

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

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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**

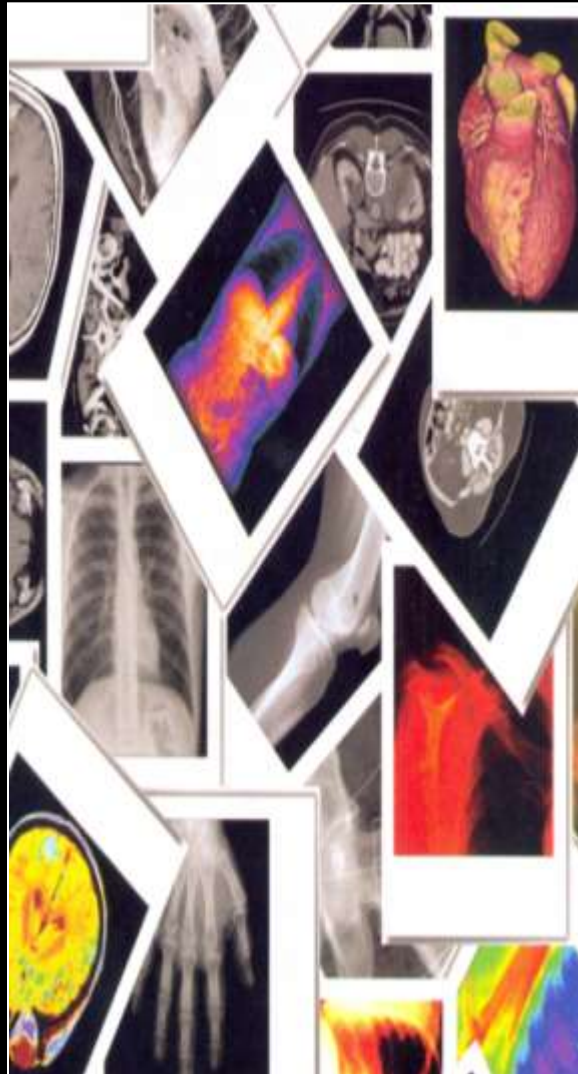
## Five Chronic Diseases Impose the Highest Cost in Healthcare Expenditures

- diabetes
  - CAD
  - CHF/COPD
  - asthma
  - depression
- 
- 70% total healthcare costs
- cancer = 8%
  - infectious diseases = 7%
  - trauma = 6%
  - ob/gynec. = 4%
  - bone and joint care = 2%

# **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

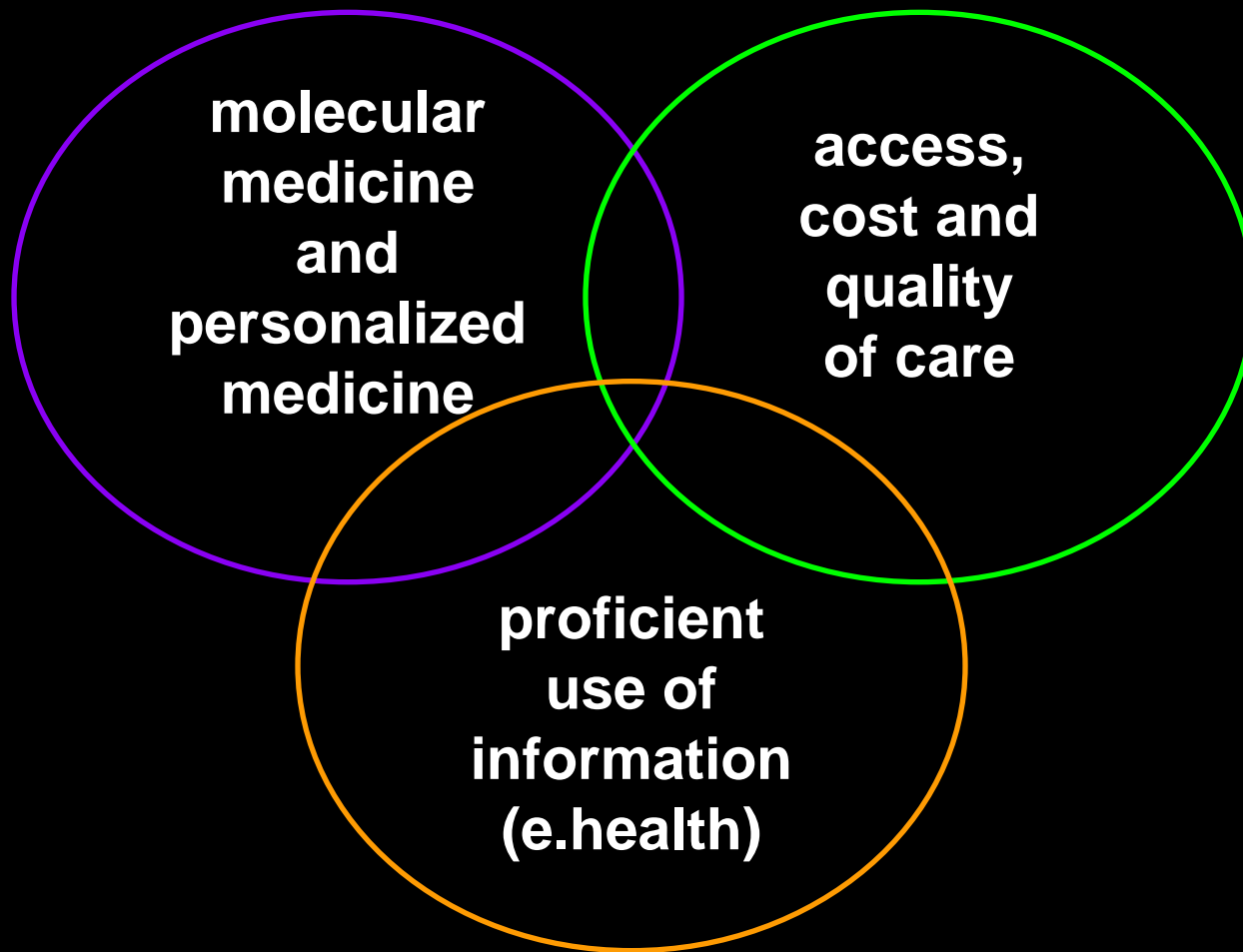
- **Economic Unsustainability**

or

**Reform and Rational Care**

**Confronting the Imbalance Between Infinite Demand and Finite Resources**

# The Three Forces Shaping the Evolution of Healthcare



**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

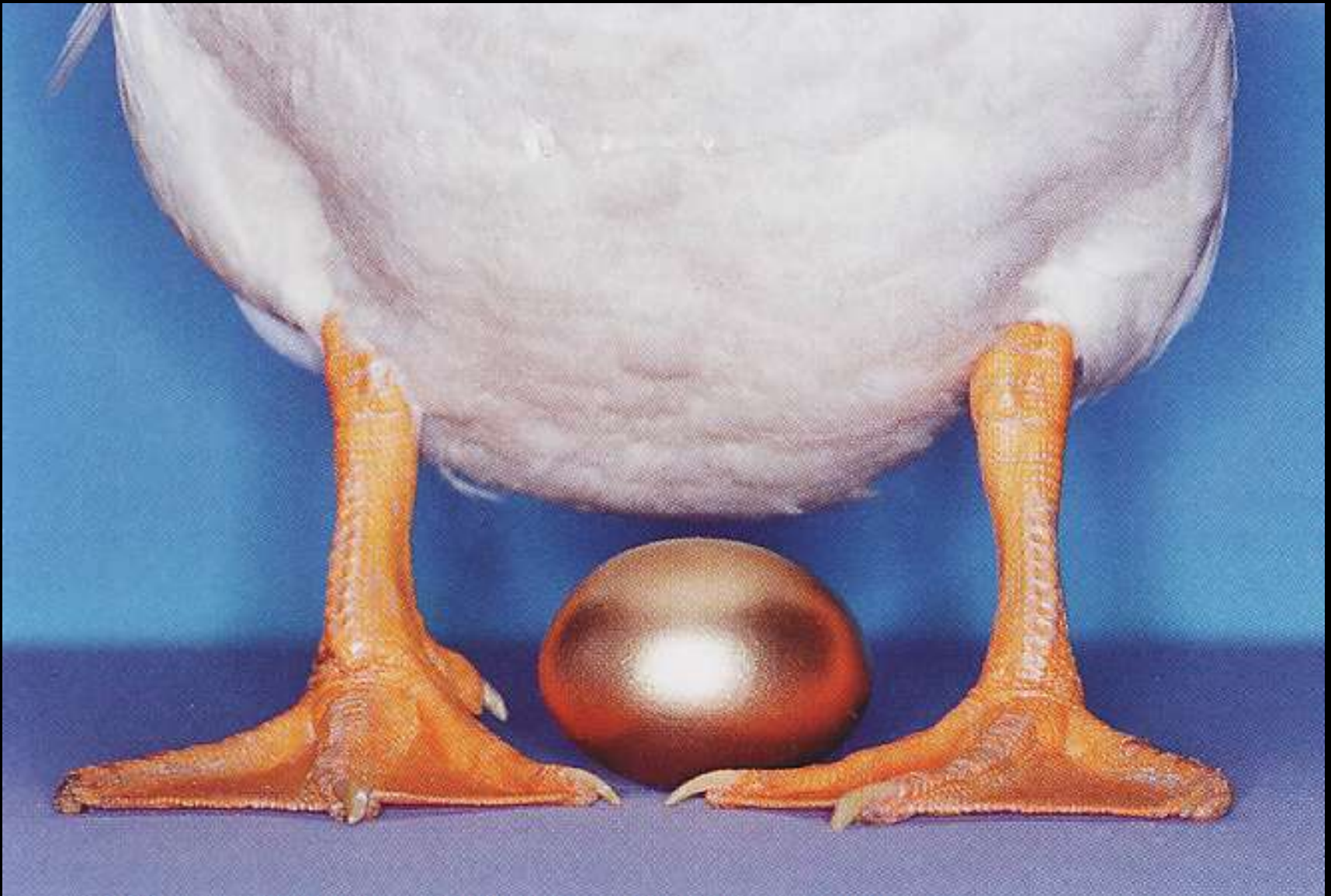


- diseases are not uniform
- patients are not uniform
- a “one-size fits all” Rx approach cannot continue



- inefficiency and waste caused by empirical Rx
- cost of futile therapy
- medical error and AEs

