What’s in Store for Personalized Medicine?

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Major Challenges in Healthcare

- Cost
- Demographics
- Access
- Variation in Clinical Practice
Major Challenges in Healthcare

- Inefficient Use of Information
- Fragmented Care Versus Integrated Care
- Duplication, Defensive Medicine & Waste
- Protracted Adoption of Innovation
New Value Propositions in Healthcare

- social and economic value of reducing disease burden will rise
  - earlier disease detection and mitigation
  - rational Rx and guaranteed outcomes
  - integrated care management of complex chronic diseases
  - extension of working life

- progressive shift from ‘reactive’ medicine to ‘proactive’ care and ‘integrated’ delivery
  - prospering in an era of increasing constraints
  - managing the limit(s) of society’s willingness and ability to pay for innovation
Personalized Medicine: Progressive Evolution Based on Increasingly Comprehensive Profiling of Disease Risk and Health Status

- Targeted Care
  - rational Rx based on profiling of underlying molecular pathology
  - MDx and disease subtyping

- Individualized Care
  - rational Rx based on comprehensive molecular profiling of individuals
    - disease subtypes and optimum Rx
    - Rx AE risk
    - disease predisposition risk and mitigation

- Personalized Care
  - integrated framework of care and longitudinal data on individual health status
  - real time remote health status monitoring
  - transition to disease prediction and preemption
From Pharmaceuticals to Pharmasuitables

Disease Subtyping:

Individual Variation and AE risk

Right Rx for Right Disease

Right Rx for Right Patient
● opening era in linking disease molecular pathology to rational Rx

● increasing payor, regulatory and public pressures for reliable ID of Rx-responsive patients

● demand for Dx-Rx combinations will intensify

● Dx-Rx combination will become an obligate element of NDA/BLA submission and product labeling

● development of Dx-Rx combinations as intrinsic components of R&D programs for investigational Rx
Pharmacogenetic Predisposition to Adverse Drug Reactions

- 1.5 to 3 million annual hospitalizations (US)
- 80 to 140 thousand annual deaths (US)
- est. cost of $30-50 billion
Molecular Diagnostics and Pharmacogenetic Profiling to Identify Individuals at Risk for Rx Adverse Events

- broader, more complex profiling platforms than MDx assays for ID of drug targets
- ID of slow metabolizer genotypes
- unknown effects of genetic and environmental confounders in AD(M)E beyond genetic variation in drug-metabolism (I-III) repertoire
- complex patterns of ethnic variation and haplotype associations impose continuum of metabolic phenotypes
Mapping the Human Pan-Genome: Identification of Ethnic Differences and Implications for Rx Efficacy and Safety

From: Ruiqiang Li et al. (January 2010) Nature Biotech. Vol. 28, p. 59
## Genetic Polymorphisms Influencing Responses to Antidepressants

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<th>Target</th>
<th>Function</th>
<th># of Papers on Association</th>
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Modified from S. Oestergaard et. al. (2009) Pers. Med. 6 (5) 501
The Human Microbiome: A Barely Understood Influence in Health

- complex meta-system
  - host, microbes, viruses, other organisms, metabolites, xenobiotics
  - is there a core microbiome?
  - how do perturbations affect disease and vice-versa?
  - does the microbiome influence xenobiotic metabolism and the metabolite spectrum?
The Hunt for Gene Loci Associated with Complex Human Diseases
Disease Predisposition Risk Profiling for Common, Multigenic Late-Onset Disorders

- slower evolution than many predict
- Genome-Wide Association Studies (GWAS)
  - high cost
  - multiple low penetrance alleles
- substantial ambiguities regarding probabilistic risk of overt disease
  - epistasis
  - epigenetics
  - environmental confounders
  - source of poor replication of GWAS studies?
The premature quest to provide consumer genomic testing (CGx) for future risk of major diseases

