Sustaining Healthcare Innovation in an Era of Constraint

Dr. George Poste
Director, Complex Adaptive Systems Initiative and Del E. Webb Chair in Health Innovation
Arizona State University
george.poste@asu.edu
www.casi.asu.edu
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 Priorities in Biomedical Innovation

- historical “progress at any price” in an environment that largely ignored cost
- shift to increasing value-conscious environment
  - improved outcomes at same or lower cost
  - reducing cost with same quality (common in sectors other than healthcare)
The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities

20% of the Population Generate 80% Cost

- chronic disease progression
- end-of-life care
- chronic disease early stage
- acute disease
- multiple co-morbidities

Health Status

- Healthy/ Low Risk
- At-Risk
- High Risk

Value

Cost
The Key Strategic Elements in the Evolution of Healthcare: Consumer: Patient Centric Care

- Molecular medicine
- Risk management
- Health status monitoring
- Optimized decisions
Molecular Diagnostics: The Key Value Driver in Improving Healthcare and Maximizing Wellness
2029

Julia discovers

a cure for leukemia

Helping women succeed in science can help us all

Determining the chemical composition of stars, uncovering Earth's inner core, interpreting DNA as a double helix, these important discoveries have one thing in common: they are often attributed to a woman. Yet despite their enormous contributions to research, women often feel like they have to push harder and work twice as hard before they can fulfill their potential.

At the Rosalind Franklin Society, we are committed to helping women at every stage of their careers achieve their dreams—because with the right support, today's dream can become tomorrow's discovery. To learn more, visit www.rosalindfranklinsociety.org.
Drug Discovery: Only for the Bold!

- sustained 'high risk' exercise
- biological complexity of chronic diseases and likely multi-focal target requirements
- uncertainty of 'high reward' absent increased predictability and evidence of clinical and economic benefits
- no obvious immediate technological solutions to dramatically shorten the protracted R&D cycle
- risk of shifting the current 'valley of death' to 'valley of dearth'
- strategic imperative to define clear value propositions for new Rx
Biodiversity, Complexity and the Challenge of Genotype-Phenotype Prediction

- non-linear relationship between genotype and phenotype
- formidable challenges for biomedical and mathematical sciences
  - individual diversity in genome organization (SNPs, haplotypes, CNVs)
  - gene-gene interactions
  - epigenetics and imprinting
  - non-coding RNA regulatory networks
  - gene-environment interactions
  - gene-Rx interactions
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  - gene-environment interactions
  - gene-Rx interactions

- has the gap between basic science and therapeutic applications widened?
- how can complexity be stratified to identify tractable approaches for diagnosis, therapy selection and disease risk predisposition?
Let’s Get Serious About Success:
A ’18-S’ Prescription!
Signatures
Mapping the Molecular Signatures of Disease: Building Integrated End-to-End Systems as the Foundation of Personalized Medicine

ID patterns of pathway and network dyregulation in disease
- “biosignatures”

automated platforms for rapid detection of multiplex analytes

PROFILE

SENSE

ACT

rapid analytics and customized data formats/visualization to guide optimum decisions by clinicians, patients and payors
“The stark reality is that although academic conception of new biomarkers is fertile, their gestation is generally interminable”

Dr. Janet Woodcock
FDA

“We’re trying to get a complete picture of where we are in the protein diagnostics business which, by the way, is not in a good place.”

“The FDA has approved one and half new (biomarker) proteins per year, flat, for the last 15 years …that pretty much proves that there’s something wrong in the biomarker pipeline”

Genome Technology April 2010 p. 35
Disease-Associated Biomarkers and Validation of Novel Molecular Diagnostics

- literature dominated by anecdotal studies
  - academic laboratories
  - small patient cohorts
  - lack of standardization
  - poor replication and confirmatory studies
- very few biomarkers subjected to rigorous validation
  - inadequate stringency in clinical phenotyping
  - case-control studies with sufficient statistical power
- widespread lack of understanding of regulatory requirements in academic research community
  - complexities imposed by multiplex tests
  - new regulatory oversight (IVDMIAs)
Success Demands a Systems-Based Approach
Adoption of New Technologies Demands a ‘Systems’ Approach to Life Cycle Analysis (LCA)

