

Personalized Medicine and Healthcare IT: Supporting the Revolution in Human Health

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Executive Summary

Personalized medicine is an emerging model of medical care that leverages continuing advances in genomics, genetic testing and bioinformatics. This new model of care uses a patient's baseline clinical, environmental, genetic and/or metabolic profile to create individually tailored diagnostic and treatment plans. Personalized medicine also uses the predictive power gained from a patient's baseline genetic profile to assess future risk of disease and suggest preventive treatment plans. Personalized medicine will dramatically change the care process, so the healthcare IT systems of tomorrow must support this new model of care.

McKesson is developing capabilities for the next generation electronic health record (EHR) to support personalized medicine in the domains of (1) enhanced disease diagnosis, (2) disease risk classification, (3) pharmacogenomics, and (4) longitudinal preventive care. To do so, McKesson is working to incorporate genetic data standards as they emerge, create knowledge visualization and representation designs that support the use of genomic medicine, and develop designs for genomic and predictive decision support and knowledge management.

Dawning of a New Era

The healthcare industry is poised for a fundamental shift in the way medicine is practiced and patient care is delivered. Today, a physician diagnoses a patient based on a number of symptoms or markers (for example, lab values) indicating a disease. Diagnosis is a complex and challenging process due to the non-specific nature of many of those indicators. For example, heart failure, which presents as shortness of breath and fluid overload, may be symptomatic of a wide range of underlying conditions. Many diseases that present in a similar manner may in fact represent a number of different molecular abnormalities that would respond differently to different therapies.

Currently, medicine is practiced according to an evidence-based approach in which a physician chooses a therapy based on statistics derived from large population studies. But this approach, which assumes a “one-sizes-fits-all” similarity among people, does not necessarily lead to the best therapy for each individual patient.

Through phenomenal breakthroughs in recent years such as the completion of the Human Genome Project and advances in rapid DNA sequencing, genetic microarray technology (which enables the automated analysis of tens of thousands of genetic variants on a single gene chip) and bioinformatics, science has advanced to the point at which an individual’s genes, gene expression, protein expression, metabolism, and other molecular factors can be understood and correlated with disease susceptibility and drug metabolism. Scientists are also beginning to understand how those molecular factors are altered in different disease states. Beginning in the next 2-3 years, the molecular basis of an individual, coupled with advanced clinical decision tools, will create a revolutionary new model of personalized care.

Health and Human Services (HHS) Secretary Michael Leavitt has described personalized care as follows:

"Personalized health care will combine the basic scientific breakthroughs of the human genome with computer-age ability to exchange and manage data. Increasingly it will give us the ability to deliver the right treatment to the right patient at the right time – every time."¹

In the September 2007 report “Personalized Health Care: Opportunities, Pathways, Resources,” Secretary Leavitt described healthcare that could:

¹ United States Department of Health & Human Services news release “HHS Secretary Leavitt Announces Steps Toward A Future of ‘Personalized Health Care,’” March 27, 2007, <http://www.hhs.gov/news/press/2007pres/20070323a.html>, accessed 3/10/08.

- Predict our individual susceptibility to disease, based on genetic and other factors;
- Provide more useful and person-specific tools for preventing disease, based on that knowledge of individual susceptibility;
- Detect the onset of disease at the earliest moments, based on newly discovered chemical markers from changes at the molecular level;
- Preempt the progression of disease, as a result of early detection; and
- Target medicines and dosages more precisely and safely to each patient, on the basis of genetic and other personal factors in individual response to drugs.²

Each of these capabilities has profound implications for the healthcare information technology systems of today and tomorrow. If we are to realize the enormous potential offered by the exciting scientific breakthroughs taking place in personalized medicine, we must significantly expand the capabilities in our clinical information technology systems to support a fundamentally new approach to patient care and health management.

Examples of Personalized Medicine and Their Implications for Healthcare IT

To best understand the power of personalized medicine, consider the following four examples that illustrate how it is having an impact on patient care today. Each example concludes with the implications for healthcare information technology as an enabler of personalized care.