# The 'Blockbuster Drug' Business Model





**AVASTIN**  
(bevacizumab)

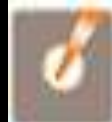
**Rituxan**  
*Rituximab*



**Herceptin**  
trastuzumab



**Tarceva**  
erlotinib  
tablets



**gleevec**  
(imatinib mesylate) tablets

**ERBITUX**<sup>TM</sup>  
CETUXIMAB INJECTION

**Tykerb**<sup>®</sup>  
(lapatinib)



**Nexavar**<sup>®</sup>  
(sorafenib) tablets



**Revlimid**<sup>®</sup>  
(lenalidomide) capsules



**SUTENT**<sup>®</sup>  
capsules

# Personalized Medicine



**“If it were not for the great variability among individuals,  
medicine might be a science, not an art”  
Sir William Osler (1892)**

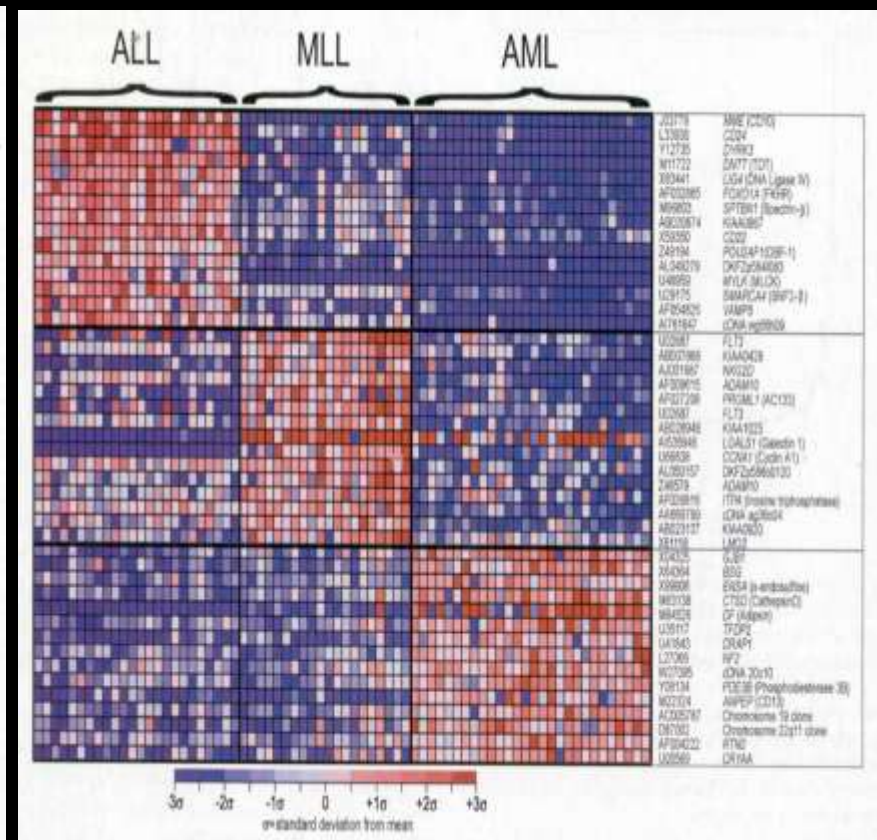
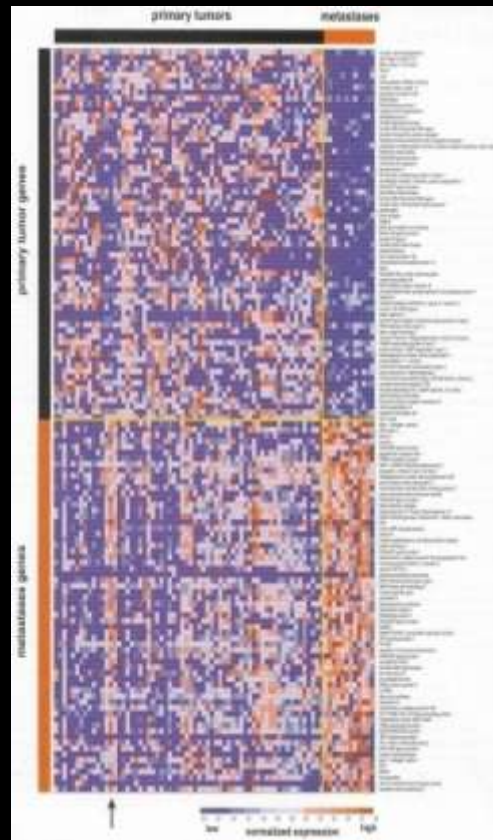
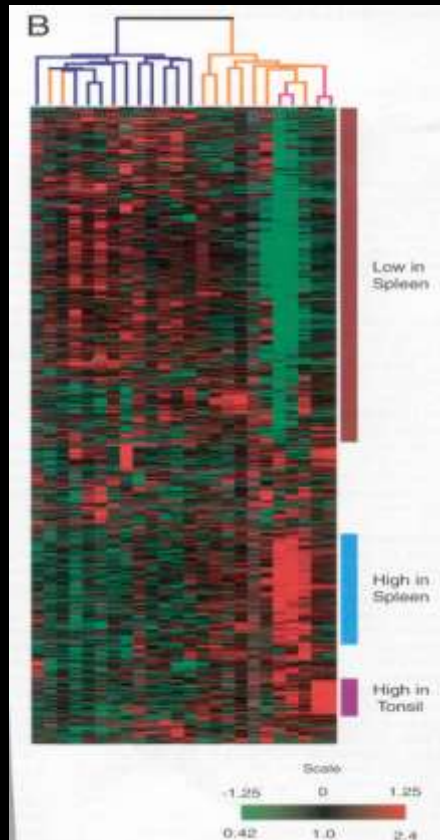
**Osler Reframed**

**“Because of the great variability among individuals,  
medicine **must** finally become a science, not an art”**

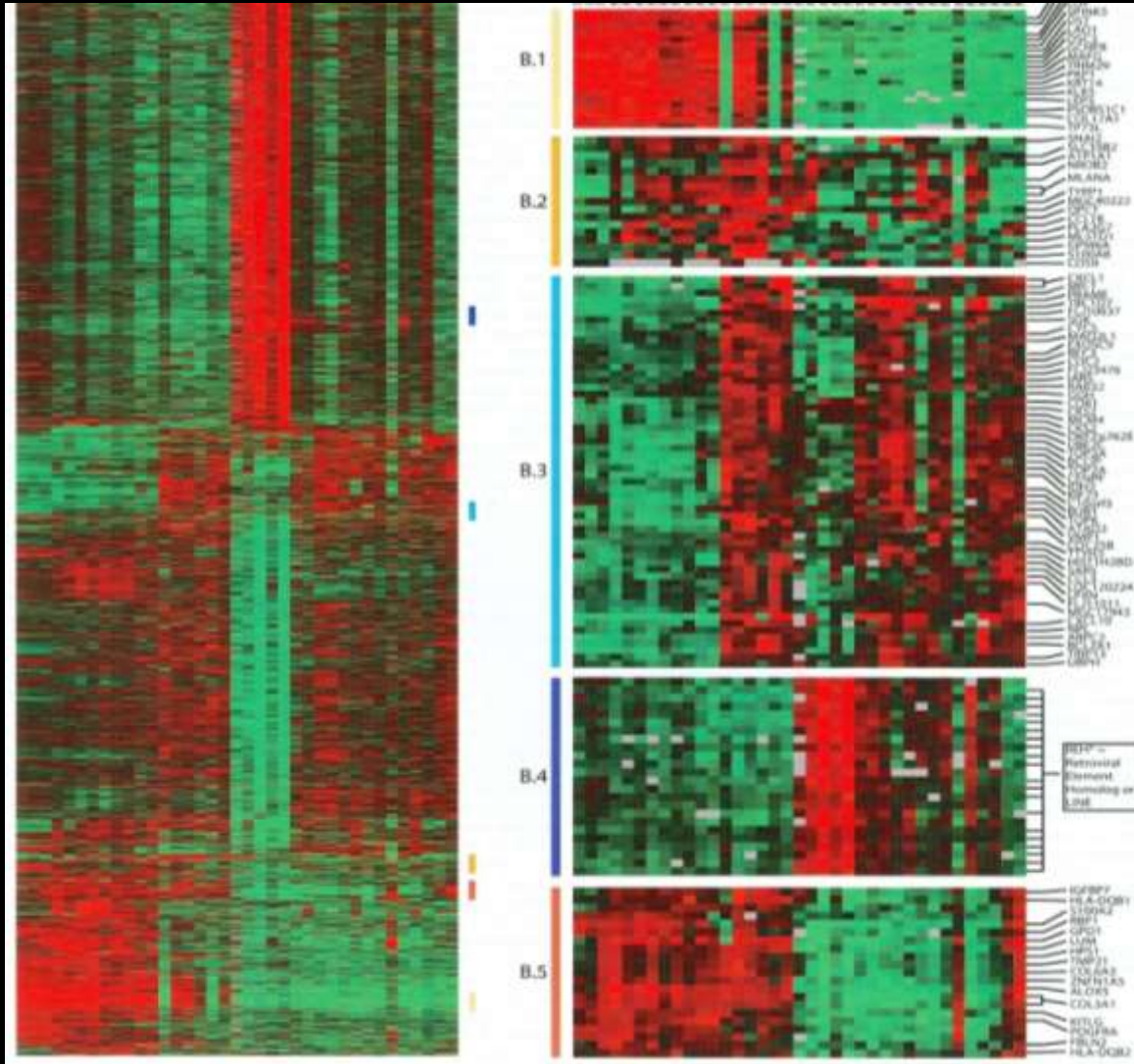
## US Healthcare Costs

- administration 35%
  - personnel costs 35%
  - procedures 18%
  - drugs 12%
  - in vitro diagnostics 0.01%
- 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