- discovery
- translation and validation
  - efficacy, safety
  - technical, clinical, regulatory
- qualification
  - levels of regulatory approval (CLIA, 510(k), PMA)
  - fit-for-purpose, clinical context
- value
  - clinical, patients, payors, society
- business model and ROI
Identification and Validation of Disease-Associated Biomarkers: Obligate Need for a Systems-Based Approaches

Biospecimens and Molecular Pathway Analysis

Biomarker Validation and Multiplex Assays

Instrumentation and Informatics

Clinical Impact and Patient Monitoring
Sourcing

Specimens

Standards and Standardization
Access to Quality Biospecimens for Medical Research: A Critical ‘Choke Point’ in Biomedical Research

Ease of Acquiring the Quality of Biospecimens

- Very easy/Easy: 8%
- Somewhat easy: 13%
- Somewhat difficult: 32%
- Difficult/Very difficult: 48%

Question Their Data Because of the Quality of Biospecimens

- Often/Always: 20%
- Sometimes: 40%
- Never/Rarely: 40%

Limit Research Scope of Work Due to the Shortage of Quality Biospecimens

- Often/Always: 19%
- Sometimes: 36%
- Never/Rarely: 45%

Challenges Associated With Legacy Biobanks and “Samples of Convenience”

- highly variable storage, curation and clinical annotation
- investigator/institutional ‘territorality’ (cf. WU case)
- ambiguous and varied informed consent provisions
  - disease specific versus blanket ‘research use’
- limited longitudinal sampling and correlation with clinical outcomes
- relative absence of normal tissue cohorts
The Importance of Standardized Methods and Data Tracking Systems for Biobanks

- **PHOEBE (EU)**
  - Promoting Harmonization of Epidemiological Biobanks in Europe

- **NCI Office of Biorepositories and Biospecimen Research**
  - National Biospecimen Network, caHUB

- **BBMRI**
  - Biobanking and Biomolecular Resources Research Infrastructure

- **P3G**
  - Public Population Project in Genomics
Stringency

- standards
- relevance
“The study of cancer cells in two dimensions seems quaint if not archaic”


“Medline search reveals that more than 80% of cancer and molecular biologists still use two-dimensional techniques”

D.W. Hutmacher (2010) Nature Materials 9, 90
A Global Map of Human Gene Expression

- 5372 microarray samples
- 206 different laboratories
- 163 different laboratories
- 369 cells, tissues, disease states and cell lines
- solid tissue cell lines cluster together rather than with respective tissues of origin or neoplasms from same lineage
  - 1217 genes upregulated in all cell lines
  - cell cycle, division and mitosis genes
Mixed-Up Cell Lines

- risk of cross-contamination of cell cultures
- 50 years of warnings
  - overgrowth by HeLa cells as ‘early culprit’
- ECV 304
  - “immortalized normal endothelial cells”: over 1000 papers
  - Wilhelm Dirks (1999) revealed as human bladder carcinoma
  - 80 papers in 2008/2009 still referencing as endothelial cells
- contamination of mesenchymal stem cell lines
  - therapeutic implications and regulatory oversight
- obligate requirement for STR profiling
- obligate adoption of validation criterion for publication
Setting Standards for Assay Platforms and Informatics

**Complex Biosignature Profiling**

<table>
<thead>
<tr>
<th>genomics</th>
<th>proteomics</th>
<th>immunosignatures</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Genomics Image]</td>
<td>![Proteomics Image]</td>
<td>![Immunosignatures Image]</td>
</tr>
</tbody>
</table>

**Signature Detection, Deconvolution and Multivariate Analysis**

- automated, high throughput multiplex assays
- novel test formats and devices (POC)
- new algorithms for complex signal/deconvolution
Enterprise Grade Biospecimen Collection, Management and Analytics: Controlling Pre-analytical and Analytical Variability

- standards, standards, standards!
  - consent and diverse regulatory/legal compliance needs
  - collection, transport, processing, analysis
  - storage and curation
  - chain of custody
  - longitudinal tracking of specimen samples, aliquots
  - integration of clinical and non-clinical data sets
  - systems integration LIMS/CTMS, GLP/GCP
  - facile data transfer to regulatory dossier/clinical EMR
  - suitability for mega-and meta-data analyses
Common Problems in MS-Based Proteomics
A.W. Bell et al. (2009) Nature Methods 6, 423

