medical information. Sixty-two percent of adults in a national poll felt that use of electronic medical records makes it more difficult to ensure patients' privacy (PR Newswire, 2007). Seventy-five percent of Internet users worry about health care websites sharing information without their permission. Seventeen percent of people in a Harris Interactive survey (2007) reported that they withhold information from medical personnel due to concerns that these individuals would disclose the data to unauthorized individuals.

The rise of personalized medicine makes these concerns even more pronounced. Genetic information, by definition, is deeply personal since genotypes, enzymes, and proteins are unique to the specific person studied. If released publicly, this information has ramifications for possible employment, economic prospects, and social relationships. If employers knew someone carried a gene that seriously increased the odds of a chronic disease, would they hire that person? Knowing the benefits of genetic testing for diagnosis and treatment does not mitigate against the possible risk of privacy violations.

There is no question that strong privacy rules are required (Goldman and Hudson, 2000). People fear discrimination or adverse job consequences from medical information not being kept confidential. In part, this is why Congress in 1996 adopted the Health Insurance Portability and Accountability Act. That legislation was designed to address patient privacy concerns and insure that appropriate safeguards were put into place. The American Recovery and Reinvestment Act has strengthened these privacy rules. The Department of Health and Human Services has a proposed rule out for public comment that would apply HIPAA rules to business associates of covered entities.

In 2008, Congress passed the Genetic Information Non-Discrimination Act prohibiting use of genomics in employment hiring or firing was very helpful in ensuring patient protection. This bill disallows health insurers from using genetic testing to determine rates and helps to reassure consumers that genomic information could not be used against them.

However, some experts question whether current privacy rules strike the right balance between privacy and innovation. A 2009 Institute of Medicine (IOM) report concluded that "the HIPAA Privacy Rule does not protect privacy as well as it should, and that, as currently implemented, it impedes important health research." The report suggests people should distinguish "information-based research" from "interventional clinical research." For research, project analysts argued that it was not feasible to get consent for all secondary uses, especially in situations where the data were "de-identified".

The IOM Report authors suggest the need to revise privacy rules to distinguish health research from practice and to allow for a "mechanism for linking an individual's data from multiple sources such as databases so that more useful databases can be made available for research in a manner that protects privacy, confidentiality, and security." In its conclusion, the report calls for a new approach to privacy, saying "effective privacy protections must be implemented in a way that does not hinder health research or inhibit medical advances."

New Approaches to Privacy and Access Control

The question for the health community is how to protect privacy and provide mechanisms for patients' access control. Technology helps in this regard because it allows patients to make decisions in more refined and differentiated ways.

Intruders leave digital fingerprints so that patients and administrators can determine who saw electronic records, what files they looked at, and how long they browsed particular parts of the record. Digital systems produce a level of accountability that is not possible with paper records and make it easier to enforce penalties where there are intrusions.

Current limits on data sharing and secondary analysis of de-identified data make it difficult to get the benefits of genomics. Data access is not just a question of the risks of unwanted information releases, but what benefits arise from data sharing. For example, it is nearly impossible to evaluate treatment effectiveness without being able to aggregate data and compare results. Researchers need to be able to re-use information so that data can be employed to improve health care quality and cut costs.

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There are particular privacy issues that arise with tissue samples and genomic information. Some experts have suggested that as few as 13 specific genetic features can identity a particular person with a 1 in a billion certainty. There are certain molecular genotypes that are rare enough to be able to identify a specific individual. Indeed, de-identified qualities nearly evaporate under the notion of personalized medicine.

It is hard to de-identify data when information is specific to a person. Health providers have a problem with patient consent for future use of a sample because they never can know all the future uses of data for research purposes. In addition de-identified tissue samples reduce the value of the specimen because the link to family history and genetic information is integral to the value of the sample for personalized medical research. Under current privacy rules, it is impossible to gain any of the benefits of genomics when patients have to approve any current or future specific use of the tissue sample.

Consent is complicated when you are unsure of future uses of samples. The Havasupai tribe recently resolved its legal dispute with Arizona State University over genetic data gathered from tribal members. University researchers used the material for research into schizophrenia and the tribe's ancestral heritage. Tribe members sued the university over what it claimed were vague consent forms. The two sides settled the dispute and the university returned blood samples to the original providers (Klosek, 2010).