# RIGHT Rx for RIGHT DISEASE SUBTYPE

**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

**SELZENTRY™**  
(maraviroc) tablets



**trofile™**  
CO-RECEPTOR TROPISM ASSAY

biosciences  
**monogram**  
The Mark of  
Individualized Medicine

**CAMPTO®**  
irinotecan



Invader® chemistry

THIRD WAVE  
TECHNOLOGIES

**COUMADIN®**  
(Warfarin Sodium Tablets, USP) Crystalline  
1 mg 2 mg 2.5 mg 3 mg 4 mg 5 mg 6 mg 7.5 mg 10 mg



Bristol-Myers Squibb

Verigene® System



Nanosphere

5-Fluorouracil

tablets  
**Xeloda®**  
capecitabine



**TheraGuide 5-FU®**

A test to predict toxicity to 5-FU/capecitabine-based chemotherapy



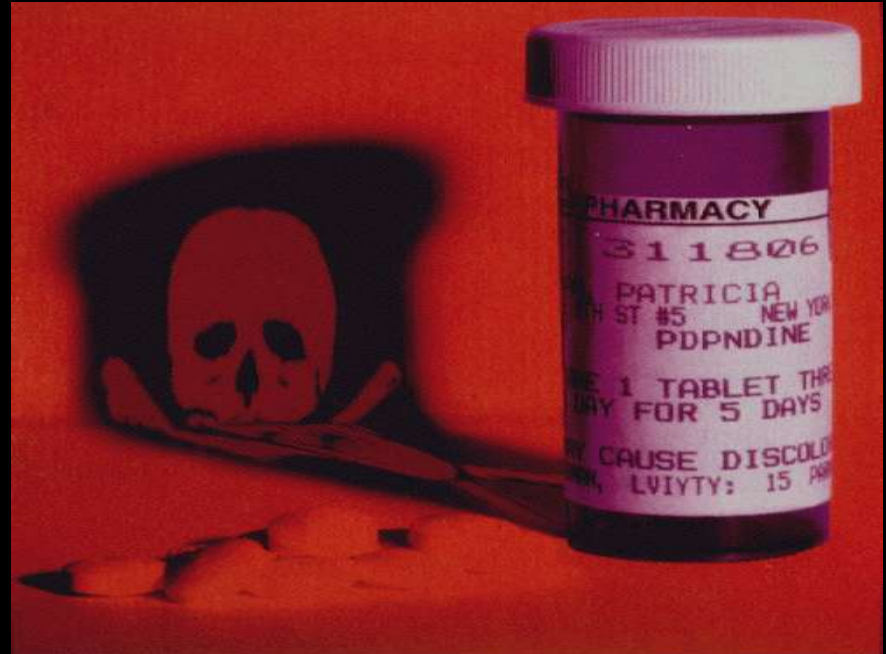
MYRIAD®

**Vectibix™**  
(panitumumab)

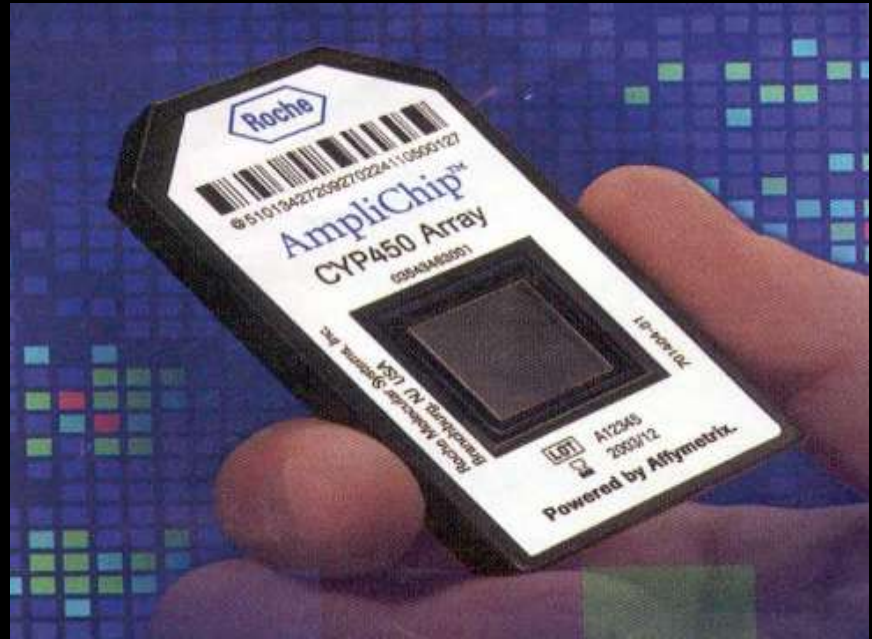
**AMGEN**

**DxS** Diagnostic  
Innovations

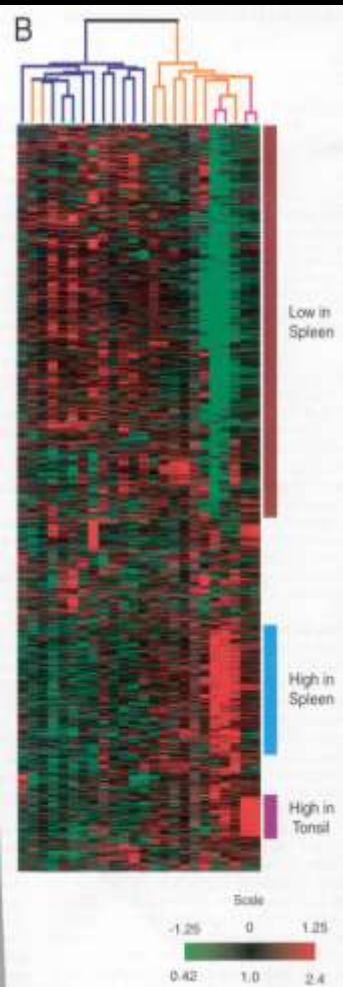
# Pharmacogenetic Predisposition to Adverse Drug Reactions



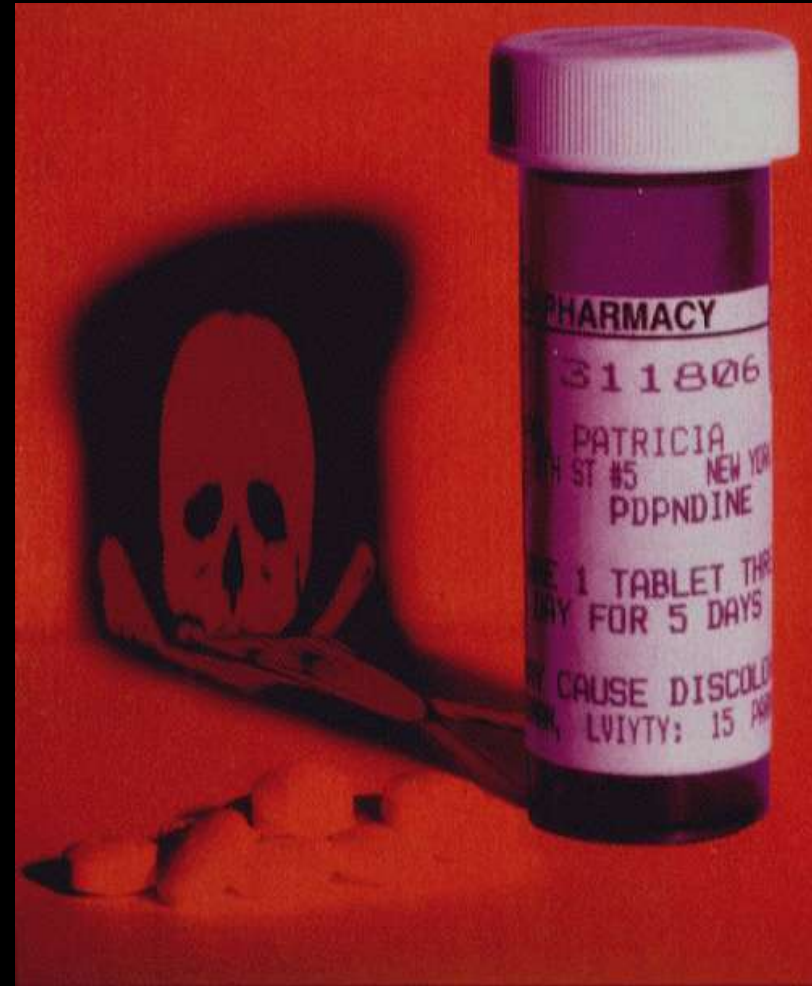
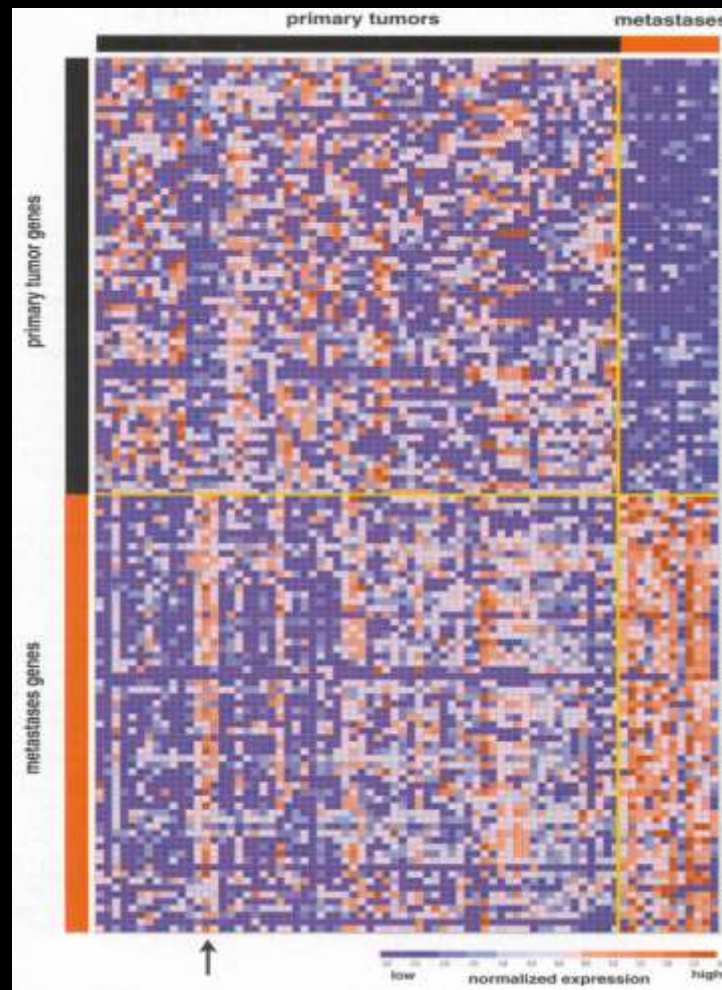
- 1.5 to 3 million annual hospitalizations (US)
- 80 to 140 thousand annual deaths (US)
- est. cost of \$30-50 billion



# Personalized Medicine: From Pharmaceuticals to Pharnasuitables



**Disease Subtyping:  
Right Rx for Right Disease**



**Reduction of Adverse  
Drug Reactions**



Diagnostic Products Corp.