- evaluation of test sample of 20 purified proteins at 5 pmole equimolar abundance
- 7/27 labs with initial correct characterization
- raw data from all sufficient to identify full 20 protein catalog and 22 derivative 1250 Da peptides
- diverse and poorly standardized databases and search engines as principal sources of erroneous reporting
  - variation in curation, annotation, comprehensiveness

• real world challenges: high complexity samples and large preanalytical (collection/storage) sample variation
• education and training to use complex technologies
• publication standards, formats and open-source dbases
“We may be lost, but we’re having a good time”

Yogi Berra
<table>
<thead>
<tr>
<th>Systems Biology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mapping Biological Pathways and the Generation of Complex Network Behaviors</td>
</tr>
</tbody>
</table>
“Our ignorance of the laws of variation is profound”

Charles Darwin
Genome Wide Association Studies of Disease Susceptibility

- 400 alleles reported for 75 diseases in 230 GWAS studies
- scale, power, logistical complexity, cost and replication
- very large sample sizes for common risk alleles and testing 500K SNPs
  - OR 1.3 requires sample size of 1000 and OR 1.1 10,000 samples
- sample pooling
  - Institutional differences in clinical phenotyping
  - impact of imputation for mixed ethnic populations
- limited clinical utility since ORs are very small
- account for only very small fraction of purported heritability of disease susceptibility
- targeted at independent effects of single genes and no insight into interaction effects
  - epistasis, rSNPs in intergenic ‘deserts’, CNVs, epigenetics and imprinting
  - challenge of replication
Mapping Disease-Associated Pathway and Network Perturbations:

**Different Challenges for MDx Versus Rx**

- intrinsic complexity of biological heterogeneity
  - molecular pathway/network perturbations
  - inter-patient variation
  - intra-patient variation with disease progression/Rx

- molecular diagnostic profiling will yield products more rapidly than the quest for novel Rx
  - Rx efficacy: action at multiple target sites?
  - Rx safety: interaction promiscuity for efficacy increases AE risk
Disruption of miRNA Connectivity in Lung Cancer

Adapted from: S. Volinia et al. (2010) Genome Research 20, 589 and T. H. Saey Science News 8/28/10
The Excessive Time And Cost Of Clinical Trials and High Failure Rates

- ‘all comers’ design versus enrichment/adaptive trials with most relevant cohorts (disease subtypes)
- inadequate phenotyping of trial populations (clinical, molecular profiling)
- insufficient knowledge of molecular pathway and redundancy in mediating non-responsiveness
- cost/delay imposed by variation in recruitment enrollment
- limited patient/MD awareness of trial enrollment outside of academic medical centers
- standards for global clinical trials
Sequencing
The Road to the Personal Genome

In the space of a single decade, the cost of mapping all your DNA will fall from the billions of dollars to the thousands. The human genome is becoming a commodity virtually overnight. It’s as if millions of households could have had dishwashers and vacuum cleaners 10 years after James Watt built his steam engine.

DNA, the “code of life,” is the ultimate binary file, a database of 12 billion bits. The data—6 billion matching sets of either the molecules adenine (A) and thymine (T) or guanine (G) and cytosine (C)—affect everything that makes you you: the color of your eyes, whether you’re moody or cheerful, and which diseases you’re most susceptible to.

Today you can purchase your very own personal genome for US $48,000 from Illumina, a San Diego biotech firm (and they’re throwing in an Apple Watch). [See “The $100 Genome,” elsewhere in this issue.] That’s a bit pricey if all you want to do is check out the genetic inheritance of Saturday’s dinner date. But by 2024, your genome will cost a mere $2500, according to TSG Partners, an Atlanta-based life sciences advisory firm, so look: health insurance companies might pick up the tab just to get their hands on the data. The current head of the Personal Genome Project, George Church, thinks it will soon be far cheaper than that—perhaps even less than the dinner itself.

Source: TSG Partners, Atlanta (www.tsgpartner.com) and George Church, Harvard Medical School (www.genomeproject.com).

Will Lost Cost Whole Genome Sequencing Change Everything?
Next-Gen and Third Generation Genome Sequencing
“Not only is there a fundamental issue of whether sequencing is clinically useful, there are huge technical issues that will take a long time to solve to get robust enough for routine clinical use”

David Altshuler, Broad Institute
Co-Chair 1000 Genome Project

“Financially, next-gen sequencing is already at the point that allows you to move it into clinical programs. Our focus is on utilization of next-generation sequencing for whole transcriptome profiling and mutation analysis …..as the future for our business.”

