Challenges and Opportunities

PERSONALIZED AND PRECISION MEDICINE

Precision medicine tailored to an individual's genetic makeup promises to detect the onset of disease at its earliest stages, preempt the progression of disease, direct the selection of optimal therapy and reduce trial-and-error drug therapies. Such approaches may increase patient adherence to treatment and the efficiency of the health care system.

The number of examples of personalized treatments and diagnostics has been growing steadily – 13 in 2006 to 72 in 2011 to 113 in 2014.[1] Continued development and adoption of personalized medicine can be attributed to several factors: the declining cost of genetic sequencing, increased commitment in the pharmaceutical industry, and an evolving public policy landscape. Yet, much remains to be done to keep up with scientific and technological advancements. For example, while biomarkers are increasingly being used to better understand patient response (see adjacent box), biomarker data cannot be used to support approval until the regulators' capacity to evaluate it catches up to the science.[2]

- 30% of all treatments in late clinical development rely on biomarker data
- 50% of all treatments in early clinical development rely on biomarker data
- 60% of all treatments in preclinical development rely on biomarker data

An economic analysis of the Onco*type* Dx® test looked at the real costs of treating women with breast cancer in a health plan with two million members. If half of the 773 eligible patients received the test, then the savings in terms of adjuvant chemotherapy, supportive care, and management of adverse events would be about $1,930 per patient tested (based on a 34 percent reduction in chemotherapy use).[3] Another study found a $604 million annual savings in annual health care cost savings would be realized if patients with metastatic colorectal cancer receive a genetic test for the KRAS gene prior to treatment.[4]

There is considerable room for improvement in overall efficacy rates for many products. For example, a 2001 study showed that the response rates of patients to medications from different therapeutic classes ranged from ~80% (analgesics) to ~25% (oncology).[5] Further, an estimated 2.2 million adverse drug reactions occur annually in the US, including more than 100,000 deaths.[6] By further elucidating why some patients respond or do not respond to a drug, and why some experience adverse reactions while others do not, we likely could improve drug safety and efficacy by specifying the population(s) in which they should be used.

Can we:

➢ deliver market changing new treatments for cancer and other diseases at an affordable price point for patients, employers, states and our nation?

➢ match treatment options to individual patients in cancer treatment?

➢ create diagnostics that will identify those who will NOT respond to expensive but effective therapeutics?

➢ use genomic markers to help identify individuals at risk for specific diseases so that they can be enrolled in early monitoring programs?

➢ incorporate genomic information into standard of care?

➢ identify genetic risk factors and assess who is at genetic risk for adverse drug reactions?

➢ create online tools to better define the risk profile of patients?

➢ develop genetic tests that give the best results and provide value to provider, patients, and payers?

➢ educate consumers on which genetic tests have been validated through evidence-based means, and are associated with reducing health care costs and improving health outcomes?

➢ educate caregivers and providers in this new field?

1. Personalized Medicine Coalition report: The Case for Personalized Medicine, available at http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_case_for_personalized_medicine.pdf
2. Tufts Center for the Study of Drug Development. Personalized Medicine Is Playing a Growing Role in Development Pipelines. Impact Report, 12 (November/December 2010): 6.
3. Genomic Health. Economic validity web site. (Available at: http://www.genomichealth.com/en-US/sitecore/content/Home/Breast/ManagedCareOrgs/EconomicValidity.aspx)
4. Shankaran V. Conference presentation at the Gastrointestinal Cancers Symposium. January 2009. (Available at: http://www.medscape.com/viewarticle/586946).
5. Lazarou J, Pomeranz B, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *JAMA*1998;279:1200–1205
6. Department of Health and Human Services Secretary's Advisory Committee on Genetics, Health, and Society. (2008). Realizing the Potential of Pharmacogenomics: Opportunities and Challenges. Washington, DC. p. 11

Chronic diseases such as diabetes, stroke, heart disease, cancer, and arthritis are the greatest threat to our nation's health. Management and treatment of these long-term medical conditions comes at a steep price. The Centers for Disease Control and Prevention (CDC) estimates the US spends 86% of health care dollars on the treatment of preventable chronic diseases.[1] The CDC also estimates that nationally, chronic diseases account for 81% of hospital admissions, 76% of all physician visits, and 91% of all filled prescriptions.

Medication nonadherence is a major cost driver in patients with chronic diseases, particularly hypercholesterolemia and diabetes. A 2012 IMS Institute for Healthcare Informatics study estimates $105 billion is attributable to medication nonadherence. The human cost and life impacts of chronic diseases also cannot be overlooked. Some of these are underscored by the following "unhealthy truths" reported by the CDC:

> **Diabetes: A Case Study of Chronic Disease Management**
> Approximately 29.1M of the United States (US) population (or 9.3%) have Diabetes Mellitus. Unfortunately, over a quarter of these individuals (27.8%) are undiagnosed. Treatment of this disease (due to high rate of complications) costs the health care system an estimated $245B, the majority directly attributed to medical related costs. By 2020, >50% of Americans are projected to either have diabetes or to be pre-diabetic. Identifying and treating this population raises a number of challenges for the health care system.

