

What's in Store for Personalized Medicine?

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

Presentation at the Personalized Medicine Conference
Arizona Biltmore in Phoenix • 9 March 2010

Major Challenges in Healthcare

Cost



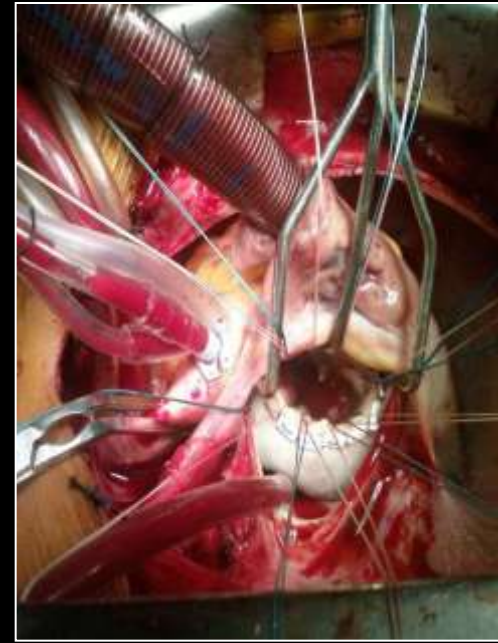
Demographics



Access



Variation in Clinical Practice



Major Challenges in Healthcare



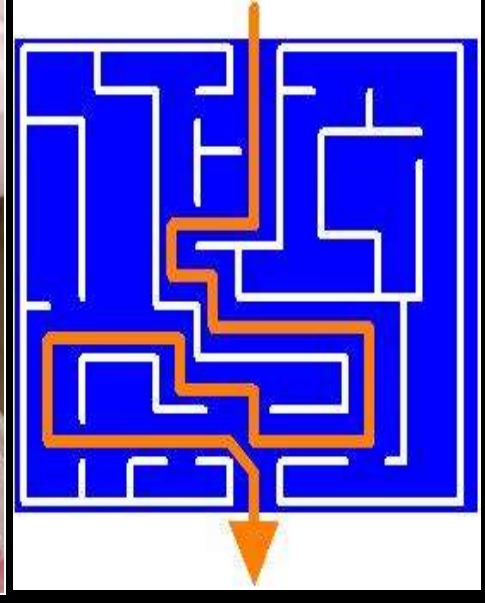
**Inefficient
Use of
Information**



**Fragmented
Care Versus
Integrated Care**



**Duplication,
Defensive
Medicine & Waste**



**Protracted
Adoption of
Innovation**

New Value Propositions in Healthcare

- **social and economic value of reducing disease burden will rise**
 - **earlier disease detection and mitigation**
 - **rational Rx and guaranteed outcomes**
 - **integrated care management of complex chronic diseases**
 - **extension of working life**
- **progressive shift from 'reactive' medicine to 'proactive' care and 'integrated' delivery**
 - **prospering in an era of increasing constraints**
 - **managing the limit(s) of society's willingness and ability to pay for innovation**

Personalized Medicine: Progressive Evolution Based on Increasingly Comprehensive Profiling of Disease Risk and Health Status

The diagram consists of three overlapping circles arranged vertically. The top circle is red and labeled 'Targeted Care'. The middle circle is green and labeled 'Individualized Care'. The bottom circle is purple and labeled 'Personalized Care'. The circles overlap in a way that suggests a progression from the top to the bottom, with each level building upon the previous one.