\$1.86 BL



Bayer HealthCare

Diagnostics Division

\$5.31 BL





\$230 MM



AmeriPath®

\$2 BL





\$185 MM





\$350 MM





\$120 MM





\$346 MM





NEW DIMENSIONS IN DIAGNOSIS





epigenomics





\$283 MM






illumina®  
making sense out of life



\$57 MM



\$89-3 MM



invitrogen™



CELERA  
an Amgen Corporation Business



**\$600 million**

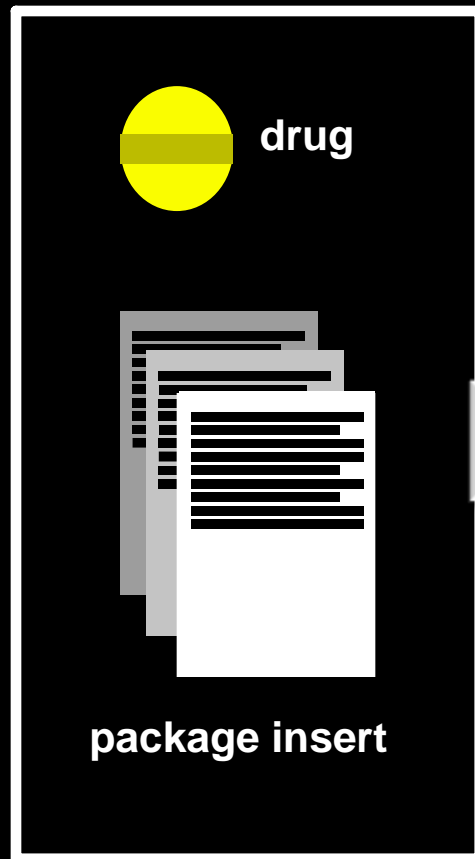


**\$3.4 billion**

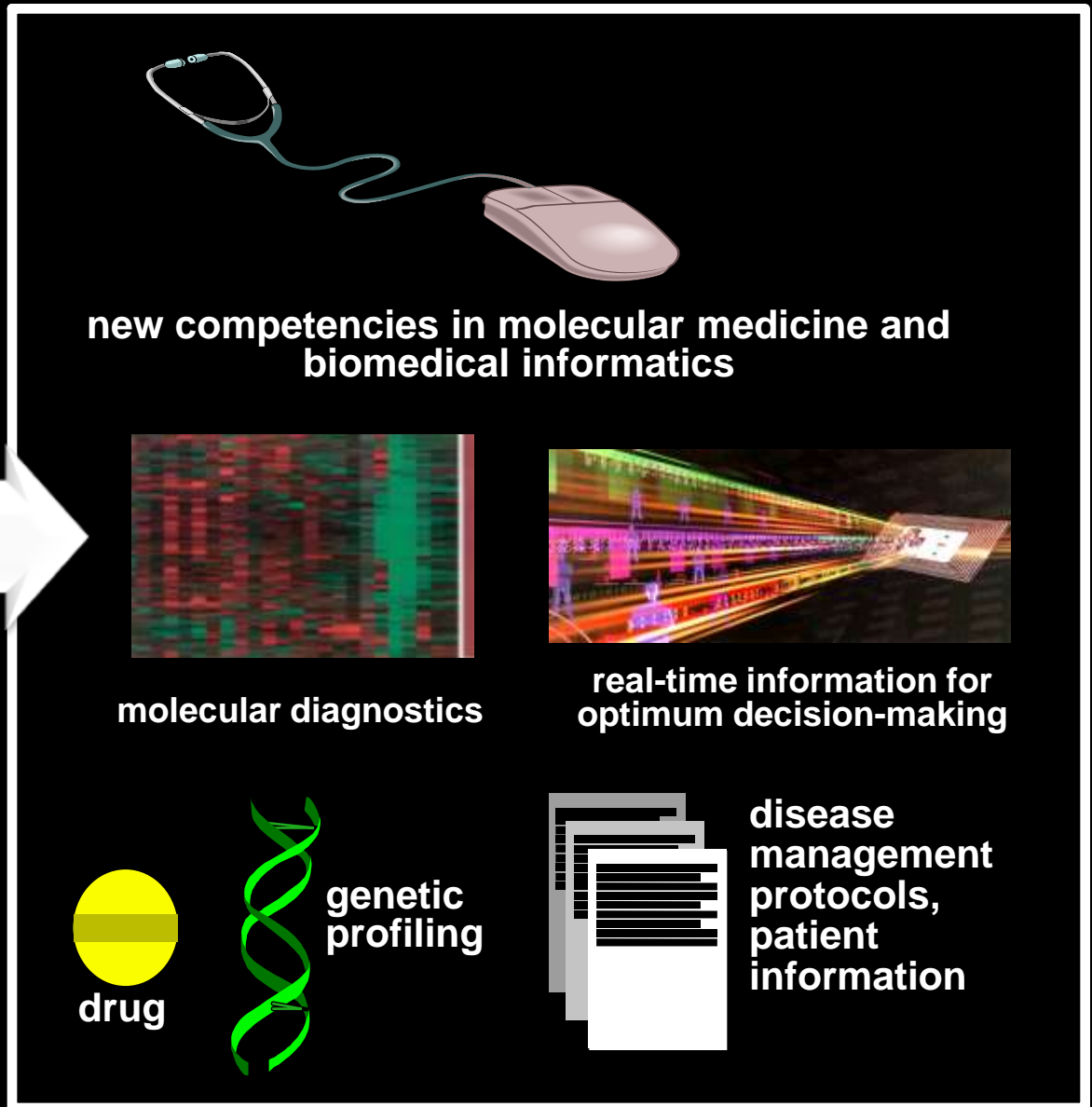


**\$1.18 billion**

# The Evolution of Molecular Medicine and Information-Based Medicine: The Foundation for Rational Care and Personalized Medicine



**Rx 2008**



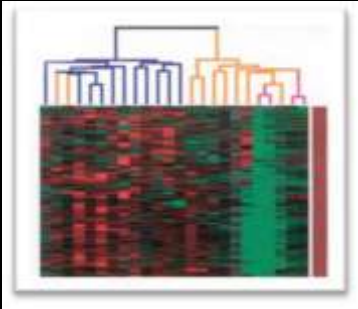
**Medicine 2018**

**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

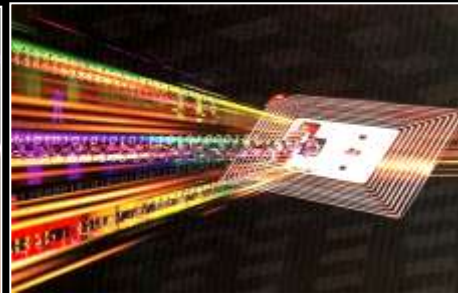
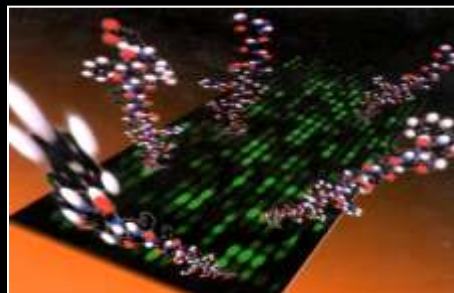
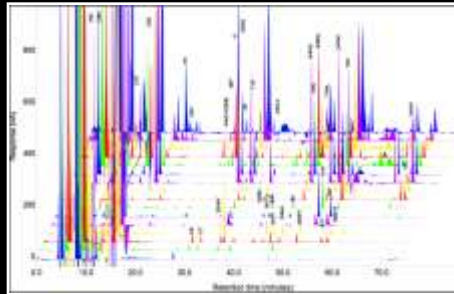
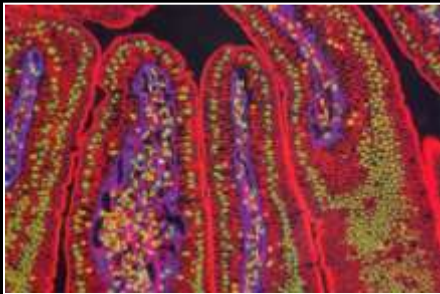


- wide variation in PGLs reported in different publications for claimed similar patients
  - minimal overlap between studies
- discriminatory power of classifiers not reproducible when tested on published cross-sets of samples
- trigger for new regulatory oversight and sophisticated validation protocols
  - 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**

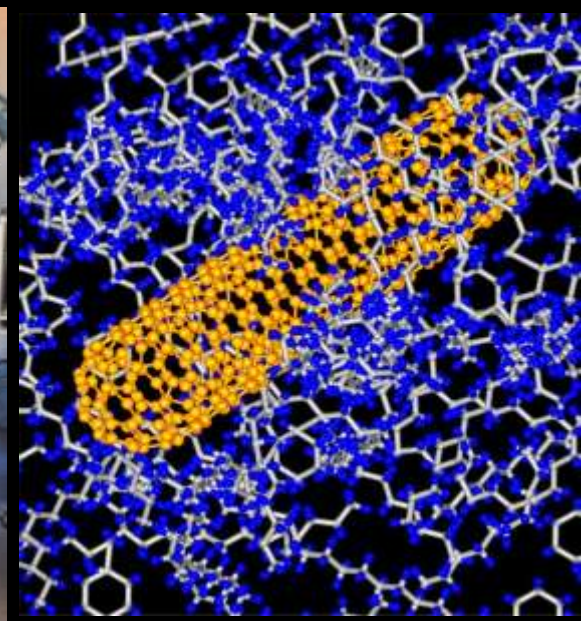
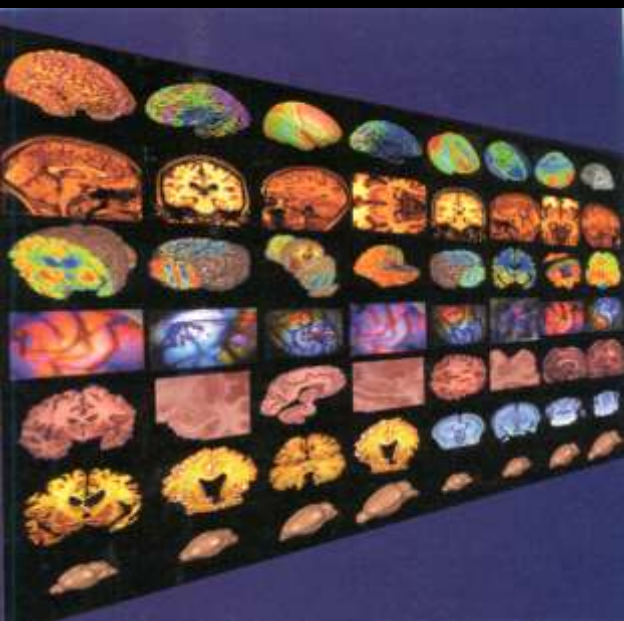
# Fundamental Issues in Clinical Validation of Biomarkers