The Centers for Pathology and Oncology Informatics and Center for Pathology Quality and Healthcare Research at the University of Pittsburgh Medical Center (2003) have developed a novel approach to patient consent on tissue samples involving what are called "honest brokers." Researchers who need information for study purposes can go to individuals designed by the center's institutional review board as honest brokers. Under particular circumstances, they can request more individualized records in order to facilitate specific research projects. This procedural mechanism represents a creative attempt to reconcile privacy and research utility.

Greater flexibility by local institutional review boards would help expedite the

integration of personalized medicine with health information technology. IRBs need to develop new models of real-time testing of cognitive systems. Its members should understand there is value not just to assessments of before and after interventions, but real-time data collection and analysis. It is hard to get human consent in large-scale research projects, but there is value in data aggregation with de-identified information. In this situation, original data can be employed to find unobserved patterns. This is an example of where the secondary use of data for research and public health purposes needs to be recognized as legitimate by local institutional review boards.

In addition, analyses would be helped by research and public health reporting exceptions. There could be limited use agreements for research purposes that allow scientists to access for purposes of comparative effectiveness. This could involve removing certain fields from the data set that are most sensitive. Administrators should not have to get new permission from patients in order to report aggregated and de-individualized data results to health officials. There is a model in the case of the U.S. Census in which personal information is collected from individuals, but aggregated data available down to the census tract and block levels are available to researchers that does not reveal individual identifiers.

There should be better understanding of ways to balance the competing needs of patients, physicians, researchers, and public health administrators. Each requires different kinds of information. For example, patient need access to medical history, vital signs, lab tests, and genomic risks. Physicians need all those things plus genomics, drug interactions, side effects, and clinical treatment guidelines. Researchers need de-identified data on medical history, vital signs, lab tests, genomics, and health outcomes. Public health administrators need data on treatments, diagnosis, financial costs and health outcomes.

The Harmonization of State Laws

The cross-border practice of medicine suffers because many states have different rules and requirements on privacy, data sharing, and access that complicate the administration of medical care. In some places, HIPAA privacy rules act as a floor, not a ceiling for stricter state laws. For example, states look for different genetic disorders in newborn screening tests. This lack of continuity makes it difficult to share information across state lines for institutions operating in various jurisdictions.

There also are substantial differences in state privacy and consent rules. A Massachusetts law has been interpreted to outline a distinction between tests done for screening purposes and those for diagnostic purposes. Ordering physicians are not able to perform genetic screening tests without the specific written consent of the patient, and tests results are available only to the ordering physician.

This means that other clinicians involved in the patient's care may not have access to this information and may end up making incorrect decisions. For

example, if a clinician is not aware that a patient has a genetic predisposition for hypertrophic cardiomyopathy, they may incorrectly diagnose their symptoms as asthma, with disastrous health consequences. Florida meanwhile has stricter rules and processes for informed consent. National health care organizations that share data across state borders must be cognizant of what the rules are in particular jurisdictions and how various regulations affect their mode of operation.

It is common for prognostic gene testing services to encounter different laws in various states. These varying legalities affect how much access emergency room physicians have to genomic information. Without access to screening tests or genetic background that assess the appropriateness of medications such as the anticoagulant drug warfarin, they may administer an ineffective treatment or prescribe the wrong medicine. Some doctors confuse asthma with heart thickening problems because they have similar symptoms and then use the wrong medication to treat the condition. Not only is this wasteful, it is dangerous to patients.

Greater harmonization of state laws would be very helpful to businesses and researchers operating across state lines. It also would speed the development of the IT infrastructure required to support personalized medicine by ensuring resources are not diverted to the peculiarities of individual state laws. The current cacophony of rules and regulations makes it difficult to know which rules to follow and which regulations apply in cross-border operations.

More attention should be devoted to preventive medicine, positive health outcomes, and reimbursement for performance as opposed to volume of business.

Ending the Catch-22 of Reimbursements

Reimbursement policies need to be better aligned with national goals. More attention should be devoted to preventive medicine, positive health outcomes, and reimbursement for performance as opposed to volume of business. Value-based reimbursement would give physicians and hospitals more of an incentive to focus on generating good health as opposed merely to ordering tests.

In 2009, the Centers for Medicare and Medicaid Services investigated whether the federal government should reimburse the costs of genetic testing of patients taking the anticoagulant drug warfarin to determine their likelihood of abnormal metabolism and health care risk. However, after extensive discussions, CMS decided not to provide blanket coverage of the genetic test because it felt that the dosing guidelines and pharmacogenomic association had not been clearly demonstrated (Downing, 2009).