Randy Scott
Executive Chairman, Genomic Health
Baby Steps in Whole Genome Sequencing for Personalized Medicine

$1000$ genome (fully costed) + $1000$ genomes = ?
Now Comes the Hard Part!
Large Scale WGS and the Primacy of Standards

- acquisition of rigorously phenotyped/matched/consented normal and disease samples
- standardization of pre-analytical and analytical methods and data reporting
- curation, ontologies, annotation, analytics for large scale databanks and federations
- new statistical/mathematical/computational approaches for multivariate, non-linear events
- regulatory validation of analytics
- customized data for different decision categories and decision-makers
Whole Genome Sequencing and Molecular Medicine: Dependency on Large Scale (Massive) Data Annotation and Analytics

- **correlation analytics**
  - SNPs, haplotypes
  - CNVs rearrangements
  - non-coding regions
  - ethnic diversity
  - epistasis
  - epigenetics
  - other ‘omics’

- **decision analytics**
  - Rx response/resistance - target(s), networks
  - Rx adverse event risk
  - prognosis/progression
  - predisposition to disease
  - environmental exposure/lifestyle confounders for predisposition

- **privacy and security**
Whole Genome Sequencing and Molecular Medicine: Dependency on Large Scale (Massive) Data Annotation and Analytics

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  - environmental exposure/lifestyle confounders for predisposition

- technical standards
- regulatory requirements
- reimbursement
- education

privacy and security

- technical standards
- regulatory requirements
- reimbursement
- education
Standards for ‘Omics’ Data Cross-Domain Integration, Open-Source Data Sharing and Computational Analysis
Semantics
Mining The Data Deluge:

- nomenclature ontologies
- liberate intelligence from multiple source formats
- interoperability challenges
- early discovery (chaos) vs. clinical trials (CDISC) vs. healthcare (HL7, SNOMED)
- urgent imperative for methodological, ontological and data storage format standards
Scale and Statistics
Validation of Disease-Associated Biomarkers

- Disease related differences are small compared to range of biological variability in the population.
- Many variables behave as QTLs with graded continuum rather than binary normal: disease separation.
- The high dimensionality small sample size (HDSS) problem:
  - High number of variables (2000-10000) and low sample size (10-100).
  - Increased risk of selection of variables due to chance (overfitting).
- Statistical powering:
  - “the 20:200:2000 rule”
- New regulatory complexities for multiplex ‘signatures’ as next-generation diagnostic tests/biomarkers.
Speed
Specter for the Cure

Specter for the Cure - Cures Acceleration Network (CAN) Act
Turning Research into Cures

STAND UP. TUNE IN.
The fight against cancer continues.

Breast Cancer Deadline
Why Now?
September 28, 2019
BreastCancerDeadline2020.org
The Distressing State of Investigational Cancer Drug Trials in the USA

- Armitage report 1997 and IOM report 2010
  - need to reduce ‘Tower of Babel’ in clinical cancer research
- Sateren et al. 2002 J. Clin. Oncol. 20, 2109
  - less than 5% cancer patients enrolled in trials
- Durivage et al. 2009 J. Clin. Oncol. 27, 337s
  - 2685 industry and NCCN trials at 14 cancer centers
  - 1455 (54.2%) failed to accrue a single patient
- Dilts et al. 2009 J. Clin. Oncol. 27, 1761
  - 296 to 481 steps to activate trials by NCI-STEP and/or cooperative groups
- NCI Operational Efficiency Working Group 2010
  - timelines that trials must achieve otherwise automatic termination
Safety
## Genetic Associations in Drug-Induced Liver Injury: Polymorphisms in Drug Metabolism Enzymes

