Technology Acceleration and Convergence: The Evolution of Novel Platforms for Improved Healthcare Delivery

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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
The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities

Health Status

Healthy/Low Risk

At-Risk

High Risk

20% of the Population Generate 80% Cost

multiple co-morbidities

end-of-life care

chronic disease progression

chronic disease early stage

acute disease

Value

Cost
Reasonable Expectations for Rational Healthcare

- what works?
- why it works?
- who it works for?
- what works best?
- when should it be used optimally?

- validated evidence
- mechanism of action
- personalized medicine
- comparative effectiveness
- best practice guidelines, standard-of-care and malpractice

VALUE
The Strategic Environment for Technology

- Disruptive Technologies
- Technology Acceleration
- Technology Convergence
- Dual-Use Technologies
The Strategic Environment for Technology

- Creative destruction, discontinuity, dislocation, inflection/tipping points, ‘Black Swans’
- Competition within a sector always arises at the margin
- New competitors/markets arise at the fusion interstices of previously separate sectors
- Adaptive agility for survival
- New legislative and regulatory oversights
- Proactive adoption of new organizational and business models/networks

- Disruptive Technologies
- Technology Acceleration
- Technology Convergence
- Dual-Use Technologies
The Three Convergent Forces Shaping the Evolution of Healthcare

- Molecular medicine and personalized medicine
- Access, cost, and quality of care
- Proficient use of information (e-health)

VALUE
Personalized Medicine and Technological and Commercial Discontinuities in Healthcare Markets

Establishing a Long-Term Strategy and New Value Propositions in a Short Term Environment
The Evolving Market for (Bio)Pharmaceutical Therapies

- **“Blockbuster” Rx**
  - empirical “one-size-fits-all”
  - population-based Rx

- **Stratified/Targeted Rx**
  - Rx targeted to patient subgroups with common molecular pathology
  - Dx-Rx combinations and Rx labeling

- **Individualized Rx**
  - relevant disease subtype
  - AE risk profiling
  - compliance monitoring

- **Personalized Healthcare**
  - integrated framework of coordinated care and longitudinal care
Molecular Diagnostics and Miniaturized Devices: A Key Future Driver in the Healthcare Value Chain

### Complex Biosignature Profiling

<table>
<thead>
<tr>
<th>genomics</th>
<th>proteomics</th>
<th>immunosignatures</th>
</tr>
</thead>
</table>

### Signature Detection, Deconvolution and Multivariate Analysis

- automated, high throughput multiplex assays
- novel test formats and devices (POC)
- new algorithms for complex signal/deconvolution
Mapping the Molecular Signatures of Disease: Building Integrated End-to-End Systems as the Foundation of Personalized Medicine

PROFILE

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

SENSE

automated platforms for rapid detection of multiplex analytes

ACT

rapid analytics and customized data formats/visualization to guide optimum decisions by clinicians, patients and payors
Disease Subtyping: Next-Generation Molecular Diagnostics (MDx) and A New Molecular Taxonomy of Disease

MDx Platforms

- massive parallelism
- miniaturization
- automation
- rapid
- POC

RIGHT Rx for
RIGHT DISEASE SUBTYPE
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)
- regulatory endorsement in product labeling
- payor adoption

Clinical guidelines

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- regulatory endorsement in product labeling
- payor adoption
Development of Companion Diagnostics and Dx Test Validation Standard

- ODAC rejection (3/2010) of Omapro for Gleevec-resistant CML due to T315I mutation

- failure to use single standardized assay for all patients
  - peripheral blood versus bone marrow
  - 1/3 tested locally; 2/3 tested centrally
  - centralized labs used different assays with 100 fold sensitivity difference for the mutation
● 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
• opening era in linking disease molecular pathology to rational Rx

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

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• 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

The New Reality (S. Burrill):
Companion Therapeutics Selected by Precision MDx
From Pharmaceuticals to Pharmasuitables

Disease Subtyping:

Individual Variation and AE risk

Right Rx for Right Disease

Right Rx for Right Patient
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
  - number of isoforms for DMPK enzymes and scale of individual variation within populations
- 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
- growing recognition of importance of variation in HLA alleles as additional risk factor
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
transcending PC and “biological egalitarianism”
non-trivial genetically-based biological variation exists in individuals and groups
ignoring such variations is illogical, poor science, poor clinical medicine and potentially dangerous
mapping group genetic diversity is fundamental knowledge
  – human evolution and trait acquisition
  – interplay of genomes and environment in determining outcomes
  – variations in disease susceptibility, xenogeneic metabolism and clinical decisions for optimum treatment
The Hunt for Gene Loci Associated with Complex Human Diseases
“Our ignorance of the laws of variation is profound”

Charles Darwin
Disease Predisposition Risk Profiling for Common, Multigenic Late-Onset Disorders

- slower evolution than many predict
- Genome-Wide Association Studies (GWAS)
  - high cost and to date low yield in terms of clinically exploitable markers
  - disease origins from multiple low penetrance alleles versus small, dominant set of high penetrance alleles
- substantial ambiguities regarding probabilistic risk of overt disease
  - epistasis
  - epigenetics
  - environmental confounders
  - source of poor replication of GWAS studies?
Disease Predisposition Risk Profiling for Common, Multigenic Late-Onset Disorders

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  - Source of poor replication of GWAS studies?

The premature quest to provide consumer genomic testing (CGx) for future risk of major diseases
Mapping the Complexity of Genome Organization

- recognition of increasing levels of organizational and regulatory complexity
  - haplotypes
  - CNV
  - indels
  - RNA universe
  - ‘dark’ elements
  - epistasis
  - epigenetics
  - nuclear compartmentalization and trans-expression
## miRNAs Associated with Solid Cancers

<table>
<thead>
<tr>
<th>Tumor</th>
<th>miRNA</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>miR-21, miR-125b</td>
<td>oncomiR</td>
</tr>
<tr>
<td>Breast cancer metastasis</td>
<td>miR-335, miR-206, miR-126</td>
<td>metastasis suppressor</td>
</tr>
<tr>
<td>Lung adenocarcinoma</td>
<td>let-7a, miR-143, miR-145</td>
<td>tumor suppressor</td>
</tr>
<tr>
<td>Lung adenocarcinoma</td>
<td>miR-17-92 cluster, miR-106b/93/25 cluster</td>
<td>oncomiR</td>
</tr>
<tr>
<td>Pancreatic ductal carcinoma</td>
<td>miR-196a, miR-196b</td>
<td>oncomiR</td>
</tr>
<tr>
<td>Ovarian carcinoma</td>
<td>miR-199a/b, miR-140, miR-145, miR-204, miR-125a/b</td>
<td>tumor suppressor</td>
</tr>
<tr>
<td>Ovarian carcinoma</td>
<td>miR-141, miR-200a/b/c</td>
<td>oncomiR</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>miR-21, miR-224, miR-34a, miR-221/222, miR-106a, miR-203</td>
<td>oncomiR</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>miR-122a, miR-422b, miR-145, miR-199a</td>
<td>tumor suppressor</td>
</tr>
<tr>
<td>Thyroid papillary cancer</td>
<td>miR-146b, miR-221, miR-222, miR-181b, miR-155, miR-224</td>
<td>oncomiR</td>
</tr>
</tbody>
</table>

From: M. Galasso et. al. (2010) Genome Medicine 2, 12
Gene Deserts: The 8q24 Region and Cancer Susceptibility

Unrooted Parsimony Tree Profiles for Clonal Evolution in B-Cell Chromic Lymphocytic Leukemia Revealed by Ultra-Deep Genome Sequencing

From: P. J. Campbell et al. (2008) PNAS 105, 13081
Length of branch is proportional to number of varying bases (evolutionary distance)
The Race for Low Cost ($<1000) Whole Human Genome Sequencing
The Evolution of Drug Discovery

- empirical screening
- cellular/receptor pharmacology
- genomics and individual molecular targets
- molecular pathways
Systems Biology: Mapping Biological Pathways and the Generation of Complex Network Behaviors
Molecular Pathways and Network Analysis: Systems Pharmacology

Deconvolution of Signaling Networks in Disease

Identification of ‘Fragile’ Nodes/Pathways for Targeted Rx
Rx Action Networks for FDA Approved Drugs