- As of 2012, nearly half of all adults (117 million people) suffer from at least one chronic condition, and 25% of adults have two or more chronic health problems. Additionally, seven of the top 10 causes of death in 2010 were chronic diseases. Two of these —heart disease and cancer—together accounted for nearly 48% of all deaths.[2]

- More than one-third of adults (~78 million people) and nearly one of five youths are obese.

- Diabetes is the leading cause of kidney failure, lower limb amputations other than those caused by injury.

- Arthritis afflicts 53 million adults and is now the most common cause of disability.

The Connecticut Department of Public Health reports similarly alarming statistics. For example, more than two million Connecticut residents - or 57% of the total population - suffer from one or more chronic diseases. Almost 91% of Connecticut adults report at least one of the following unhealthy behaviors: smoking, being overweight or obese, eating less than five servings of fruits and vegetables per day, and not meeting physical activity recommendations.

Individuals with chronic conditions are often high utilizers of the medical system, and if this utilization is inefficient, costs expand and quality suffers. Health care costs for people with chronic conditions average $6,032 annually - five times higher than for those without such a condition. Motivating consumers to change, reduce, or eliminate unhealthy behaviors remains a main obstacle to addressing preventable health conditions.

Can we:

- ➢ develop approaches to manage the total cost of care?
- ➢ develop predictive models that identify at-risk people without undue loss of privacy?
- ➢ reduce the cost of clinical lab monitoring in chronic diseases while improving outcomes?
- ➢ modify at-risk behaviors in a patient centric manner?
- ➢ develop scalable psychological approaches to modify at-risk behaviors?
- ➢ develop cost-effective screening tests to identify early-on patients with diabetes or pre-diabetes?
- ➢ develop more cost-effective treatments than currently exist to prevent and treat diabetes?
- ➢ develop cost-effective interventions to reduce the risk of diabetes and prevent obesity?
- ➢ develop cost-effective interventions that can reduce the morbidity of diabetes and obesity?
- ➢ optimize management for congestive heart failure and ischemic heart disease?
- ➢ increase overall treatment plan adherence and modify the behavior of non-adherent patients?

---

[1] Centers for Disease Control and Prevention (CDC), Chronic Disease Prevention and Health Promotion (date unavailable), available at http://www.cdc.gov/chronicdisease/.
[2] Ibid.

Behavioral health conditions affect one in five Americans and drive healthcare costs of $57 billion per year, according to SAMHSA -- the Substance Abuse and Mental Services Administration. Patients with behavioral health issues incur higher healthcare costs, but generally do not receive the care they require to resolve or control these conditions.

Mental and substance use disorders exact more than $700 billion annually in costs related to crime, lost work productivity and health - more than the cost of diabetes and cancer combined.[1] SAMHSA estimates that in 2012, 9.6 million adults in the US had a serious mental illness, 23.1 million Americans aged 12 and older needed treatment for substance use, and 2.2 million children (aged 12 to 17) had a major depressive episode. These disorders are among the top conditions that cause disability and carry a high burden of disease in the US, resulting in significant costs to families, employers, and publicly funded health systems. SAMSHA estimates that by 2020, mental and substance use disorders will surpass all physical diseases as a major cause of disability worldwide. In Connecticut alone, substance use disorders are the 6th leading cause of death overall having claimed nearly 900 lives in 2013 -- 7 times more than car accidents or homicides and 1.5 times more than diabetes.

> **Substance Use Disorders: A Case Study for Behavioral Health Management**
> The prevalence of substance abuse (alcohol or drugs) amongst the US population is growing. Indeed, 8.2% of the population aged 12 and older has a substance use disorder. The management of this problem is responsible for a significant portion of health care costs; i.e., the direct and indirect costs associated with substance abuse in the US are ~$36B annually. This amount includes costs related to medical interventions including Emergency Department visits, inpatient/outpatient treatment, and substance abuse prevention and treatment research.

Prevention of substance abuse disorders through identification of the at-risk population would be very helpful, but effective early detection strategies are not available. Broadly effective treatment strategies are also not available: those who eventually achieve sustained remission have on average 5 relapses prior to remission. It is not clear which drugs will work with which patients; and it is difficult to identify those patients who need the most intensive therapy (inpatient). Thus in the rehabilitation phase, the availability of approaches to stratify individuals for specific treatments is also unclear. This disease is increasing in prevalence, and the cost of caring for this disease is escalating rapidly.

Adults with serious mental illness (SMI) die, on average, 25 years earlier than the general population, and the rates of illness and death in this population have been on the rise.[2] People with SMI also have disproportionately high rates of mortality from the preventable conditions, including cardiovascular and pulmonary disease, that are among the leading causes of death in the general population. Further, co-occurring substance use disorders are prevalent among individuals with SMI. The mental health and substance abuse systems are often entirely separate, and both are segregated from the physical health system. This fragmentation of the health care system can lead to inappropriate care, disjointed care, gaps in care, and redundant care, and can result in increased health care costs. Management of behavioral health conditions requires new approaches as we strive to improve the healthcare system.