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- Genome-Wide Association Studies (GWAS)
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  - source of poor replication of GWAS studies?
The Trajectories for Molecular Medicine

- Technology convergence
  - Life sciences
  - Engineering
  - Computing

Exponential growth of research data

Data → Time
The Trajectories for Molecular Medicine

Addressing the Void in Translation and Design of New Delivery Models
The Trajectories for Molecular Medicine

- Translational medicine and clinical validation
- Regulatory standards
- Clinical utility and reimbursement
- Routine clinical adoption

Data

Time
Deriving Value from “-Omics”

- useful only when correlated with additional parameters
  - clinical outcomes
  - clinical utility
  - actionable information
  - demonstrable economic value
Disease-Associated Biomarkers and Validation of New Molecular Diagnostic for Personalized Medicine

- literature dominated by anecdotal studies
  - academic laboratories
  - small patient cohorts
  - poor replication and confirmatory studies
- lack of standardization
- very few biomarkers subjected to rigorous validation
  - case-control studies with sufficient statistical power
  - inadequate stringency in clinical phenotyping
- widespread lack of understanding of regulatory requirements
  - complexities imposed by multiplex tests
  - new regulatory oversight (IVDMIAs)
Increased Legislative Interest in Standards, Oversights and Regulation of Molecular Diagnostic Testing

- (2008) In Vitro Diagnostic Multivariate Index Assays (IVDMIAs)

- (2009) Quality, Regulation and Clinical Utility of Laboratory-Developed Tests


- (2009) Secretary’s Advisory Committee on Genetics, Health and Society (SACGHS)

- (2009) SB 42: Post-CLIA Bioinformatics Services
Reimbursement for Diagnostic Tests

The Imperative for Value-Based Pricing versus Current Cost-Based Models

- inadequate US Medicare coding and payment mechanisms
  - outmoded, out-dated, lacking in transparency, inconsistently applied

- inappropriate assignment of existing CPT codes to new tests

- engagement of third party payers who derive economic/clinical value from new Dx
K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy

- higher response in patients with K-RAS versus mutant-K-RAS
- estimated $604 million/year savings (ASCO)

clinical guidelines

- regulatory endorsement in product labeling

payor adoption
“I’m afraid that the vast majority of oncologists will either ignore the guidelines or fail to execute the knowledge contained in the guidelines”

Dr. Lee Newcomer
Head, Oncology Services
United Healthcare
Health Affairs (2008) 27, 41
“The Task Force found that patents are not “powerful” incentives for conducting genetics research disclosing genetic discoveries or investing in development of genetic tests but that they limit access to genetic tests”

Dr. James Evans, Chair, SACGHS
How Much New Technology Can We Afford?
- selection of comparators
- shortcomings in clinical phenotyping/outcomes classification
- retrospective data and meta-analyses versus cost/complexity of prospective studies
Nice Gets Nasty (or Rational?)
Personalized Medicine: Consumer-Centric Healthcare: A Key Driver

- Structural shift in healthcare delivery from encounter-/procedure-driven to incentives for integrated disease management
- Clinical and economic benefits of coordinated care of complex chronic conditions
- Cost-shifting to consumers
- Lifestyle and disease risk mitigation
- New information intermediaries
- Cost-driven transitions from ‘passive patient’ to ‘engaged consumer’
The Costs of Non-Compliance with Rx Regimens

- $177 billion projected cost
- 20 million workdays/year lost (IHPM)
- 40% of nursing home admissions
- Projected 45-75% non-compliance (WHO)
- 50-60% depressed patients (IHPM)
- 50% chronic care Rx (WHO)
On Body: In Body Sensors and Devices

Objective

- remote monitoring of health status

Applications

- multi-feature monitoring and broadband wireless networks
- ubiquitous sensing
- enhanced autonomy for in-home aged
- proactive alerting and intervention to mitigate health incidents
- monitoring of patient compliance
- coupled linkage to remote Rx dispensing for efficient disease management
Connected Care
Technology-enabled Care at Home