**Drug-Target Networks**

- 788/890 share targets with other Rx

**Target-Protein Networks**

- 305/394 targets interact with two or more Rx

Network Pharmacology and Drug Discovery: Key Principles

- there are few single molecular targets for Rx action
- effective Rx requires modulation of pathways
- there are no linear pathways, only networks and subnetworks
- there are also highly interconnected networks/subnetworks between tissues
  - e.g. modulation of liver network induces changes in pancreatic islet network
Mapping Pharmacogenomic Molecular Networks

*Tanimoto coefficient of 166 structural features
Building Pharmacogenomic Drug: Network Datasets

83,338 concept terms for subtree of pathology descriptors

4068 concept terms matched to SNOMED-CT

726 diseases/2022 drugs

3517 approved drug indications, 8130 off label uses

12,460 genes (proteins)/400 drugs
The Complexity of Cancer Genomes

**LUNG CANCER**
Cancer: small-cell lung carcinoma

- Sequenced: full genome
- Source: NCI-H209 cell line
- Point mutations: 22,910
- Point mutations in gene regions: 134
- Genomic rearrangements: 58
- Copy-number changes: 334

**Highlights:**
Duplication of the CHD7 gene confirmed in two other small-cell lung carcinoma cell lines.


**SKIN CANCER**
Cancer: metastatic melanoma

- Sequenced: full genome
- Source: COLO-829 cell line
- Point mutations: 33,345
- Point mutations in gene regions: 292
- Genomic rearrangements: 51
- Copy-number changes: 41

**Highlights:**
Patterns of mutation reflect damage by ultraviolet light.


**BREAST CANCER**
Cancer: basal-like breast cancer

- Sequenced: full genome
- Source: primary tumour, brain metastasis, and tumours transplanted into mice
- Point mutations: 27,173 in primary, 51,710 in metastasis and 109,078 in transplant
- Point mutations in gene regions: 200 in primary, 225 in metastasis, 328 in transplant
- Genomic rearrangements: 34
- Copy-number changes: 155 in primary, 101 in metastasis, 97 in transplant

**Highlights:**
The CTNNAL1 gene encodes a putative suppressor of metastasis that is deleted in all tumour samples.


**BRAIN CANCER**
Cancer: glioblastoma multiforme

- Sequenced: exome (no complete Circos plot)
- Source: 7 patient tumours, 15 tumours transplanted into mice (follow-up sequencing on 21 genes for 83 additional samples)
- Genes containing at least one protein-altering mutation: 685
- Genes containing at least one protein-altering point mutation: 644
- Copy-number changes: 281

**Highlights:**
Mutations in the active site of IDH1 have been found in 12% of patients.

Selected Targeted Agents With Potential as Breast Cancer Therapeutics

- Angiogenesis:
  - Sexaminib
  - SU6668
  - Bevacizumab
  - HuMV833
  - Cilengitide
  - Vitaxin 2
  - CAI
  - Endostatin
  - Angiostatin
  - Thalidomide
  - Neovastat
  - 2-Methoxy Estradiol
  - Sorafenib
  - Sunitinib
  - Vandetanib
  - Motesanib diphosphate

- Matrix Metalloproteinases:
  - Batimastat BB-94
  - Marimastat BB-2516
  - BMS-275291
  - BAY 12-9566
  - COL3

- Growth Factors (e.g., TGFα):
  - Cilengitide
  - Erlotinib SU6668
  - Sexaminib
  - Gefitinib
  - Trastuzumab
  - Lapatinib

- Cyclin D1
  - Cdk
  - CDK4
  - CDK6
  - c-Myc
  - E2F
  - Cyclin A
  - Cyclin B

- Survival Factors (e.g., IGF1)
  - TGFβ
  - HGF
  - IGF1

- Hormones (e.g., Bombesin, Estrogen)
  - G-Protein
  - Ad Cycl
  - PKA

- Changes in Gene Expression
  - c-Myc
  - E2F
  - Cyclin D1
  - Cyclin E

- Cell Proliferation (Cell Cycle)
  - Cell Death (Apoptosis)
  - Caspase 3
  - Cytochrome C
  - FasL
  - Death Factors (e.g., FasL)