Disease Diagnosis

Personalized medicine promises entirely new ways to diagnose illness. For example, in a disease called polycythemia vera (PCV), red blood cells reproduce uncontrollably and cause the blood to become too thick, which in turn can cause strokes, clots, poor circulation and other problems. Currently, the standard way to diagnose PCV is by a process of elimination of other causes of a high level of red blood cells. This elimination is done through a number of tests, including one for red blood cell mass that is very difficult to perform. However, the acquired genetic mutation that causes

² "Personalized Health Care: Opportunities, Pathways, Resources," U.S. Department of Health & Human Resources, September, 2007, <http://www.hhs.gov/myhealthcare/news/personalized-healthcare-9-2007.html>, accessed 3/10/08.

PCV has been identified as JAK2. In academic centers, the diagnosis of PCV is made simply by looking for the JAK2 genetic mutation in someone who has an elevated blood count. If the genetic mutation exists, the person definitely has PCV. Through these kinds of molecular tests, diseases will be diagnosed earlier, expensive and/or insensitive tests will become obsolete, and appropriate therapeutic interventions will be started sooner. Earlier intervention will improve patient outcomes and reduce the cost of late stage interventions, both in terms of human suffering and monetary expense.

Implications for healthcare IT: Electronic medical records will need to incorporate standardized information from genetic testing into patient profiles and feed relevant, machine-interpretable results into knowledge management applications that support physicians in making differential diagnoses.

Disease Classification and Risk Stratification

Many illnesses may present in the same manner, but we are now learning that there may in fact be multiple different biochemical variations causing the same presentation. For example, science may eventually discover that there are actually 20 different kinds of congestive heart failure among people presenting the same symptoms, not the single kind that most physicians think of today. Using gene expression arrays (gene chips) and other molecular techniques, it is now possible to better classify diseases and use that knowledge for more precise prognostic and treatment purposes.

As another example, a woman who is diagnosed with early stage breast cancer faces a difficult decision. Should she undergo chemotherapy – a toxic, difficult, and dangerous regimen – to prevent future recurrence, or should she do nothing and hope the tumor never returns? The decision is critical. A woman may become seriously ill or even die from the chemotherapy regimen, but if the tumor recurs there may be no chance for a cure. There is now a test called Oncotype DX that analyzes the gene expression of 22 genes in the tumor. Based on a complex algorithm, the clinician and patient are presented with a risk model that classifies the woman as low, medium, or high risk for recurrence and allows them to make a better informed decision about treatment. Thus a low risk patient is spared from expensive, toxic chemotherapy that is less likely to be needed, while a high risk patient receives chemotherapy that will help prevent recurrence. Before these genetic tests, there were not such informed methods for patients or physicians to determine the best course of action.

Implications for healthcare IT: As molecular-based knowledge of different diseases progresses, it will need to be translated into risk models that can be integrated with electronic patient profiles and provider order entry applications to drive informed decision making on the part of patients and their care providers.

Pharmacogenomics

People metabolize and respond to different drugs in different ways. However, physicians usually prescribe medications to all individuals in the same way, making only basic adjustments for criteria such as body weight or age. Then they follow biomarkers (for example, a PSA lab result in a patient with prostate cancer) or the patient's symptoms to determine if a given therapy is working. As scientists are beginning to understand how an individual's biochemical makeup impacts drug response and metabolism, this knowledge can be incorporated into clinician decision making so that medication therapies can be chosen and dosed more appropriately. Using this type of individual-specific information to optimize medication therapy is called pharmacogenomics.

As an example, warfarin is a medication used to "thin" or anticoagulate a person's blood when a person has had a blood clot, has an artificial valve, or has certain irregular heart rhythms. It is a commonly used drug but it is difficult to use safely and effectively because it is nearly impossible to know what dose an individual will require to achieve adequate anticoagulation. It is not uncommon for a patient to sit in a hospital on IV anticoagulation therapy waiting day by day for their blood to become "thin" enough on the oral warfarin to go home.

Fortunately, the metabolism of warfarin is becoming better understood. Now, by incorporating genetic knowledge into a dosing algorithm, it is possible to understand 50-60% of the variability associated with warfarin dosing. By using this type of knowledge, clinicians can now better predict the time required to achieve appropriate anticoagulation and minimize the risk of side effects such as excess anticoagulation and bleeding. The test required for this dosing algorithm can now be performed in under a day, but so far it is only being done in specialized centers and labs.