<table>
<thead>
<tr>
<th>Drugs</th>
<th>High-risk genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perhexiline</td>
<td>CYP2D6*3, *4, *5, and *6</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>GSTM1 null</td>
</tr>
<tr>
<td>Tacrine</td>
<td>GSTM1 and T1 null</td>
</tr>
<tr>
<td>Troglitazone</td>
<td>GSTM1 and T1 null</td>
</tr>
<tr>
<td>Diverse</td>
<td>GSTM1 and T1 null</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>GSTM1 non-null, RFC1 G80A</td>
</tr>
<tr>
<td>Anti-TB drugs</td>
<td>NAT2*5, *6, *7, CYP2E1 c1/c1, MnSOD T/C or C/C, GSTM1 null</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>UGT2B7*2, CYP2C8 haplotype, ABCC2 C24T</td>
</tr>
<tr>
<td>Tolcapone</td>
<td>UGT1A haplotype</td>
</tr>
<tr>
<td>Indinavir</td>
<td>UGT1A1*28, UGT1A3 T66C-UGT1A7 T57G</td>
</tr>
<tr>
<td></td>
<td>UGT1A1*6</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>UGT1A1*28, UGT1A3 T66C-UGT1A7 T57G</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>TPMT*3A and *3C</td>
</tr>
</tbody>
</table>

**Genetic Associations in Drug-Induced Liver Injury: Polymorphisms in Immune-Related Pathways**

<table>
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<th>High-risk genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flucloxacillin</td>
<td>HLA-B*5701</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>HLA-DRB1<em>1501-DRB5</em>0101-DQB1*0602</td>
</tr>
<tr>
<td>Clavulanate</td>
<td>HLA-DQA1<em>0102-DQB1</em>0602</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>HLA-A<em>3303, HLA-DQB1</em>06</td>
</tr>
<tr>
<td>Ximelagastaran</td>
<td>HLA-DRB1<em>07, HLA-DQA1</em>02</td>
</tr>
<tr>
<td>Anti-TB drugs</td>
<td>HLA-DQB1*0201</td>
</tr>
<tr>
<td>Diverse</td>
<td>HLA-DRB1<em>15, DQB1</em>06</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>IL-10-627A and IL-4-590T</td>
</tr>
<tr>
<td>Tacrine</td>
<td>IL-6-597A-572G-174G haplotype</td>
</tr>
</tbody>
</table>

- third leading US Rx
- $9 billion annual sales
- biologically inactive dosage form
  - hepatic metabolic activation by CYP2C19
- carriers of loss of function CYP2C19 alleles non-responsive
  - 30% European ancestry, >50% Asians
- FDA black box warning (March 2010)
  - risk in ‘poor metabolizers’
- slow uptake of routine genotyping
- new momentum from launch of Medco and CVS/Caremark genotyping services?
If You Build It Will They Pay?
Adoption of Disruptive Innovation

- new technology/service that simplifies a complex/costly problem
- business model that allows market adoption of the simplified solution at low(er) cost
- incentivized supply and demand to reinforce the disruption
If You Build It, Will They Pay?
Adoption of Disruptive Innovation

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“If it isn’t billable – it isn’t going to happen”

- value-based versus cost-based reimbursement
- new billing codes
- reimbursement for professional analysis of remote patient monitoring data streams
How Much New Technology Can We Afford?
NICE Gets Nasty (or Rational?)

Logos of various pharmaceutical companies are displayed on the page.
### What Are We Willing to Pay for Added Months of Survival in Cancer

<table>
<thead>
<tr>
<th>Lifetime cost above standard care</th>
<th>If cancer is on par with other diseases ($150,000 per life year gained), months of added overall survival benefit needed</th>
<th>Treating cancer as worthy of much higher reimbursement ($250,000 per life year gained), months of added overall survival benefit needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>$50,000</td>
<td>4 months</td>
<td>2.4 months</td>
</tr>
<tr>
<td>$100,000</td>
<td>8 months</td>
<td>4.8 months</td>
</tr>
<tr>
<td>$150,000</td>
<td>12 months</td>
<td>7.2 months</td>
</tr>
<tr>
<td>$200,000</td>
<td>16 months</td>
<td>9.6 months</td>
</tr>
<tr>
<td>$250,000</td>
<td>20 months</td>
<td>12 months</td>
</tr>
<tr>
<td>$300,000</td>
<td>24 months</td>
<td>14.4 months</td>
</tr>
<tr>
<td>$350,000</td>
<td>28 months</td>
<td>16.8 months</td>
</tr>
<tr>
<td>$400,000</td>
<td>32 months</td>
<td>19.2 months</td>
</tr>
<tr>
<td>$450,000</td>
<td>36 months</td>
<td>21.6 months</td>
</tr>
<tr>
<td>$500,000</td>
<td>40 months</td>
<td>24 months</td>
</tr>
</tbody>
</table>

