Innovation In Healthcare Delivery –
Unavoidable Realities and Stark Choices:
Future Challenges and Opportunities

Keynote Address, ILSI – Biomed Israel 2008
Tel Aviv, 28 May 2008

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A Few Current Challenges for the US Healthcare System

- $2.3 trillion dollar expenditures (2007): 16% of GDP ($1 in every $7)
- Escalating and unsustainable fraction of GDP
- Highest per capita expenditure in OECD
- $510 billion cost of chronic disease
- 2 million annual hospital-acquired infections
- 2.5 million hospitalizations due to adverse Rx reactions
- Highly variable treatment patterns
- Slow diffusion of best practices
- No reserve capacity for disasters, epidemics or pandemics
Healthcare Costs are Unevenly Distributed

- 0.5% patients consume 25% of healthcare budget
- 1% consume 35%
- 5% consume 60%
- 10% consume 70%
- 50% consume 3%
- 75% of cost is for patients with chronic diseases

*Source: Healthcare Reform Now
G. Halvorson, Chairman and CEO
Kaiser Foundation Health Plan and Hospitals
Wiley, NY 2007 p.2
Five Chronic Diseases Impose the Highest Cost in Healthcare Expenditures

- diabetes
- CAD
- CHF/COPD
- asthma
- depression
- cancer = 8%
- infectious diseases = 7%
- trauma = 6%
- ob/gynec. = 4%
- bone and joint care = 2%

70% total healthcare costs
Market Distortions and Perverse Incentives in Modern Healthcare Delivery

- focus on late-stage detection and intervention
  - high cost
  - low reversibility

- multiple reimbursements for fragmented (siloed) care versus integrated management of patient needs

- illness versus wellness

- inadequate social and economic incentives for wellness
How Much New Technology Can We Afford?
Knowing What Works (or Doesn’t)

- Pervasive Inefficiencies and Errors in Healthcare Created by Empirical Care and Lack of Robust Outcomes and Performance Data
The Threat Posed by Unconstrained Growth in Healthcare Costs

- fiscal balance of governments
- cost structure of employers/companies
- incomes of individual patients
- inequity in access to care
- eroded quality of care
- rationed end-of-life care
- political inertia and eventual draconian rationing policies
E7 hypertension
- 2005: 639 million
- 2025: 1.2 billion

E7 diabetes
- 2005: 140 million
- 2025: 228 million

Accelerating impact of chronic diseases in E7
- Urbanization and pulmonary disease
- Deteriorating environmental quality and occupational exposures
- Diabesity, CVD
- Tobacco-use

Chronic diseases account for 80% of E7 mortality but earlier onset than in G7
The Urgent Imperative to Control the Growing Global Threat from Infectious Diseases
Global Health: Understanding the Implications of Major Economic and Environmental Dislocations
The Strategic Future of Healthcare

- Economic Unsustainability
- Reform and Rational Care

Confronting the Imbalance Between Infinite Demand and Finite Resources
The Three Forces Shaping the Evolution of Healthcare

- molecular medicine and personalized medicine
- access, cost and quality of care
- proficient use of information (e.health)

DEMONSTRATING VALUE
Aligning Incentives

- changing the value proposition in healthcare
- from cost to value
- from fragmented interventions to integrated care
- from late intervention in chronic disease to prediction, prevention and earlier detection and intervention
- from empirical Rx to rational Rx targeted to the underlying causal molecular pathologies
- escalating importance of Dx/PDx in the healthcare value chain
The Strategic Environment for The Pharmaceutical and Biotechnology Industries
Challenges for the Pharmaceutical and Biotechnology Industries

- Escalating R&D costs without concomitant gains in productivity
- Sustained high failure rates of candidate Rx in advanced clinical trials
- Intensified assault from politicians and media
  - Rx price, Rx safety, patents
- Payor pressures and regulatory creep for comparative trials before Rx approval
- Increasingly stratified global markets
- Demographic trends in G8/OECD and pressures for price controls
- Neglected diseases of developing world (DDW)
The Strategic Environment for the Pharmaceutical and Biotechnology Industries

- prospering in an environment of increasing constraints
- managing the limit(s) of society’s willingness and ability to pay for innovation
- harnessing unprecedented opportunities for rational therapeutics and personalized care
- building new alliances to improve clinical and economic outcomes from rational Rx use
  - integration of Dx, Rx, Ix