Can we:
- develop cost effective screening tools to identify those most at risk, while maintaining patient confidentiality?
- match patients to interventions (e.g., drugs, behavioral modification, psychotherapy) for maximum effectiveness? Can we devise earlier intervention strategies?
- identify the patients most likely to relapse and better engage them in the most intensive treatment?
- identify those who are unlikely to respond?
- develop scalable online approaches can be developed to replace for face-to-face interventions?
- improve interventions and not price them out-of-reach of most patients?
- determine the extent to which there a genetic predisposition to substance abuse? Can genetics help distinguish different patterns of response to various treatments?
- develop pain medications that have negligible abuse potential?

1. U.S. Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress. A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
2. Parks J et al., *Mortality and Morbidity in People with Serious Mental Illness*, National Association of State Mental Health Program Directors, October 2006, available at. http://www.nasmhpd.org/docs/publications/MDCdocs/Mortality%20and%20Morbidity%20Final%20Report%208.18.08.pdf

Healthcare is a dynamic industry and the pace of change relative to regulation, reimbursement and technology is rapid. The ability to exchange patient information among disparate systems is an important contributor to the "triple aim" of improving health outcomes, improving health care quality and lowering health care costs.

According to the Department of Health and Human Services, 20 percent of preventable medical errors are caused by the lack of immediate access to health information. One of every seven primary care visits is affected by missing medical information. Other studies have shown that medical errors result in as many as three million preventable adverse events each year, driving as much as $17 billion in excess annual medical costs and as many as 98,000 deaths per year.[1,2] Several of the most common causes of medical errors can be substantially addressed by improved medical device interoperability, including drug errors (accounting for 20 percent of adverse events), diagnostic errors (17 percent) and failure to prevent injury (12 percent). [1,2]

Connectivity and interoperability also have implications in remote areas. Monitoring of individuals with multiple chronic conditions has been shown to reduce hospitalizations, hospital readmissions and ER visits for more than 80 percent of respondents and boosted disease self-management for nearly all monitored patients. Other targets of a remote monitoring strategy included frequent utilizers of hospitals and emergency rooms (ERs) (62 percent) and the recently discharged (52 percent). [3]

In a report that assessed the value of electronic healthcare information exchange and interoperability (HIEI) between providers, independent laboratories, radiology centers, pharmacies, payers, and public health departments, it has been estimated that fully standardized HIEI could result in a net savings of $77.8 billion annually[4]. Though numerous steps have been taken to improve healthcare connectivity and interoperability, there is still a significant gap in implementing a streamlined population health management approach, according to a Patient-Centered Primary Care Collaborative report.[5]

Can we:
  ➢ achieve this truly connected healthcare system of the future?
  ➢ identify the key elements necessary for advancing interoperability and improving the quality, efficiency, and safety of health care delivery industry-wide?
  ➢ use IT to drive consistency in treatment and decision support?
  ➢ create "medical neighborhoods" – linking primary care physicians (PCPs) with specialists?
  ➢ better coordinate hospital care with handoffs to PCPs?
  ➢ arrange for HIPAA compliant transfer of images and information among caregivers?
  ➢ better track admissions, discharge and transfers and link this information to PCPs
  ➢ achieve multipayer solutions – unified forms, procedures, and standards?
  ➢ deliver care remotely, with less patient travel and more efficient use of caregivers' time?
  ➢ maximize office efficiency by matching patient demand with physician schedules?
  ➢ better monitor health status, adherence, movement, and vital signs via wearable devices with automatic synchronization?
  ➢ leverage existing technologies to provide online psychiatric care/psychological counseling?
  ➢ store personal genomic information to be mined over time for actionable markers as new discoveries are made?
  ➢ provide alerts for markers for adverse events to drug response that automatically inform patients and physicians?

1. Jha AK, Chan DC, Ridgway AB, Franz C, Bates DW. Improving safety and eliminating redundant tests: cutting costs in U.S. hospitals. Health Aff (Millwood). 2009;28(5):1475-1484.
2. Kohn LT, Corrigan JM, Donaldson MS, editors. To err is human: building a safer health system [Internet]. Washington: National Academy Press; 2000 [cited 2012 Oct 25]. Available from: http://www.nap.edu/catalog.php?record_id=9728.
3. Healthcare Intelligence Network's inaugural survey on Remote Patient Monitoring (March 2014), available at inaugural survey on Remote Patient Monitoring
4. The value of health care information exchange and interoperability, available at. http://www.ncbi.nlm.nih.gov/pubmed/15659453
5. Managing Populations, Maximizing Technology: Population Health Management in the Medical Neighborhood, available at: http://www.pcpcc.org/download/4378/PCPCC%20Population%20Health%20FINAL%20e-Version.pdf?redirect=node/200274&utm_source=HIT+Consultant&utm_medium=content&utm_campaign=report