- 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

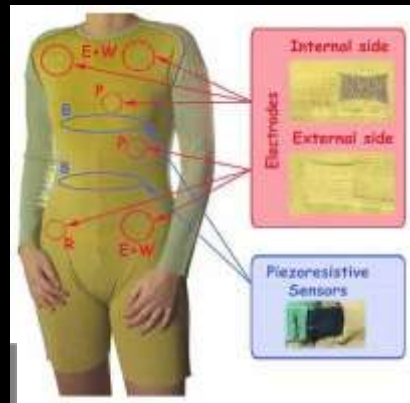
## **Reimbursement for Diagnostic Tests**

- **inadequate US Medicare coding and payment mechanisms**
  - **outmoded, 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**

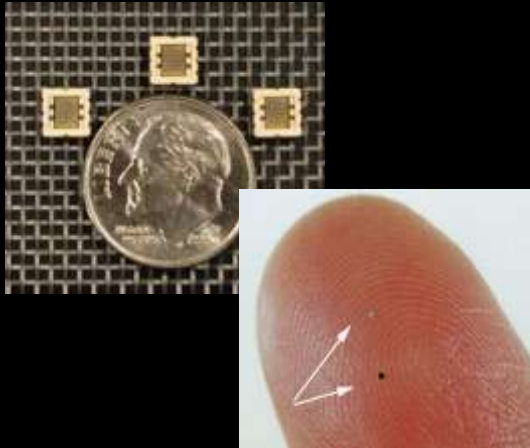
# The Increased Importance of Advances in Engineering and Computing in Healthcare Delivery



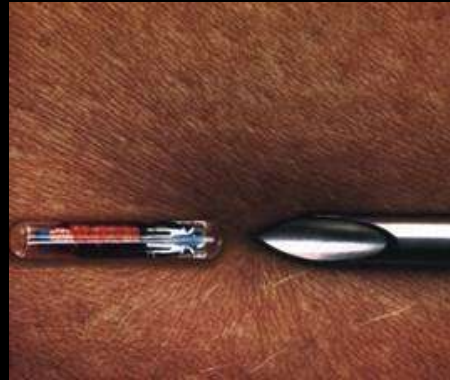
# On Body: In Body (OBIB) Sensors for Real Time and Remote Monitoring of Individual Health Status



# OBIBs and Body Area Networks (BAN's) for Remote Monitoring of Health



**Microtags**



**In-Body Wireless Tags**



**Environmental  
Sensors**

- **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)

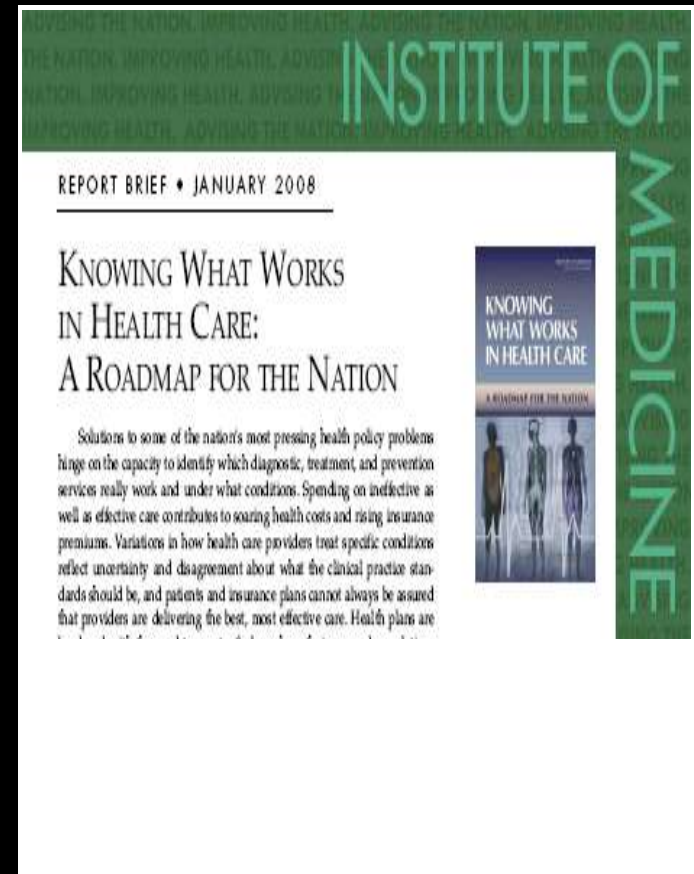
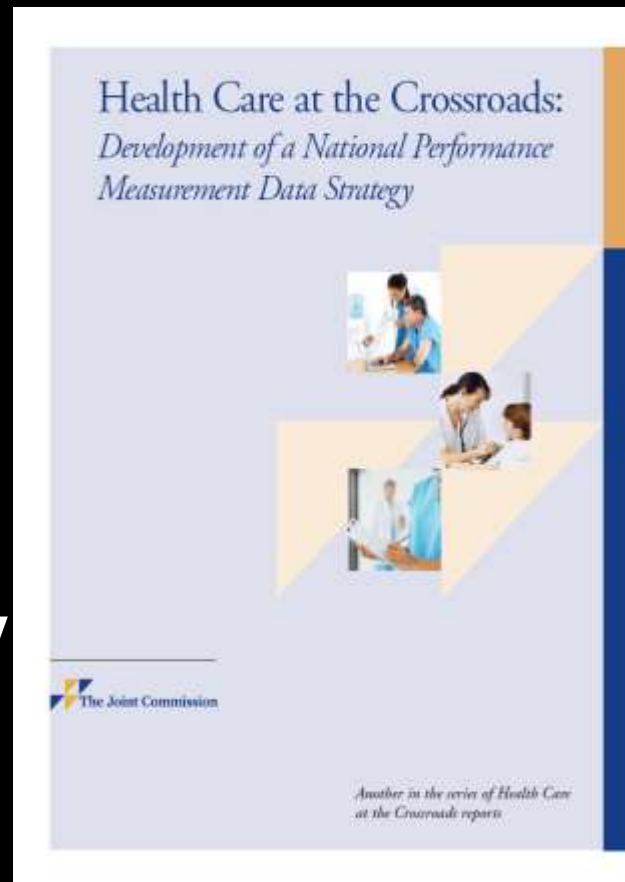
# Smart Pills and Smart Containers: Improving Patient Compliance



- 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

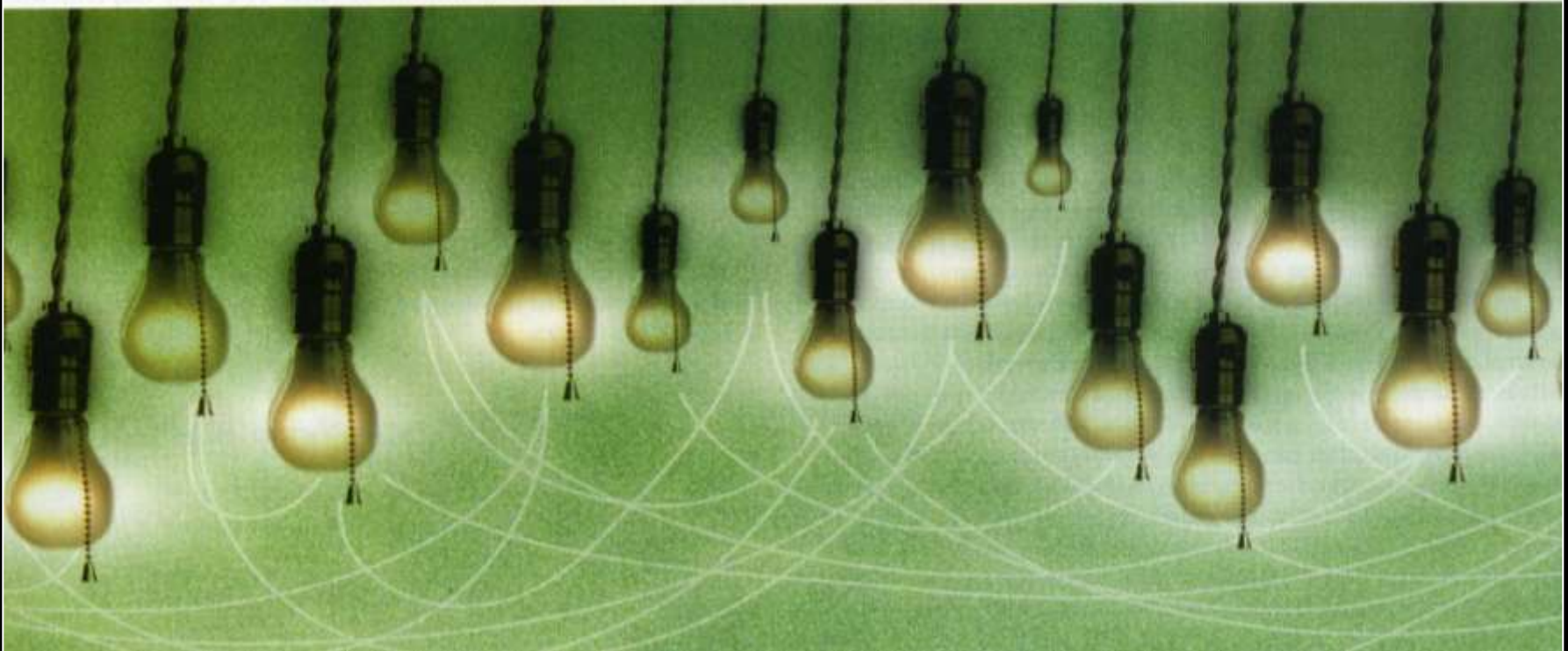


- **lack of investment to establish practical metrics for longitudinal assessment of quality, outcomes and value**
- **continued investment in low-priority/high cost care over high-benefit care exacerbates current market distortions**
- **new incentives**
  - **superior clinical and economic outcomes via coordinated care in chronic disease**
  - **shift focus from reimbursement of uncoordinated procedures/interventions to rewards for disease mitigation and wellness**