- Clinical Options.com/oncology
Network Pharmacology, Pathway Redundancy and Drug Resistance ($D^r$)

- **D-1** and **D-2**
- **D-1$^r$** and **D-2$^r$**

**susceptible to both D-1/D-2**

**mutation confers resistance to D-1**

**distal pathway mutations confer resistance to both D-1/D-2**
Systems Pharmacology and Molecular Pathways
Network Analysis

- ‘connectivity’ maps
  - correlations between genomic signatures and sets of proteins involved in Rx action
- Rx ‘promiscuity’
  - spectrum of ‘target’ effects required for optimum efficacy
  - network redundancy and Rx non-responsiveness/resistance
- Rx ‘pleiotropy’
  - off-target effects and adverse event risk(s)
- ‘synthetic lethal’ screening
  - ID new Rx oncology targets in co-dependent genes required for cell survival
- ‘minimum knockout’ modeling
  - ID/predict smallest number of drug targets to fully block a cellular process
High Content Cellular Screens: Cyto-omics

- rapid expansion of single cell analysis methods
- linking gene expression to functional pathways/networks/compartments
- obvious requirement to validate in vitro/ex vivo phenotypes to events in vivo
  - higher level of ‘stochastic’ drift in vitro?
  - failure of 2D cultures to mimic complex signaling environment of organized multi-cellular tissues
- parallel evolution of technologies for imaging in vitro and in vivo for biomarker validation
New Incentives for R&D Investment in Diagnostics, Drugs and Vaccines to Outpace Infectious Diseases
The Valley of Dearth: The Consequence of Declining R&D Investment in Antibiotic Discovery*

- 75% decrease in antibacterials approved from 1983 to 2009
- only 16 agents currently in Phase II / III clinical trials
  - only 3 as new ‘classes’ with novel mechanisms of action
  - absence of agents for therapy of AMR in Gram-negative bacilli
  - lack of systemic agents in advanced development for organisms resistant to all current antibacterials

The Growing Challenge Posed by Antimicrobial Drug Resistance (AMR)

**NO ESKAPE**

*Enterococcus faecium*

*Staphylococcus aureus*

*Klebsiella Pneumoniae*

*Acinetobacter baumannii*

*Pseudomonas aeruginosa*

*Enterobacter species*
New US-EU Task Force (2 Nov. 2009)
- encourage R&D on new antimicrobial drugs
- yet to be defined strategy/funding

The I0 X ’20 Initiative (20 Nov. 2009)
- grand challenge to develop 10 new antibiotics by 2020

Multi-Country Program on AMR (12 Jan. 2010)
- € 12.4 million
“Millions demand it, millions refuse it, and millions don’t know what to think”

John Carroll
Editor, FierceBiotech (23 Oct. 2009)
Vaccine Safety: Informing the Misinformed
Vaccine Safety: Media Sensationalism and Celebrity Quackery
“Faked Pandemics- a Threat for Health”

- Motion to COE by Wolfgang Wodarg, Chair, Healthcare Committee, January 2010
- “WHO in cooperation with some big pharmaceutical companies and their scientists re-defined pandemics and lowered the alarm threshold”
- “Those standards forced politicians...... to sign marketing commitments for vaccines against swine flu and spend billions to catch up with the alarming scenario that big pharma, media and WHO are spreading”

Source: Scrip News 6 Jan. 2010
Media Sensationalism and Public Response to H1N1 Threat

The Economist

The pandemic threat
How scared should you be?

The New Yorker

The end is near sale

Swine Flu Panic Timeline

Last Week

AHHHHHHH!!