DEMONSTRATING THE VALUE OF RX
Inescapable Realities for the Pharmaceutical and Biotechnology Industries

- Rx margins are not sustainable
- comparator and pharmacoeconomic trials will increase development costs
- the power of the payor
  - reimbursement will shift to value-based outcomes
  - CMS, insurers, employers, nations
- intensified political and public pressures for improved quality and outcomes in healthcare
Ignoring The Obvious in Clinical Practice

- diseases are not uniform
- patients are not uniform
- a “one-size fits all” Rx approach cannot continue

- inefficiency and waste caused by empirical Rx
- cost of futile therapy
- medical error and AEs
The ‘Blockbuster Drug’ Business Model
“If it were not for the great variability among individuals, medicine might be a science, not an art”
Sir William Osler (1892)

“Because of the great variability among individuals, medicine must finally become a science, not an art”
# US Healthcare Costs

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>administration</td>
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<tr>
<td>personnel costs</td>
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<tr>
<td>procedures</td>
<td>18%</td>
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<tr>
<td>drugs</td>
<td>12%</td>
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<tr>
<td>in vitro diagnostics</td>
<td>0.01%</td>
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- Diagnostic tests influence 85% of clinical actions
Molecular Diagnostics and Biomarkers: The Fundamental Technology Platforms For Molecular Medicine and the Future Healthcare Value Chain
Disease Subtyping: Next-Generation Molecular Diagnostics (MDx) and A New Molecular Taxonomy of Disease

Dx Platforms
• massive parallelism
• miniaturization
• automation
• rapid
• POC

B1 skin, B2, melanocytes, B3, melanoma, B4 and 5 metastatic melanoma
From: C. Haqq et al. (2005) 102, 6092
The Emergence of Drug: Diagnostic Combinations

Invader® chemistry

5-Fluorouracil
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
Personalized Medicine: From Pharmaceuticals to Pharmasuitables

Disease Subtyping: Right Rx for Right Disease

Reduction of Adverse Drug Reactions
$600 million

$3.4 billion

$1.18 billion
The Evolution of Molecular Medicine and Information-Based Medicine: The Foundation for Rational Care and Personalized Medicine
A Realistic Strategy for the Delivery of Rational Healthcare?
Or
An Erstwhile Intellectual Pursuit Doomed to be Dashed on the Rocks of Siloed Science, Clinical Conservatism or Commercial Myopia?
Predictive Gene Lists (PGLs) of Altered Gene Expression in Cancer as Diagnostic and Prognostic Tests

- wide variation in PGLs reported in different publications for claimed similar patients
  - minimal overlap between studies
- discriminatory power of classifiers not reproducible when tested on published cross-sets of samples
- trigger for new regulatory oversight and sophisticated validation protocols
  - IVDMIAs (FDA)
The Multi-Factorial Nature of Common Diseases and the Challenge of Mapping Robust Panels of Disease Biomarkers

- genetic heterogeneity creates phenotypic heterogeneity
- complexity of GWAS mapping of the contributions of multiple ‘small effects’ gene loci
- modulation of ‘genotypic risk’ by genetic and environmental factors
  - epistasis, methylation, indels, copy number
  - lifestyle, xenobiotic exposure
  - prior/concurrent Rx
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**
Fundamental Issues in Clinical Validation of Biomarkers

- cost, effort and **CURATION STANDARDS** for biobanks
- analysis of variability
  - inter-and intra-subject variation
  - inter-laboratory variation
- cost and infrastructure to conduct population-based longitudinal trials
- flawed clinical trial design
  - heterogeneous patient cohorts
  - inadequate statistical power, overfitting, bias
- compatibility/receptivity of test format with clinical practice
- regulatory oversight
- coding and reimbursement
Reimbursement for Diagnostic Tests

- inadequate US Medicare coding and payment mechanisms
  - out moded, out-dated, lacking in transparency, inconsistently applied
- no effort to link reimbursement to value
- inappropriate assignment of existing CPT codes to new tests
- engagement of third party payers who derive economic/clinical value from new Dx
  - Genomic Health Oncotype Dx
The Increased Importance of Advances in Engineering and Computing in Healthcare Delivery
On Body: In Body (OBIB) Sensors for Real Time and Remote Monitoring of Individual Health Status
OBIBs and Body Area Networks (BAN’s) for Remote Monitoring of Health

- design standards
  - IEEE Task Force TG6 802.15
- privacy and security standards
On Body: In Body Sensors and Devices