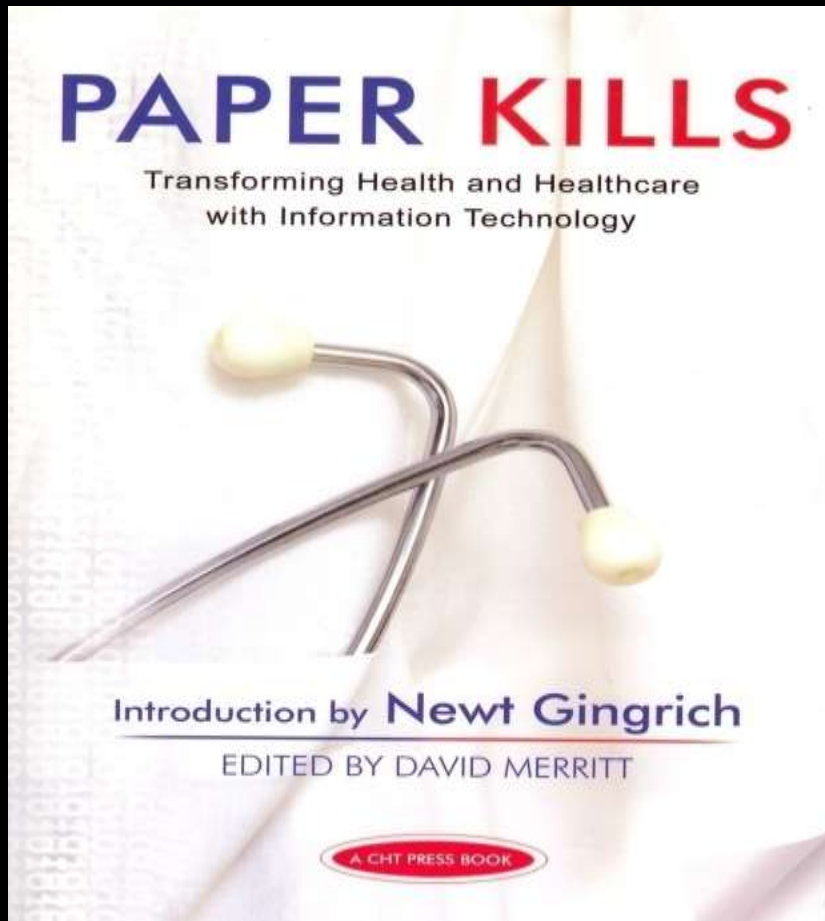
# Information-Based Medicine



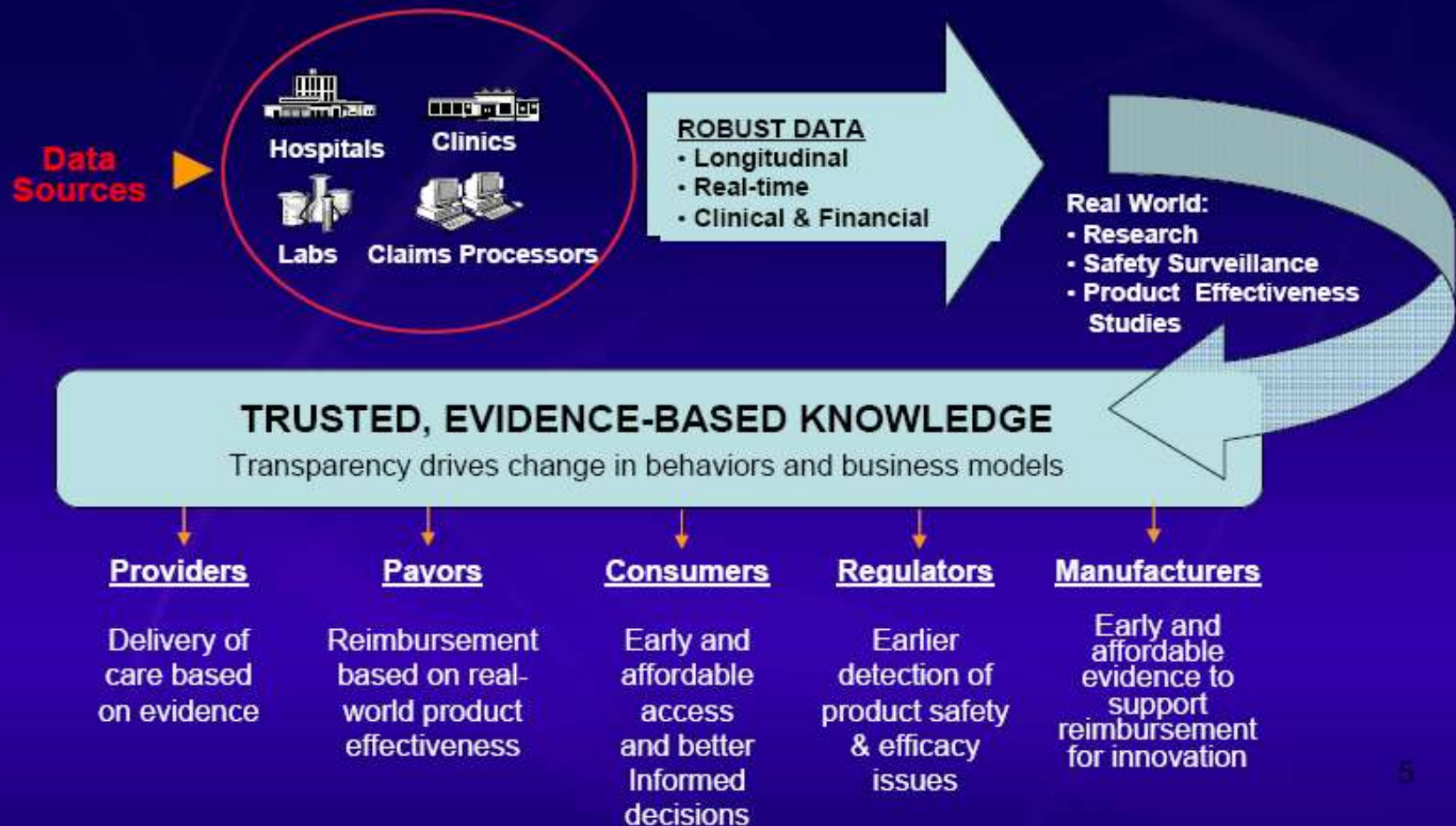
HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT



# **Paper-Based Medical Records: Fragmented Care, Unacceptable Errors and a Major Hurdle to Performance Analysis**



# Interoperable EMR is a Critical Enabler





# **Managing the Economic and Clinical Impact of Aging Demographics and Complex, Chronic Conditions**

# Challenges in the Management of Complex Chronic Conditions and Co-Morbidities

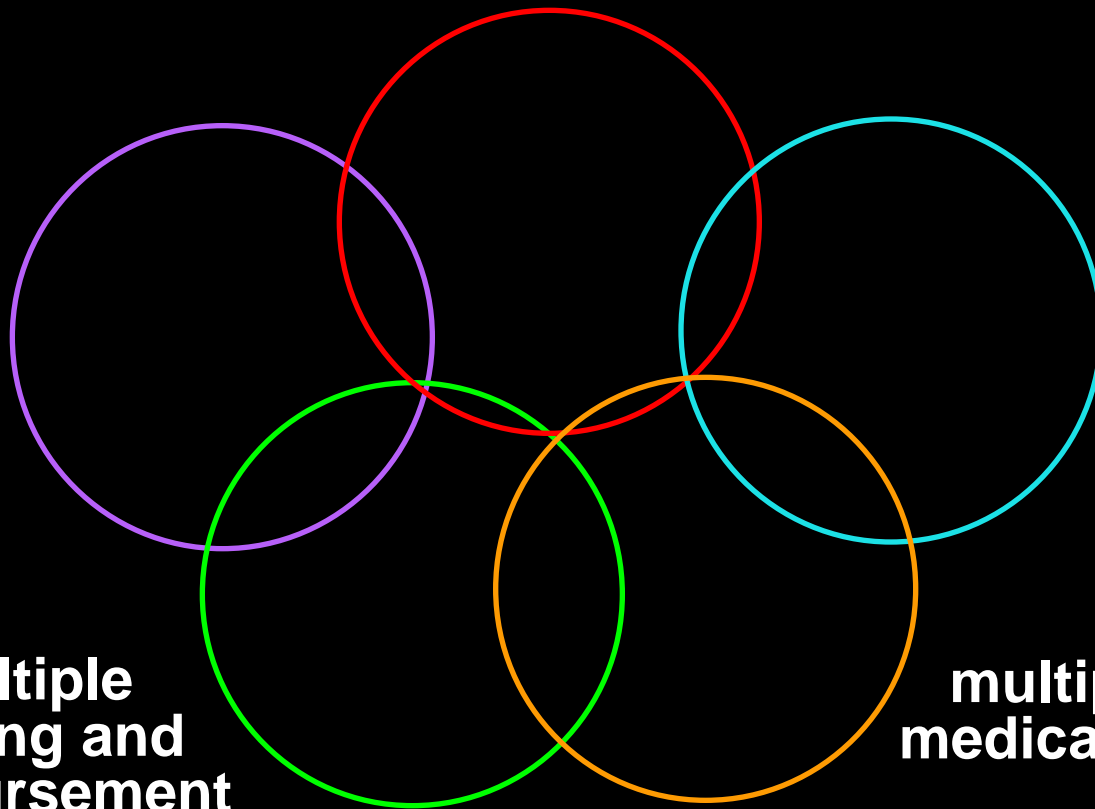
multiple conditions

multiple  
providers

multiple  
treatments

multiple  
coding and  
reimbursement  
policies

multiple  
medications



## **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**

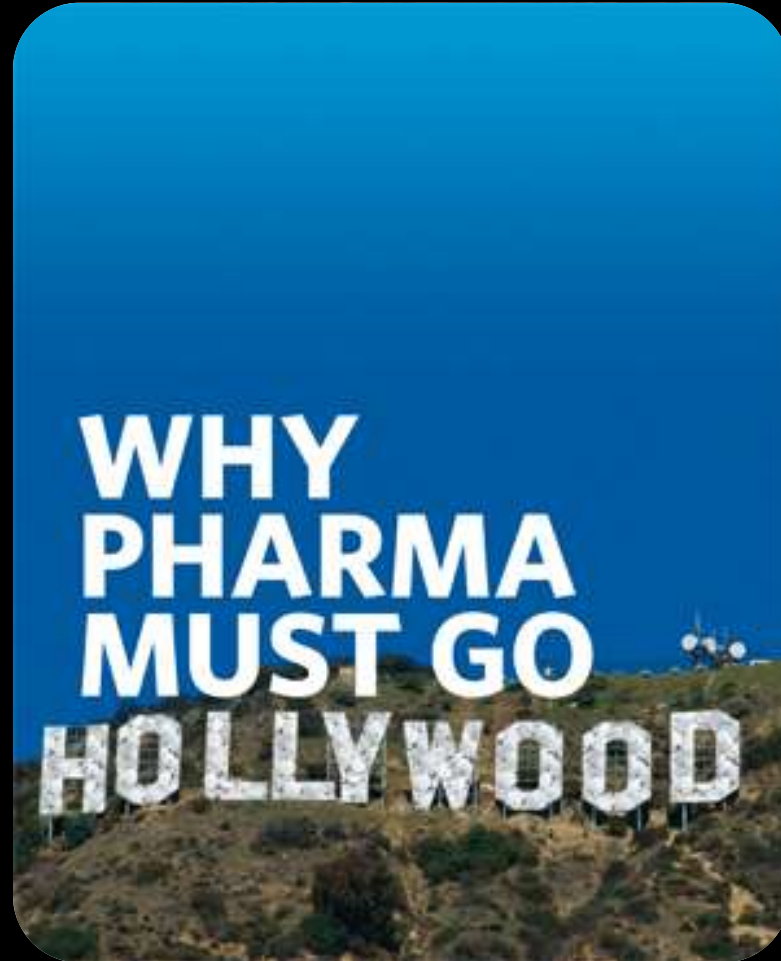
## Personal Medical Records (PMRs)