In recognition of the possibility that genetic background might be relevant for treatment outcomes, CMS did establish a process for test reimbursement if it were part of a large-scale randomized clinical trial research project. The CMS Coverage with Evidence Developmental (CED) allows Medicare reimbursement for testing on patients enrolled in a formal assessment. There is a catch-22 where insurers do not wish to reimburse unless there is demonstrated evidence yet it is hard now to validate the value of genetic tests because it is difficult to complete large randomized

studies with gene data. CMS CED represents an example of how reimbursement policies can be adapted, but this is only a first step.

At the same time, current coding protocols do not facilitate the case for genetic information because they do not distinguish various types of genetic tests. This weakness makes it impossible to establish the efficacy of genomic information for medical treatment. Reimbursement policies clearly need to change so that financial incentives are better aligned with policy goals and desired outcomes.

In the case of genetic testing, it is important to distinguish between reimbursement for performing the test and interpretive services. The physical test where you sequence the base pair and run a DNA analysis is reported on the clinical laboratory fee schedule by a hospital or laboratory, and does not include the professional work to interpret and make sense of the data. Some insurers are starting to reimburse for the actual test.

However, there is insufficient reimbursement for physicians and qualified health care practitioners who interpret test results and help patients understand the significance of the information. In many cases, these individuals are paid less than $10 per report, and this is inadequate for making the greatest use of genomic information. With the costs of genetic testing dropping rapidly, the cost of interpretation is becoming a bigger share of the genomic analysis. This situation does not provide proper incentives for the application of interpretive services.

Rapid Learning Feedback Mechanisms in Clinical Care

One of the biggest current problems is the isolation of research and clinical care. Future medicine needs to be "translational" in nature with a means to update knowledge as new discoveries are found. Right now, it is difficult to integrate advances in medical research into treatment guidelines that are accessible to physicians. There need to be ways to speed up the feedback loops so that new discoveries get incorporated into treatment (Institute of Medicine, 2010a).

Administrators collect an extraordinary amount of information but too little of it is integrated or put into form that is usable for secondary purposes. For example, there are millions of medical claims that are filed, but no way to determine which specific tests are performed. This makes it impossible to identify what lessons we can learn from the data.

There is weak feedback from research to clinical care. It is hard to incorporate the latest research findings into clinical settings. Researchers do not like to share data before publication, and there is great emphasis on the risks of information-sharing and little attention to possible benefits of system integration. We need data sharing both for research and public health purposes (Walker, 2010).

Faster knowledge management enables "rapid learning" models and evidence-

based decision-making on the part of physicians and public health officials (Etheredge, 2010). Integrated databases help researchers to log on and test ideas. High-speed networks, integrated data sets, and research registries facilitates hypothesis-testing and allows clinicians to draw on the latest knowledge about medical treatment (Etheredge, 2010).

In the long-run, it would be valuable to have information both on clinical care and financial management. Integrating cost information into clinical data would allow care-givers to determine what the best clinical options at the best cost. Of course, it is notoriously difficult to evaluate medical cost information. Hospitals provide discounts and rebates so there are proprietary considerations in terms of cost material. Few patients pay list costs for treatments and Medicare often reimburses only 60 percent of actual costs. In this situation, it is hard to get standard accounting codes that help others determine which payees get which discounts.

Predictive Modeling in Physician Practices

As more information on treatment, lab tests, genomics, and financial costs get integrated into health care, it creates a major problem for physicians. It is hard to incorporate information from medical history, vital signs, genetic background, and lab testing into diagnosis and treatment when there is a flood of information. Knowledge integration may create systems that exceed the cognitive capabilities of care-providers to interpret the information. For example, there are 7,900 current procedural terminality (CPT) codes established by the American Medical Association and 80,000 diagnostic codes so it is hard for physicians and public health professionals to figure out what to do with all the information.

Predictive modeling represents a way for physicians to move towards systematic and evidence-based decision-making. Computer models monitor the range of information and predict what treatments are likely to be most effective given the range of symptoms observed.

Aided decisions can help modelers develop decision trees for physicians in the style of "what if" statements. If patients have certain symptoms, what are the logical tests to run and treatments to suggest? Patient- and lab-reported information on symptoms, value statements, co-morbidities, vital signs, renal and heart performance still are central to diagnosis. With the addition of biomarkers and gene testing, predictive models help physicians decide the best course of action. The U.S. Department of Health and Human Services hopes to add learning models to its last stage of financial incentives for health care providers engaged in "meaningful use" of certified systems. This requirement will enable health information technology to integrate clinical, outcome, and research information.