Healthcare

**Application**
- remote monitoring of health status

**Objectives**
- proactive alerting and intervention to mitigate health incident
- coupled linkage to Rx dispensing for efficient disease control
- enhanced autonomy for in-home aged
- monitoring of patient compliance
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)
Smart Pills and Smart Containers: Improving Patient Compliance

- high definition logos and bar codes
- electronic ID
- covert chemical taggants
- pearlescent coatings
- RFID tags
Assessment of New Technology and Outcomes

- $2.3 trillion healthcare economy
- $110 billion R&D investment
- $0.9 million on technology assessment
- lack of investment to establish practical metrics for longitudinal assessment of quality, outcomes and value
- continued investment in low-priority/high cost care over high-benefit care exacerbates current market distortions
- new incentives
  - superior clinical and economic outcomes via coordinated care in chronic disease
  - shift focus from reimbursement of uncoordinated procedures/interventions to rewards for disease mitigation and wellness
Information-Based Medicine
Paper-Based Medical Records: Fragmented Care, Unacceptable Errors and a Major Hurdle to Performance Analysis
Interoperable EMR is a Critical Enabler

Data Sources
- Hospitals
- Clinics
- Labs
- Claims Processors

ROBUST DATA
- Longitudinal
- Real-time
- Clinical & Financial

Real World:
- Research
- Safety Surveillance
- Product Effectiveness Studies

TRUSTED, EVIDENCE-BASED KNOWLEDGE
Transparency drives change in behaviors and business models

Providers
- Delivery of care based on evidence

Payors
- Reimbursement based on real-world product effectiveness

Consumers
- Early and affordable access and better informed decisions

Regulators
- Earlier detection of product safety & efficacy issues

Manufacturers
- Early and affordable evidence to support reimbursement for innovation
Managing the Economic and Clinical Impact of Aging Demographics and Complex, Chronic Conditions
Challenges in the Management of Complex Chronic Conditions and Co-Morbidities

- multiple conditions
- multiple treatments
- multiple providers
- multiple medications
- multiple coding and reimbursement policies
Consumer Directed Healthcare Plans

“Until the person receiving the product is responsible in some fashion for the costs, there will be no incentive to spend responsibly”

Scott Serota
CEO, BCBS Association of Chicago
Chief Executive Magazine, March 2007 p. 50
After a Short Stay in America, Michelangelo's David Returned to Europe
The Case for Wellness

- 30-60% of health plan claims are related to health risks that are modifiable by nutrition, exercise, stress reduction, etc.

- Well-managed employer health and productivity management programs return $6-15 for every dollar spent.

- Cost of smoking: healthcare cost of smoking over a lifetime = $220K per person = $40 in healthcare cost per pack of cigarettes smoked!

- 67% of the US population is overweight or obese, and 22% of current healthcare costs are obesity-related.

Source: Wellness Councils of America
Personal Medical Records (PMRs)

Promoting Wellness
Telecommunications and Media Industry Convergence: Implications for Healthcare
The Infocosm: Emerging Networks of Global Connectivity
A Burgeoning Infocosm and An Expanding Metaverse

- ubiquitous sensor networks
- connectivity from deep blue to deep space to inner space
  - everything is a reporter
  - everything goes everywhere
  - everybody sees everything
  - everything moves fast
Herd Behavior: 1.3 Million Bathers, Coney Island 1951

Herd Behavior: 2008 Social Networks and Virtual Communities

The Changing Nature of Social Interaction
Consumer-Directed Healthcare

- leveraging social-and peer-networks
- increased role of fitness industry and entertainment in healthcare
  - “success via distraction”
- “virtual touch”
  - web-based medical consultation and diagnostic algorithms
  - generational gap in need for physical interaction with physician
we see
one doctor, many experts.