## Promoting Wellness



# Telecommunications and Media Industry Convergence: Implications for Healthcare



# The Infocsm: 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



# 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

*Walgreens*

As far as you want to go.™

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**WAL★MART®**

Save money. Live better.™



Your potential. Our passion.<sup>™</sup>  
**Microsoft**

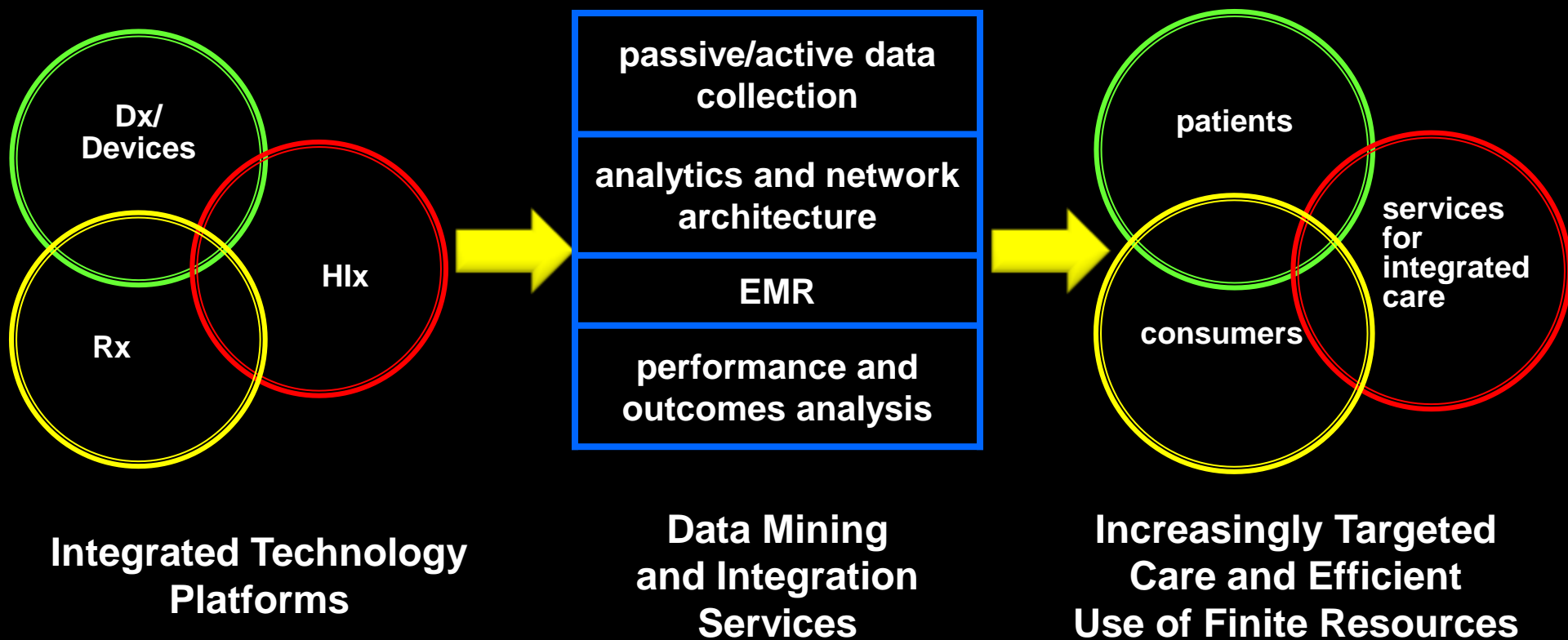


**we see**  
one doctor, many experts.

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](http://microsoft.com/potential)