Source: Pink Sheet 13 Sept 2010. Adapted from S. Ramsey, FHCRC, ASCO 2010
“I have a very romantic view of the NHS”

Interview in Health Affairs
April 2010

Dr. Donald Berwick
Current Payor Value Propositions Do Not Align with Clinical/Economic Value of Molecular Diagnostics

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
Services
Wellness:

The Most Broad and Most Valuable Definition of Successful Healthcare

Consumers at the Center
Engaging Consumers and Patients for Wellness and Greater Responsibility for Mitigation of Health Risk(s)

- entitlement mentality
- lack of accountability
- lack of transparency in pricing and evidence-based performance to guide choice
- cost-shifting
  - a negative but blunt economic driver
- economic incentives
  - positive drivers for wellness
  - employers, payors, taxation policies
- providing tools and information to support informed choices and improved outcomes tracking
Engaging Consumers and Patients for Wellness and Greater Responsibility for Mitigation of Health Risk(s)

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INADEQUATE OPTIONS/SYSTEMS
FOR ROUTINE REMOTE HEALTH STATUS MONITORING
Sensors
Sensor Networks for Remote Health Status Monitoring
Wireless Integrated Data Systems

- geolocation data (where)
- temporal information (when)
- contextual information (what)
Personal Health Systems: On-Body: In-Body Sensors (OBIBs)

- wearable
- portable/mobile
- point-of-care
- implantable
- multi-parametric
- interoperability with electronic records

Mobile Health (mHealth)
m.Health

Remote Health Monitoring and Chronic Disease Management

Lifestyle and Fitness

Information for Proactive Health Awareness (Wellness)
## Major Target Markets for Wireless Medicine

<table>
<thead>
<tr>
<th>Disease</th>
<th>*Patients</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s</td>
<td>5 million</td>
<td>vital signs, location, activity, balance</td>
</tr>
<tr>
<td>Asthma</td>
<td>20 million</td>
<td>respiratory rate, FEV, air quality, oximetry, pollen count</td>
</tr>
<tr>
<td>Breast CA</td>
<td>3 million</td>
<td>ultrasound self-exam</td>
</tr>
<tr>
<td>COPD</td>
<td>10 million</td>
<td>respiratory rate, FEV, air quality, oximetry</td>
</tr>
<tr>
<td>Depression</td>
<td>19 million</td>
<td>medication compliance, communication</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21 million</td>
<td>glucose, hemoglobin ATC</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>5 million</td>
<td>cardiac pressures, weight, blood pressure fluid status</td>
</tr>
<tr>
<td>Hypertension</td>
<td>74 million</td>
<td>continuous blood pressure monitoring, medication compliance</td>
</tr>
<tr>
<td>Obesity</td>
<td>80 million</td>
<td>smart scales, caloric in/out, activity</td>
</tr>
<tr>
<td>Sleep Disorders</td>
<td>15 million</td>
<td>sleep phases, quality, apnea, vital signs</td>
</tr>
</tbody>
</table>

From: West Wireless Health Institute, Medtech Insight, August 2009
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)
Intelligent Medicine Dispensers for Enhanced Rx Compliance

Gaming for Health:
Wireless Devices for Health Status Monitoring

Zio™ Patch

Cardionet  Biotronik  Omron

AMD  Chealcomm  Vitatelemedicine

Corventis  Sotera Wireless

Card Guard  Airstrip Technologies

LG  Intouch Health  Medic4all

Q-Connect  Vitalograph

LifeCOMM  AT&T  Nokia

Qualcomm  Verizon  Myca

Orange  Medonline  Google
“This isn’t a device it’s a service.”

Jeff Bezos
CEO, Amazon
You, Me and Health in a Networked World

- mobile
- multimedia
- monitored
- measured
- me, and those like me
- multiple markets of one, but primarily ME!
Social Media and Social Networks
Social Networks and Consumer: Patient Empowerment

Source: R&D Directions May 2010
“Real personalized medicine should begin long before we’re faced with pharmacology.”

“Our health information is too important to leave to an archaic, insular system.

If there’s no longer a need to rely solely on a doctor’s advice for treatment and care, why should we be expected to artificially limit our options.”