This Week

EH...
Maintaining Global Preparedness for a High Virulence Pandemic

- **H1N1**: high transmissibility - low virulence/mortality
- **H5N1**: low transmissibility – high virulence/mortality
- **H5N1 x (H1N1) or (X)**: potential for devastating pandemic
Emerging Infections:
Combating “Agent-X”

- new infectious agent
  - natural or nefarious origin
- highly virulent, high transmissibility
- major gaps in public health preparedness
  - outmoded vaccine technologies and production methods
  - inadequate scale of vaccine manufacturing infrastructure
  - cost and lead time for new vaccine production facilities
  - lack of novel Rx classes
  - high cost and protracted R&D cycles
- inadequate investment incentives
- public policy neglect
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 Evolution of Drug Discovery

- systems biology
  - elucidation of biological networks and their regularity
- regenerative biology
  - reprogramming cell function and directed differentiation (ESC/iPS)
- synthetic biology
  - de novo design of novel organisms and a new industrial ecology
- predictive biology
  - information flow in complex adaptive systems
“Biomedical research in academia has been very successful in generating an immense amount of information, leading to a true revolution in molecular medicine”

S. Albani and B. Prakken

TRUE OR FALSE?
The Trajectories for Molecular Medicine

- Exponential growth in research data

- Time

- Data

- Translational medicine and clinical validation

- Regulatory standards

- Clinical utility and reimbursement

- Routine clinical adoption
Knowledge and Evidence Doesn’t Translate Easily into New (or Rational) Behaviors

- science (impact is too often unknown or abstract)
- industry (incremental timidity driven by short-term focus on markets and stock valuation)
- payors (cost control)
- physicians and healthcare professionals (status, revenue and recognition)
- patients (unaware and uninvolved in healthcare decisions)
- politicians (populism and short-term fixes)

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
Data: The Fastest Growing Resource on Earth
Standards for ‘Omics’ Data
Cross-Domain Integration,
Open-Source Data Sharing
and
Computational Analysis
The Open Biomedical Ontologies

Cell Ontology (CL)

ZFIN
Zebrafish Anatomical Ontology

Plant Ontology (PO)

The Open Biomedical Ontologies

Common Anatomy Reference Ontology

Environment Ontology

The Open Biomedical Ontologies

Phenotypic Quality Ontology (PATO)

The Gene Ontology

Gene Ontology (GO)

Chemical Entities of Biological Interest (ChEBI)

Disease Ontology (DO)

Sequence Ontology (SO)

Ontology for Clinical Investigations (OCI)

OBO Relation Ontology

Ontology for Biomedical Investigations

Protein Ontology (PRO)

RNA Ontology (RnaO)

http://www.nature.com/nbt/journal/v25/n11/fig_tab/nbt1346_T2.html
The Rise of Open-Source Networks and Consortia

FDA/Severe Adverse Events (SAE) Consortium
“Managing Mega-Data”: (Who Knows Wins)

volume

scale

global networks

heterogeneity

integration
How Much New Technology Can We Afford?
“We must acknowledge that the cost of drug discovery is becoming outrageous and, if it continues to grow at the present rate, new drugs will be unaffordable for any country in the world.”

Sir Michael Rawlins
Chairman,
UK National Institute for Health and Clinical Excellence (NICE)

UK National Institute for Health and Clinical Excellence (NICE)
Nice Gets Nasty (or Rational?)
Knowing What Works (or Doesn’t)

- Pervasive Inefficiencies and Errors in Healthcare Created by Empirical Care and Lack of Robust Outcomes and Performance Data
Comparative Effectiveness Research (CER)

- Superficial appeal of rational policy belies the complexity of rigorous CER
  - endpoints/outcomes
  - methodological and reporting standardization
  - stringency of patient selection/treatment regimen/compliance
  - prospective versus retrospective data
- Payor engagement and impact on reimbursement policies
  - predisposition to choose lower cost intervention(s)?
  - risk of abuse and rationing of care

Who sets priorities and evaluation criteria?
Who Defines Best Practices?

- controversy over US Preventive Task Force (USPTF) recommendations on mammograms for women age 40-49
- endorsed by ACP
- opposed by ASCO and NCCN
- USPTF did not address cost but it dominated public debate
- “should policy makers set a price on saving a life?”
Patient Safety: The Dimension of the Problem

- Overt Error
- Non-Compliance
- Adverse Rx Event

- Hospital-Acquired Infections
- Cost of Hospital Re-admissions
- Inaccurate, Inaccessible or Ignored Information

Certain medicines may affect your ability to drive.
Wellness:

The Most Broad and Most Valuable Definition of Successful Healthcare

Consumers at the Center
Consumer Behavior and Healthcare Costs

“diabetes” $200 billion

smoking $190 billion
alcohol $20 billion
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)
Health Status Monitoring and the Promotion of Wellness

On-Body: In-Body Sensors (OBIBs) and Remote Monitoring of Health Status
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)
## 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*
● first generation remote health monitoring devices

● MD payment for analysis of data streams from remote monitoring
  – Cardionet, Medtronic

● White House Broadband Plan (3/16/10)
  – FDA and FCC to establish oversight process for e.health devices
  – HHS to develop reimbursement methods to accelerate adoption
  – FCC to allocate wireless spectrum for BANs
The Infocosm: Emerging Networks of Global Connectivity
Healthcare Records:
Proliferating Paper and Primitive Electronic Systems
“Meaningful Use”
EHR Incentive Programs Funded by ARRA 2009

- proposed rule and fact sheet comment deadline 2/28/10
- www.cms.hhs.gov/recovery/11-healthit.asp

- interim final rule: comment deadline 2/28/10
- http://healthit.hhs.gov/standardsandcertification
Telecommunications and Media Industry Convergence: Implications for Healthcare
“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
Wireless Technologies: Consumer and Clinical Markets Converge
Pharma and Healthcare Social Media (Non-Brand Sponsored) Patient Communities

CancerCompass
- Community network about Multiple Chemical Sensitivity
- Blog and social network about Multiple Chemical Sensitivity

Autism151
- Campaign to pull our community together and offer a brighter, more positive view of autism

CureTogether
- Anonymously track and compare health data, to make more informed treatment decisions and contribute data to research

Cancer Survivors Network
- Discussion board featured on cancer survivors

Advanced Breast Cancer Community
- Information source online community advanced (metastatic) breast cancer patients, caregivers

Daily Strength
- Safe, anonymous online support groups focused on over 500 specific challenges

Depression
- Social network where like-minded people can communicate with each other and offer peer support

G GUARDIAN
- Health informatio

Circle of Sharing
- Helps cancer patients and caregivers get personalized information about the disease, and share that information

Disaboom
- Information and resources for people with disabilities

CareFlash
- Place to submit, retrieve and share information and well-wishes surrounding a loved one’s health circumstances

American Diabetes Association
- Discussion board featured on diabetes

CROHN'S & COLITIS FOUNDATION OF AMERICA
- Discussion groups and forums

eDrugSearch.com
- Search engine for Americans interested in purchasing safe, low-cost prescription drugs from prescreened international pharmacies

Be Well
- Expert-guided communities where you have access to authoritative information about health topics

Cancer TV
- Discuss health informatio

Healia
- Health informatio

Struggling with disorders and chronic illness

Humanizing Healthcare
- Social network where like-minded people can communicate about drug safety

Pharma and Healthcare Social Media (Non-Brand Sponsored) Patient Communities
In-Home Health Connection: Engaging the Elderly
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
The Doctor Will See You Online

- immediate access to care for patients
- patients submit medical records to company
- flexible engagement of MDs for additional income generation
- complementary tier of access
- billing and insurance services
- liability issues
The Dominant Future Element in Primary Healthcare Delivery???
A New Healthcare Ecosystem Arising From Technology and Market Convergence

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

MDx/Devices
Rx
HLx
<table>
<thead>
<tr>
<th><strong>Research</strong></th>
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<tr>
<td>• national resources network for biomedical R&amp;D</td>
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<td>• expanded private: public partnerships</td>
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<td>• reform of academic funding model to promote interdisciplinary research</td>
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<th><strong>Reimbursement</strong></th>
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<td>• value-based pricing</td>
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<td>• new coding for molecular medicine</td>
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<td>• new models for HTA and CER</td>
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<th><strong>Regulation</strong></th>
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<td>• rebalancing benefit: risk evaluation and abandonment of ‘zero-risk’ delusion</td>
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<tr>
<td>• validation standards for Dx-Rx and high complexity Rx</td>
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Genes and Intellectual Property

14 March 2000

5 February 2010 Report

29 March 2010 SDNY Court Decision

16 April 2010 WSJ Editorial
The Coming Convergence in 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
The Coming Convergence in Healthcare Delivery

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