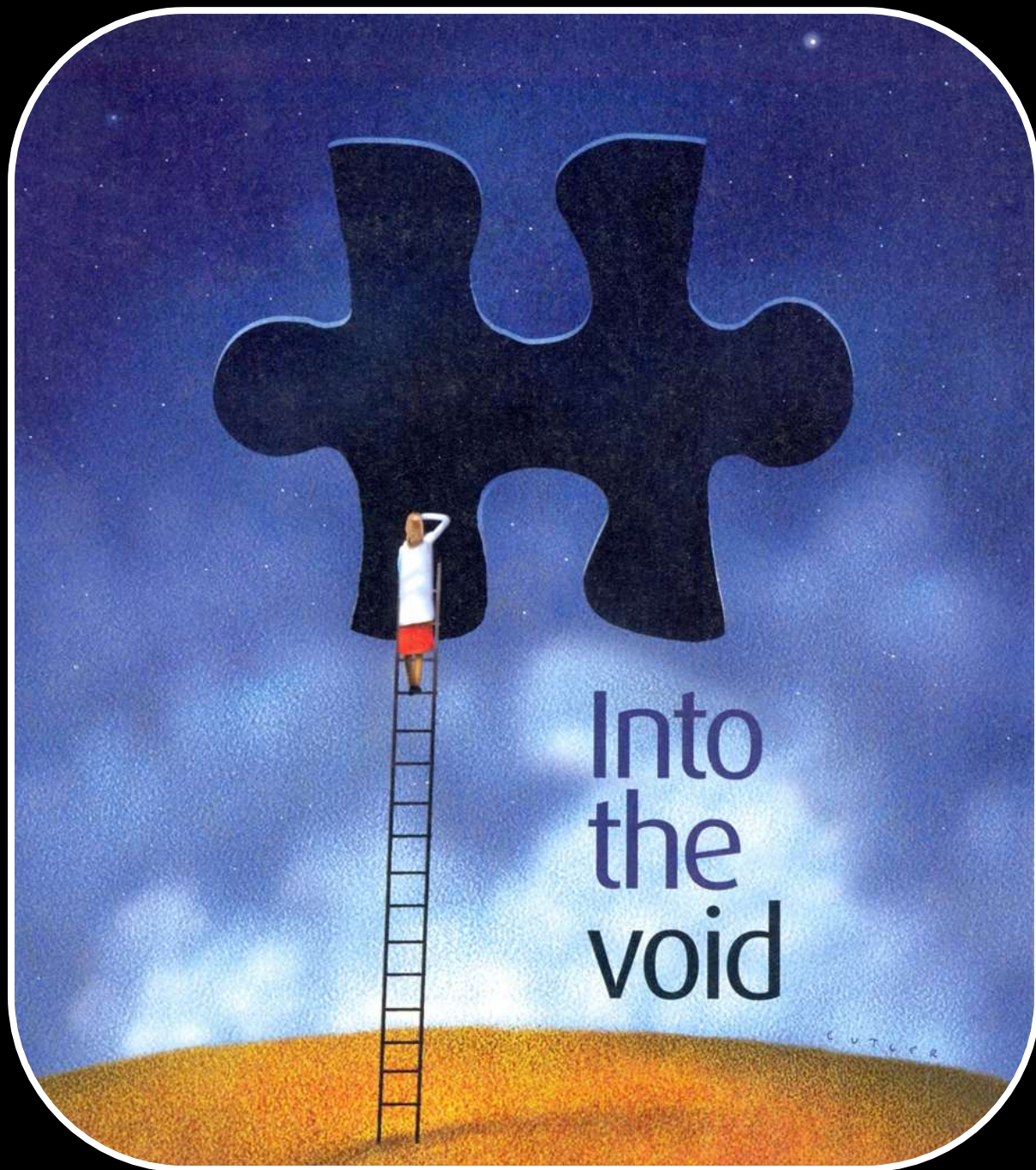


# A New Healthcare Ecosystem Arising From Technology Convergence



# 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

CUTLER

# 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**

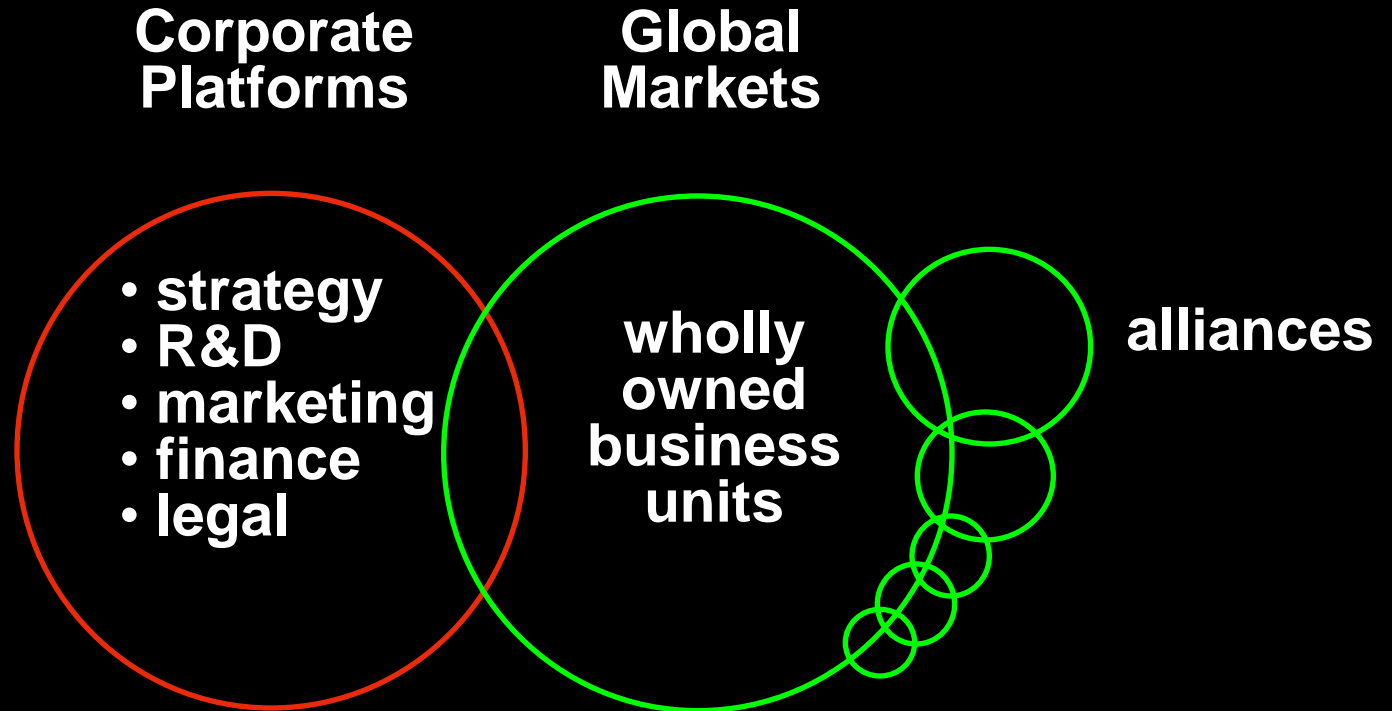
## **Connectivity**

- **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**

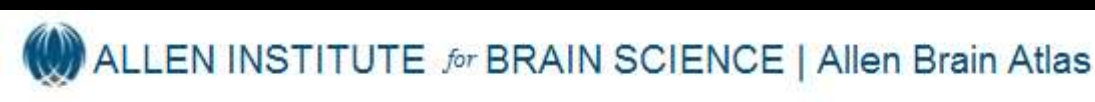
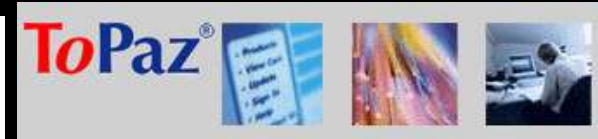
# The Traditional Business Model for Pharmaceutical Companies



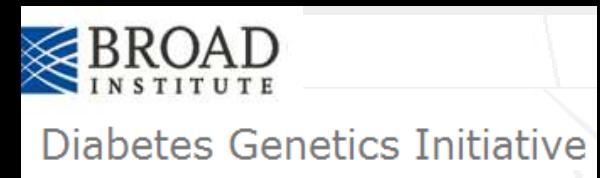
## **Creating a New Network of Connected Expertise to Accelerate Innovation in Healthcare R&D**

- **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



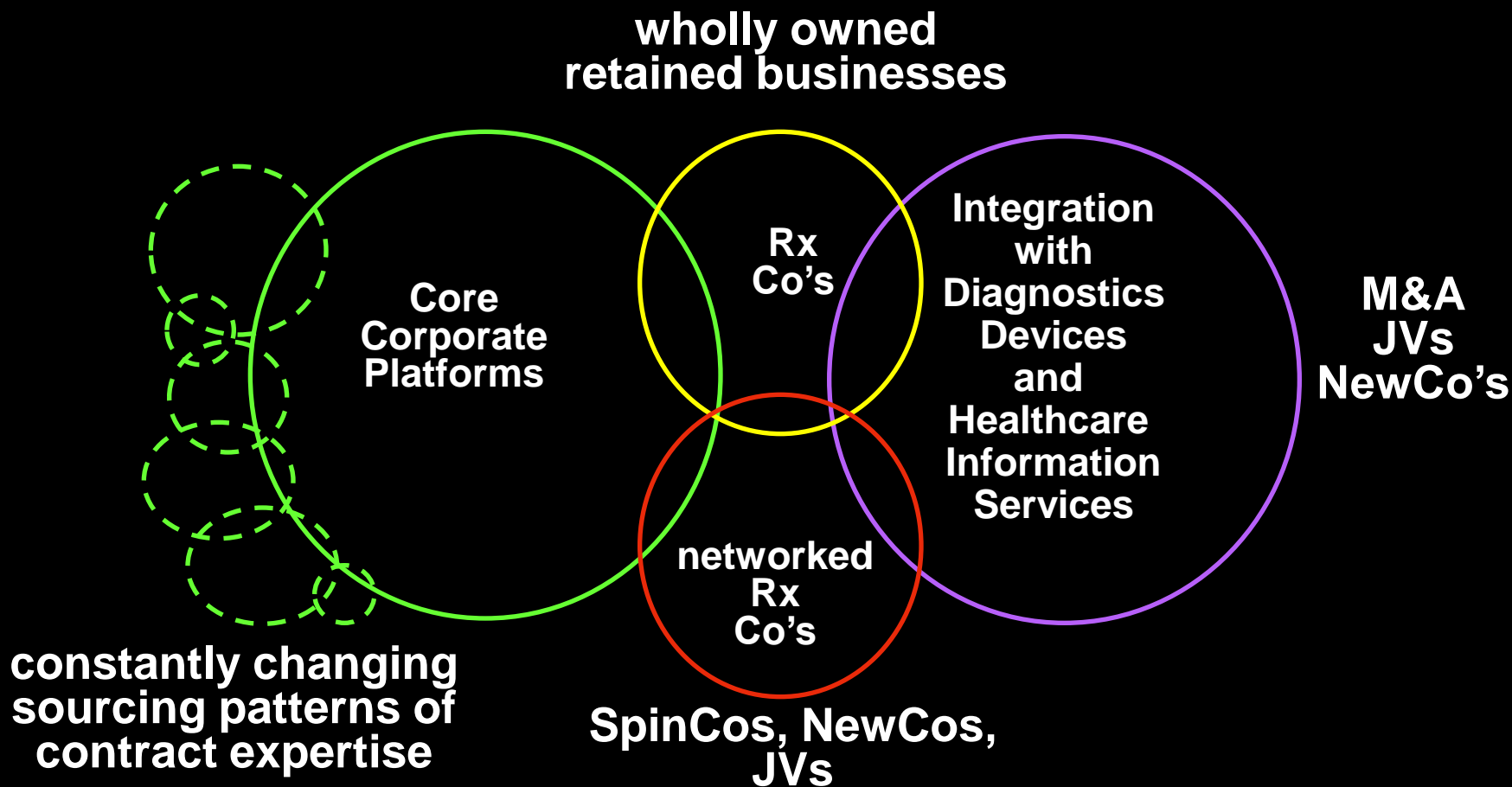
FDA/Severe Adverse Events (SAE) Consortium



## **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



## **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**

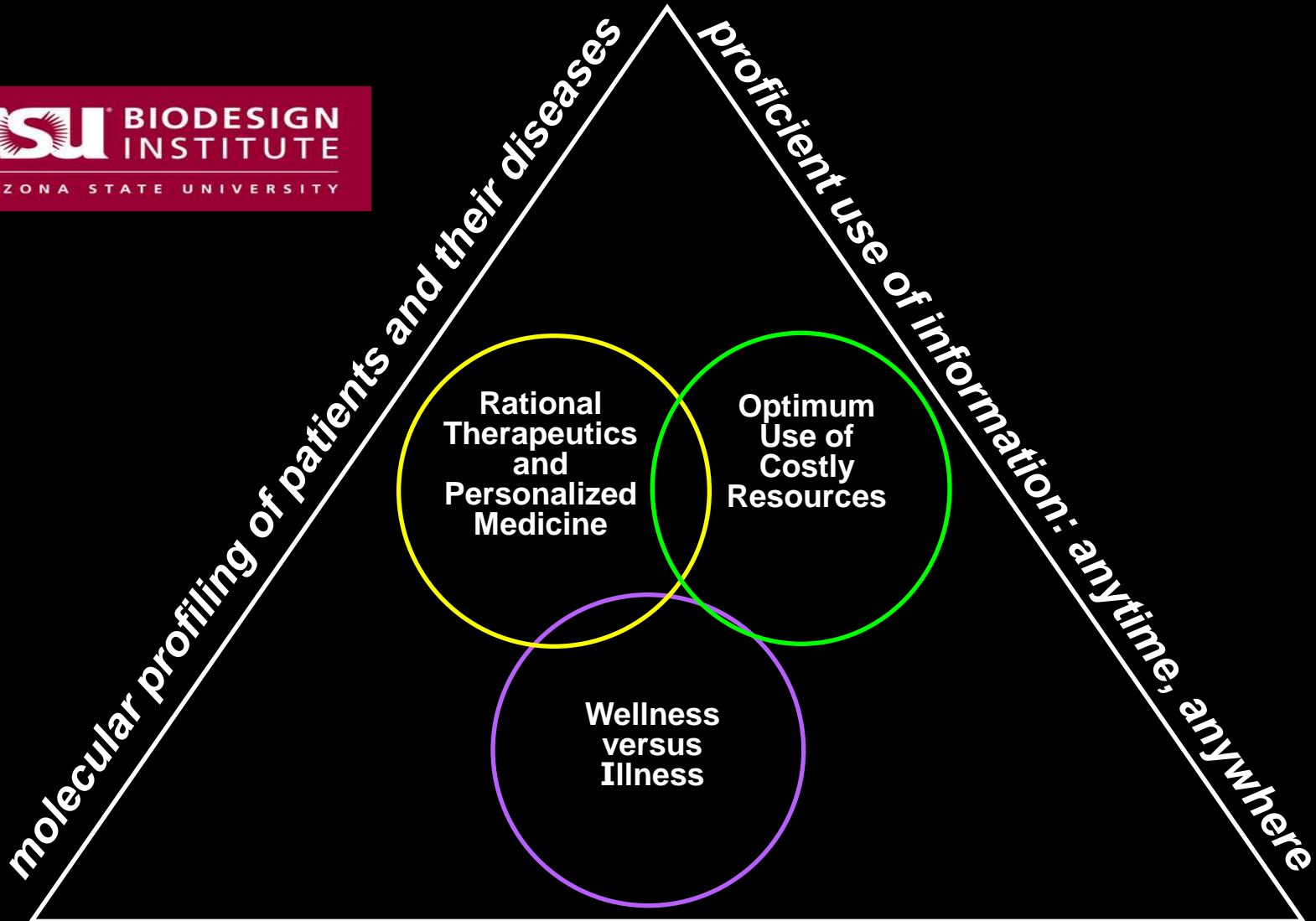
- **end-to-end continuity in use of internet and wireless technologies**
- **from routine remote monitoring of health status to advanced critical care**

- **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





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**Innovation for  
Global  
Challenges**