Implications for healthcare IT: Electronic treatment planning and clinical order entry systems in all care environments will need to incorporate the rapidly growing and highly complex knowledge base in pharmacogenomics to provide far more sophisticated levels of decision support than are available today.

Preventive Care

A person's risk of developing many diseases is directly related to that individual's genetic makeup. A growing number of adult onset diseases can often be linked to genetic defects that an individual is born with, including such common diseases as colon cancer, ovarian cancer, breast cancer and macular degeneration.

Today, physicians make educated guesses about a person's genetic makeup based on family history. Then they typically incorporate this information into the general preventive health recommendations for their patients. But through genetic testing, it is now possible to incorporate a whole new level of knowledge and precision into disease prevention from birth onward.

For example, hemochromatosis is a disease caused by defects in a person's ability to metabolize iron. It typically presents with non-specific symptoms, such as low blood sugar levels, chronic fatigue, and arthritis, which are often treated without ever identifying the underlying cause. Eventually, the patient frequently develops diabetes and later on, severe heart or liver failure will occur. By that time it is too late to treat the underlying disease, and the patient will die. However, when hemochromatosis is diagnosed early, its progression can be halted or prevented by the simple treatment of phlebotomy, or the regular removal of blood as is done with blood donation.

Approximately 9% of the population has one copy of the defective gene associated with hemochromatosis, and if you have two copies (one each from both of your parents), you will most likely develop the disease. By testing for the disease at an early age, a person can live a normal, healthy life with a simple intervention. This is an example of how genetic knowledge can help prevent serious health complications and the diminished quality of life and treatment costs associated with them.

Implications for healthcare IT: The individualized level of lifetime health planning implied in the example above does not even exist in today's electronic medical records. Such systems will not only need to incorporate an enormous amount of information from genetic testing into the patient profile but will also require comprehensive knowledge synthesis to help providers interpret these genetic defects, determine appropriate lifetime care plans for the patient, and support regular reminders and interventions through intelligent rules and alerts.

Personalized Medicine: Industry Issues

There are a number of key industry issues that must be addressed to drive widespread adoption of personalized medicine by healthcare providers in the community as well as participation by consumers.

- **Privacy Concerns.** There is great concern among consumers that if genetic data is not protected, payers or employers will be able to stratify individuals and put those with genetic defects at a disadvantage. Congress has finally passed legislation to address this concern. On May 1, 2008, the House passed the Genetic Information Nondiscrimination Act (GINA) by a vote of 414 to 1. The Senate had previously passed GINA on April 24th, 2008 by a vote of 95 to 0. The act will protect individuals against discrimination based on their genetic information when it comes to health insurance and employment. The long-awaited measure, which had been debated in Congress for 13 years, will pave the way for people to take full advantage of the promise of personalized medicine without fear of discrimination.
- **Inadequate Reimbursement Models.** Many of the new genetic tests are not yet covered by health insurance plans as those organizations are awaiting more definitive evidence of the economic value of incorporating genetic testing. In addition, care providers are not reimbursed for providing the additional education that patients need to understand genetic test results. Finally, because our healthcare financial model is dominated by volume-based reimbursement and because financial incentives to prevent disease do not exist for most of the stakeholders in healthcare, the concepts in lifetime care and health management are not a priority for providers. However, recent pilots by the Centers for Medicare and Medicaid Services (CMS) indicate that fundamental changes in this model are coming which will require providers (hospitals, primary care providers and specialists) to coordinate care for patients across settings while sharing in common reimbursement models.
- **Lack of Common Data Standards.** While there are some standards to represent genetic and molecular data for the scientific community such as the Human Gene Nomenclature, there are very limited standards for the transmission and representation of molecular data by healthcare IT systems. Common data standards will be critical for computer-readable sharing of genetic information.
- **Need for Public and Provider Education.** There are legitimate public concerns regarding genetic and molecular testing as well as inadequate

knowledge of these topics among consumers and care providers. Industry organizations such as the Personalized Medicine Coalition, government agencies such as HHS, the Food and Drug Administration (FDA) and CMS, professional organizations and patient advocacy groups must escalate the priority given to these issues and create tools for all stakeholders to understand the implications of personalized medicine.