Microsoft is partnering with industry leaders to develop the health care system of the future. By creating a seamless national network that provides a more efficient flow of medical information, health care providers are better informed, patients better served. Find out more at microsoft.com/potential.
A New Healthcare Ecosystem Arising From Technology Convergence

Integrated Technology Platforms

Data Mining and Integration Services

Increasingly Targeted Care and Efficient Use of Finite Resources
The Coming Era in Healthcare

- dramatic (unprecedented change)
- discontinuity (new technologies)
- demographics (graying societies)
- dislocation (markets, physician training)
- disaggregation (vertically-integrated business)
- dependency (new inter-relationships)
- data (R&D, outcomes and standards of care, risk management)
- Darwinian (new competitive pressures)
Into the void
The Coming Convergence in Healthcare Delivery
The Coming Convergence in Healthcare Delivery

Technologies
- medicine, engineering, computing

Clinical Practice
- molecular medicine and increasingly customized care
- diagnostic, drug and device combinations
- POC testing

Performance
- outcomes and comparative effectiveness
- reduced error and improved compliance

Realigned Incentives
- integrated care for complex chronic diseases
- earlier disease detection and risk reduction
- wellness versus illness
- health status monitoring
The Coming Convergence in Healthcare Delivery

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

Connectivity
- integrated care networks for chronic disease
- social networks and informed consumers
- new supplier networks of specialized turnkey expertise
- value added ‘content’ services for clinical data mining
Re-Inventing the Pharmaceutical and Biotechnology Industries

- changing the industry versus changing with the industry
- escaping the myopia of current markets and investor horizons
- organizational re-structuring and process re-engineering are insufficient for survival
- imagination not imitation
- creation of unimagined products, services and businesses
  - integration of Dx, Rx and Ix
- creating new competitive space
The Traditional Business Model for Pharmaceutical Companies

Corporate Platforms
- strategy
- R&D
- marketing
- finance
- legal

Global Markets
- wholly owned business units
- alliances
Creating a New Network of Connected Expertise to Accelerate Innovation in Healthcare R&D

- ever faster generation of new information
- current R&D ecosystem is too fragmented to fully leverage novel content and shared learning
- rise of new business models of ‘expertise networks’ that eclipse current monolithic single company innovation models
The Rise of Open-Source Networks and Consortia

- NCBI
- Entrez, The Life Sciences Search Engine
- ToPaz
- PLoS one
- caBIG
- Cancer Biomedical Informatics Grid
- International HapMap Project
- ALLEN INSTITUTE for BRAIN SCIENCE | Allen Brain Atlas
- W3C
- World Wide Web Consortium
- PubMed
- The Cancer Genome Atlas
- Science Commons
- The Neurocommons
- Critical Path Institute
- Improving the Path for Innovative Therapies
- PGRN
- Creative Commons
- NCI Biomarkers Consortium
- Clinical Semantics Group

FDA/Severe Adverse Events (SAE) Consortium
Virtual Pharma: New Organizational Models for Leverage of Open-Source Services

- PharmaCommons: integration of rapidly expanding open-source datasets
  - discovery, toxicology, clinical trials
- network of web-based turn-key contract services
- China/India/other low cost sites will dominate
- worldwide pricing/parallel importing from lowest priced countries
- patents devalued
- new role of BigPharma as integrator to generate value across the entire disease episode spectrum
  - wellness to terminal care
The Extended Enterprise: Sustaining Competitiveness in an Era of Technical and Commercial Convergence

- Core Corporate Platforms
- Wholly owned retained businesses
- Integration with Diagnostics Devices and Healthcare Information Services
- M&A JVs NewCo’s
- Rx Co’s
- Networked Rx Co’s
- SpinCos, NewCos, JVs
- Constantly changing sourcing patterns of contract expertise
Building Health Technology Networks

- extended enterprise design: the next competitive frontier
- transition of vertically-integrated industries into horizontally-integrated ecosystem of alliance networks
- web-based routing and tracking of materials and knowledge for competitive capture (time/scale) of turnkey expertise centers
- agility in managing the choreography of ever shifting alliance networks as a core competency
Healthcare Information Networks: AORTA: Always On Real Time Access

- end-to-end continuity in use of internet and wireless technologies
- from routine remote monitoring of health status to advanced critical care

- comprehensive connectivity
  - plus
- collapsing time
  - plus
- global networks
From Ambiguity to Certainty: Competitive Superiority via Analysis of a Burgeoning Infocosm

- new intermediaries for analysis/packaging of healthcare data
- global sourcing of data and expertise
- lower transactional costs
- higher efficiency in use of expensive, finite resources
- increasingly predictable cost structure and predictable performance of products and procedures
- improved clinical and economic outcomes
Building The Strategic Platforms for Integrated Healthcare Delivery

Rational Therapeutics and Personalized Medicine
Optimum Use of Costly Resources
Wellness versus Illness

earlier detection and prevention of disease episodes
coordination of care for complex chronic diseases.
Innovation for Global Challenges