State of Technology in Aging Services According to Field Experts and Thought Leaders

By:
Majd Alwan, Ph.D.,
Center for Aging Services Technologies (CAST)
American Association of Homes and Services for the Aging (AAHSA)

and

Jeremy Nobel, M.D., M.P.H.,
Harvard School of Public Health

Report Submitted to: Blue Shield of California Foundation

February 2008
The Infocosm: Emerging Networks of Global Connectivity
Wireless Technologies: Consumer and Clinical Markets Converge
iPhone Apps for Your Health and Fitness
Pharma and Healthcare Social Media (Non-Brand Sponsored) Patient Communities

- CancerCompass: Social network about Empowering cancer patients to make informed decisions.
- the CANARY REPORT: Blog and social network about multiple chemical sensitivity.
- Face to Face Health: Healthcare social utility designed to connect people, humanizing healthcare.
- Community network: Share stories, encouragement, and friendship.
- disaboom: Place to submit, retrieve and share information and well-wishes surrounding a loved one’s health circumstances.
- Autism151: Campaign to pull our community together and offer a brighter, more positive view of autism.
- Advanced Breast Cancer Community: Information and resources for people with disabilities.
- CROHN'S & COLITIS FOUNDATION OF AMERICA: Discussion board featured on diabetes.
- American Diabetes Association: Discussion groups and forums.
- eDrugSearch.com: Search engine for Americans interested in purchasing safe, low-cost prescription drugs from pre-screened international pharmacies.
- GGUARD: Social network where like-minded people can communicate with each other and offer peer support.
- DailyStrength: Safe, anonymous, online community advanced (metastatic) breast cancer patients, caregivers.
- CureTogether: Expert-guided communities where you have access to authoritative information about health topics.
- Cancer Survivors Network: Discussion board featured on cancer survivors.
- healia: Discussion board anonymously share health information.
- Circle Of Sharing: Helps cancer patients and caregivers get personalized information about the disease, and share that information.
- Be Well Data: Share information learn about cancer across the web.
- CareFlash: Place to submit, retrieve and share information and well-wishes surrounding a loved one’s health circumstances.
Molecular Diagnostics as a Key Element in the Evolution of Integrated Healthcare Delivery

- Molecular Profiling (Dx/PDx)
- RiskAlerting and Tracking
- Health Status Monitoring
- Increased Personal Responsibility for Wellness
- Incentives for Risk Mitigation
A New Healthcare Ecosystem Arising From Technology and Market Convergence

- **Dx/Devices**
- **Rx**
- **HLx**

**Integrated Technology Platforms**

**Dx/Devices**

- **Rx**

**HLx**

- **Dx/Devices**

**passive/active data collection**

**analytics and network architecture**

**EMR/PMR**

**performance and outcomes analysis**

**Data Mining and Integration Services**

**Increasingly Targeted Care and Efficient Use of Finite Resources**

**patients**

**consumers**

**services for integrated care**
Technology Acceleration and Convergence in Healthcare Delivery
Technology Convergence and Implications for Healthcare Delivery

**Technologies**
- biotechnology, medicine, engineering, computing, telecommunications and social media

**Clinical Practice**
- molecular medicine and increasingly customized care
- diagnostic, drug and device combinations
- POC testing and remote monitoring
- reduced error and improved compliance
- improved outcomes

**Realigned Incentives**
- integrated care for complex chronic diseases
- earlier disease detection and risk reduction
- wellness versus illness
- remote health status monitoring
Technology Convergence and Implications for Healthcare Delivery

**Consumers**
- increased personal responsibility for health
- new incentives for wellness/compliance
- health status monitoring

**Connectivity**
- integrated care networks for chronic disease
- social media networks and informed consumers
- new supplier networks of specialized turnkey expertise
- value added ‘content’ services for clinical data mining
- clinical decision-support systems