- **Challenges for Clinical Practice.** Related to the need for provider education described above, clinicians will face specific challenges as they begin to incorporate personalized medicine into everyday practice. The explosion of knowledge in a field already overflowing with new evidence-based literature will make it extremely hard for clinicians to keep up. They will need to continually update knowledge in four main areas:
 1. Which tests are available and the diagnostic indications associated with those tests
 2. How to interpret test results
 3. How to incorporate test result interpretations into treatment planning decisions (i.e., what should a provider do with a risk score?)
 4. How to communicate with patients and their families about test results and risk scores

All of these challenges will be exacerbated by a relative shortage of geneticists and genetic counselors compared with the demand for information that the spread of personalized medicine will generate. Since nurses have traditionally been responsible for providing patient education in many care settings, this trend will likely have a profound impact on nursing practice.

- **Consumerism.** There are a growing number of new companies targeted to consumers such as 23andMe and Navigenics that provide broad-based genetic testing to consumers primarily for “infotainment” purposes. In addition, other molecular diagnostic companies such as Myriad Genetics are directly advertising to consumers the ability to test for specific genetic markers, such as BRCA for breast cancer. Some consumers may become more informed than their providers, but consumers will still look to their providers for assistance in the interpretation of genetic test results.

McKesson's Strategy for Personalized Medicine

Personalized medicine can more accurately diagnose and classify disease, tailor and optimize drug therapies to achieve the best outcomes and minimize adverse events, assess an individual's risk for disease, and act as the basis for longitudinal and lifetime care of the patient. Therefore, McKesson anticipates that personalized medicine will have a profound impact on healthcare, including delivery models, clinician workflow and individual health planning.

McKesson is developing strategies for personalized medicine in its Predictive Care Solutions group, a new group formed in June 2007 and focused on building innovative solutions to address new and emerging challenges in the healthcare. The Predictive Care Solutions group is a part of the Life Sciences area within the Health Systems organization of the McKesson Provider Technologies division.

Our initial strategies for personalized medicine will focus on enhancements to the Horizon Clinicals® product portfolio that will leverage these concepts and the new requirements that genomic and other individual biochemical data will create. The primary focus will be on these areas:

- **Data Representation and Standards.** Genomic and molecular information presents challenges in data representation and storage. As standard nomenclatures become established in the industry, Horizon Clinicals solutions will be enhanced to support these new terminology sets.
- **Knowledge Visualization.** The visualization of genomic information also poses challenges in presenting complex data in a clinically useful manner. We foresee enhancements to Horizon Health Summary™ that will allow clinicians to review genetic test results in a way that will optimize an individual's care – both predictively and holistically.
- **Genomic and Predictive Decision Support and Knowledge Management.** Advances in disease management and health maintenance related to genomics are reported on in the medical literature and general media on almost a daily basis. With genomic information, diseases can be diagnosed and classified more accurately. Risk models can be integrated into McKesson's decision support constructs to give predictive clinical guidance to the clinician and characterize a patient's risk for disease. Pharmacogenomic calculators and alerts can help optimize and tailor a patient's therapies. As new genotype-phenotype associations are discovered, this knowledge can be incorporated for presentation to the

clinician. In February, 2008, McKesson announced a strategic agreement with Proventys, Inc., a personalized medicine knowledge service provider that utilizes cutting-edge predictive modeling to enable these types of personalized clinical decisions at the point of care. McKesson plans to incorporate Proventys' risk prediction capabilities into our core clinical decision support solutions. The knowledge management infrastructure within McKesson's Horizon Architecture™ technology strategy will facilitate this assimilation, and of new predictive information as it becomes available.

Additionally, the concepts of personalized medicine can add value to many other solutions in the McKesson portfolio. We are evaluating how best to integrate these concepts into other McKesson products.

Conclusion

Groundbreaking scientific discoveries in areas such as genomics are rapidly propelling the practice of medicine into a revolutionary new era of personalization. This new age of individualized care holds enormous potential to improve human health through a far more proactive approach than typically occurs today, focusing on disease prevention and early intervention instead of on simply reacting to illness. As a leader in healthcare innovation, McKesson will be at the forefront of incorporating knowledge breakthroughs in personalized medicine into the everyday practice of clinicians through our advanced healthcare IT solutions supporting the care process.

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