Thomas Goetz
Deputy Editor of Wired
Virtual Medicine Networks:
Increasingly Integrated Care and Continuity of Care

- rapid, real time access
- clinical specialties
- health records
- lab data
- drug interactions
- electronic Rx prescribing
Integration of Services and Simplification of Services
Demographic Trends and the Clinical and Economic Burden of Complex, Chronic Conditions/Co-Morbidities

- 23% Medicare beneficiaries have 5 or more conditions
- Polypharmacy and AEs
- Poor patient compliance
- Multiple physician/venue encounters
- Poor communication/coordination between siloed healthcare services
- Procedure-based reimbursement versus care continuum integrated
Connected Care

Technology-enabled Care at Home

Produced by the Deloitte Center for Health Solutions

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
In-Home Health Connection: Engaging the Elderly
Molecular Diagnostics and Health Information Systems as the Key Elements in the Evolution of Integrated Healthcare Delivery

- Risk
- Health Status Monitoring
- Incentives for Risk Mitigation

- Increased Personal Responsibility for Wellness
- Risk Alerting and Tracking

- Molecular Profiling Dx/PDx
Data: The Fastest Growing Resource on Earth
“Managing Mega-Data”

volume

scale

global networks

heterogeneity

integration
A New Healthcare Ecosystem Arising From Technology and Market Convergence

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

**Integrated Technology Platforms**

**Data Mining and Integration Services**

- passive/active data collection
- analytics and network architecture
- EMR/PMR
- performance and outcomes analysis

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

**Patients**

**Consumers**

**Services for Integrated Care**
The Expanding Universe of Health Information Resources: Redefining Physician:Patient Relationships

- MD-centric monopoly
- paternalistic decisions and passive patients
- institutional control
- paper records
- fragmented information and portability barriers
- centralized testing analysis and expert interpretation

- patient-centric markets
- engaged patients/consumers
- individual custody
- EHR/PMRs
- seamless integration and mobility
- increasingly decentralized, automated analysis and decision algorithms
- remote health status monitoring
Sociology
“I respect the seriousness of death.
I’ve had many occasions to meditate on its intrusions.
….the way the message was delivered.
Frankly, it made me furious.”

Sen. Edward Kennedy
True Compass. A Memoir. 2009
Patients

- want information regarding treatment options
- increasingly informed about options via web sources but want professional input to assist in interpretation
- generation-dependent preference/expectancy for shared role in decision-making
- improved outcomes and increased compliance when patients are engaged and informed

- major cultural gap in professional-patient interactions
- time and cost to healthcare professionals
- lack of professional familiarity/competencies in molecular medicine
“do you understand”: physician paternalism and patient timidity
- a dangerous combination

impact on increased incidence of Rx/treatment errors, non-compliance and hospital readmissions

challenge for healthcare professionals
- time and money but large component originates in culture/training
- often hold different perception to patients and priorities versus increasing problem in managing chronic disease and multiple co-morbidities

the sociology of medical training and practice
- hierarchical, authoritarian, paternalistic
- inadequate focus on team-based healthcare delivery
SILOS
and
THE SOCIOLOGY OF RESEARCH
AND CLINICAL MEDICINE
Forging a New R&D Framework for Biomedical Research and Public Health

- fragmented, uncoordinated, siloed R&D activities versus systems-based integration
  - dominance of investigator-driven research via funding decentralized academic laboratories
  - alarming lack of standardization of methods, tools and data reporting
  - poor data replication and barrier to metaanalysis
  - insufficient use of public:private partnerships to drive scale and standards
Forging a New R&D Framework for Biomedical Research and Public Health

- leverage still unique and unmatched capabilities
  - intellectual and cultural capital
  - financial and infrastructure resources
- aggressive reform of national research planning, organization and funding
  - coordinated, multidisciplinary programs with requisite scale
  - increasing standardization as foundation for proficient assembly/analysis of large scale data
  - oblige engagement of private sector partnerships to receive funding
  - authority and accountability
- imperative for radical and, by definition, disruptive changes
The Key Strategic Elements in the Evolution of Healthcare

- Molecular diagnostics for disease prediction, prevention, and earlier detection
- Biomarkers for health status profiling
- Risk management
- Health status monitoring
- Optimized decisions
- E-care: EMR, PHR integrated care and wellness
- Prevention
- Disease subtyping and Rx choice
- Compliance
- m. health