One example of this approach is Kaiser's Archimedes model (Eddy, 2009). This approach uses data on blood pressure and sugar levels to chart optimal health. The compilation of information allows computers to determine who the individual

outliers and the probability of illness developing given their life histories and genetic makeup.

Breast cancer is an area where effective predictive models have been developed. It is the illness where scientists have made the most progress at identifying biomarkers and determining how to personalize treatment to one's genetic composition. It is the leading edge of innovation in terms of personalized medicine.

But there remain questions of how best to validate models. Scientists need clinical diagnosis and treatment data linked to health outcomes to determine what works. Approaches that allow learning over time, adapt to new research and new procedures, and feed into predictive models represent a promising way to improve health care.

Our healthcare system requires a seamless and rapid flow of digital information, including genomic, clinical outcome, and claims data, in order to become more efficient, effective, and truly personalized.

Duke University partners with 100 institutions in an effort to collect the same data from every patient before and after treatment. They follow 80 different data points, and employ that information to make decisions on interventions and treatments. They monitor self-reported symptoms and personalize the treatment based on clinical and psychological needs.

Geisinger Health System has made progress at using material on patient background and symptoms to predict 6 to 24 months in advance for half of its members who is most likely to develop congestive heart failure (Adams, Mounib, and Shabo, 2010). They have validated this model based on probabilistic reasoning and can report that if someone has certain symptoms, there is a certain probability he or she has heart failure. This helps physicians make decisions on diagnosis and treatment. Public health officials need to incorporate predictive models in physician practices.

Conclusion and Key Recommendations

To summarize, this report has outlined a number of ways to promote a better use of health information technology to enable personalized medicine. There needs to be policy and operational changes that facilitate connectivity, integration, reimbursement reform, and secondary analysis of information. Our healthcare system requires a seamless and rapid flow of digital information, including genomic, clinical outcome, and claims data, in order to become more efficient, effective, and truly personalized. Research that studies data in real-time expedites learning and helps determine what works and how physicians can tailor treatments to individual circumstances.

Currently, there are problems in terms of interoperability, standards, data sharing protocols, privacy, predictive modeling, and rapid learning. Scientific innovation in the areas of genomics, imaging, and computing is far ahead of public policy. The result is a policy regime that constrains innovation, and does not help physicians, researchers, or patients receive the full benefits of these advances.

There are eight changes that would enable personalized medicine:

1) creating "meaningful use" rules from the Office of National Coordinator of the Department of Health and Human Services that facilitate more effective use of health information technology for personalized medicine.

2) reducing the isolation of health research from clinical practice, and creating mechanisms that connect information from multiple sources into databases for secondary usage.

3) developing privacy rules that strike the right balance between privacy and innovation.

4) having differentiated codes for various molecular or genetic tests so that researchers can link genomic information to disease diagnosis and treatment.

5) building data systems and language semantics that help researchers compare, evaluate, and frequently update information.

6) enabling feedback loops so that new discoveries get incorporated into treatment. Faster knowledge management would enable "rapid learning" models and evidence-based decision-making on the part of physicians and public health officials.

7) deploying predict models in physician practices to help them handle the flow of information from medical history, vital signs, genetic background, and lab testing into diagnosis and treatment.

8) funding CMS and NIH projects demonstrating the value of innovation in health care.

It is clear that our system needs better interoperability, improved data sharing, more balanced privacy controls, the development of rapid learning feedback models, and deployment of predictive modeling for physician practices. Once these changes are put into place, the United States will be in a much stronger position to gain the benefits of personalized medicine for patients, care-givers, and the health system as a whole. The result will be a healthier population getting medical care at a more reasonable cost.

If the United States does not move forward, it risks missing an opportunity to be a technical leader in health care. Other countries, such as the United Kingdom, France, Germany, Singapore, and China, are moving forward with personalized medicine and health information technology. Their governments are investing financial resources to facilitate the advancement of genomic medicine. The U.S. needs a policy framework that facilitates the implementation of genomics into health care. It should consider beacon programs that seed the market for further innovation. Not only will this improve health care, it will create high-value medical technology jobs for the American economy.

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