**Targeted
Care**

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

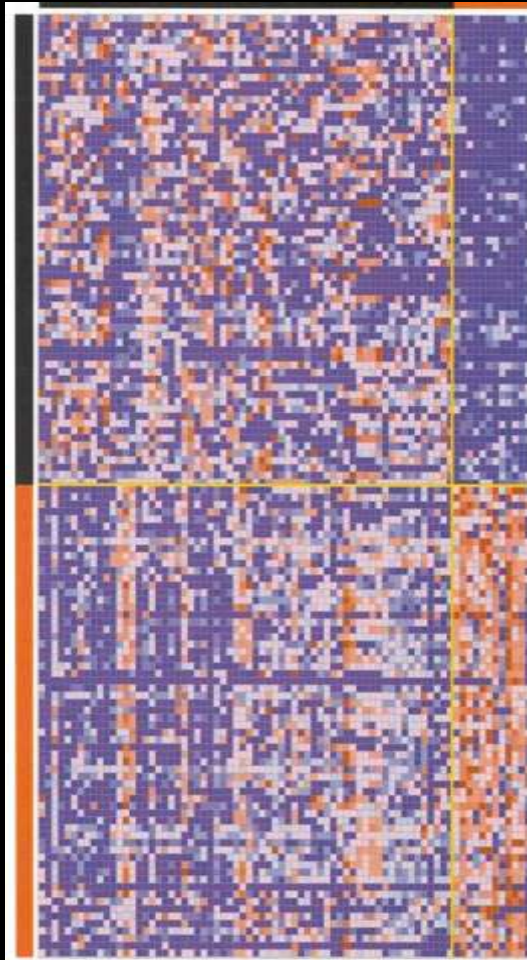
**Individualized
Care**

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

**Personalized
Care**

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

Personalized medicine: Key Drivers



Science



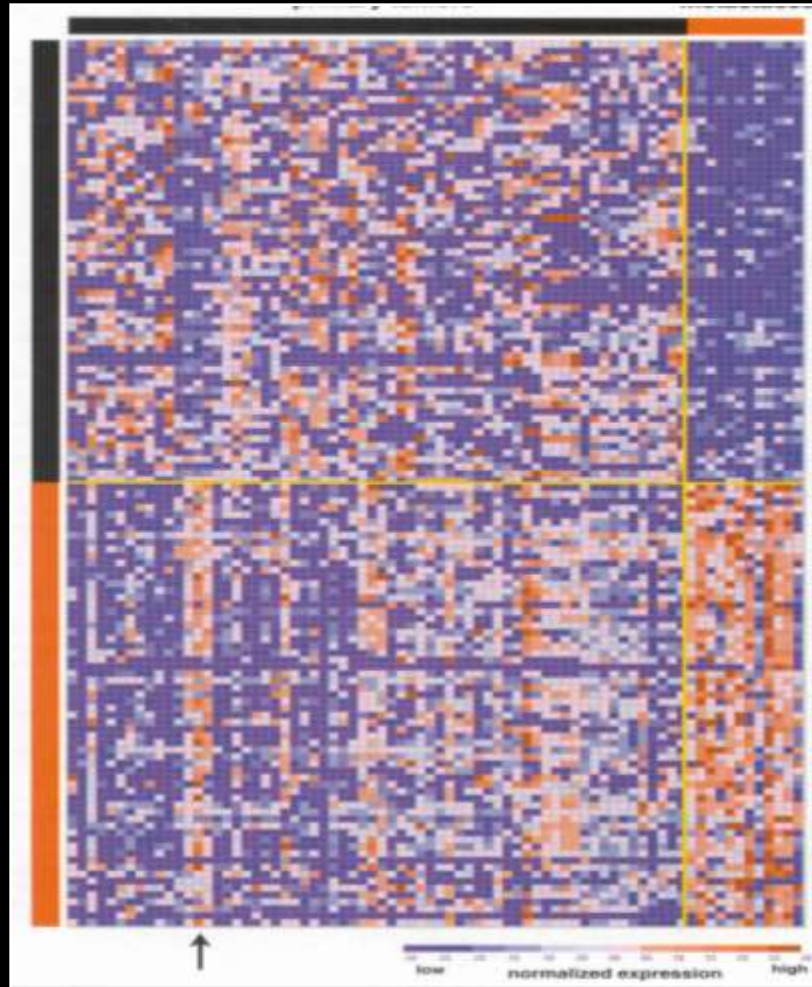
Policy



Cost and Outcomes

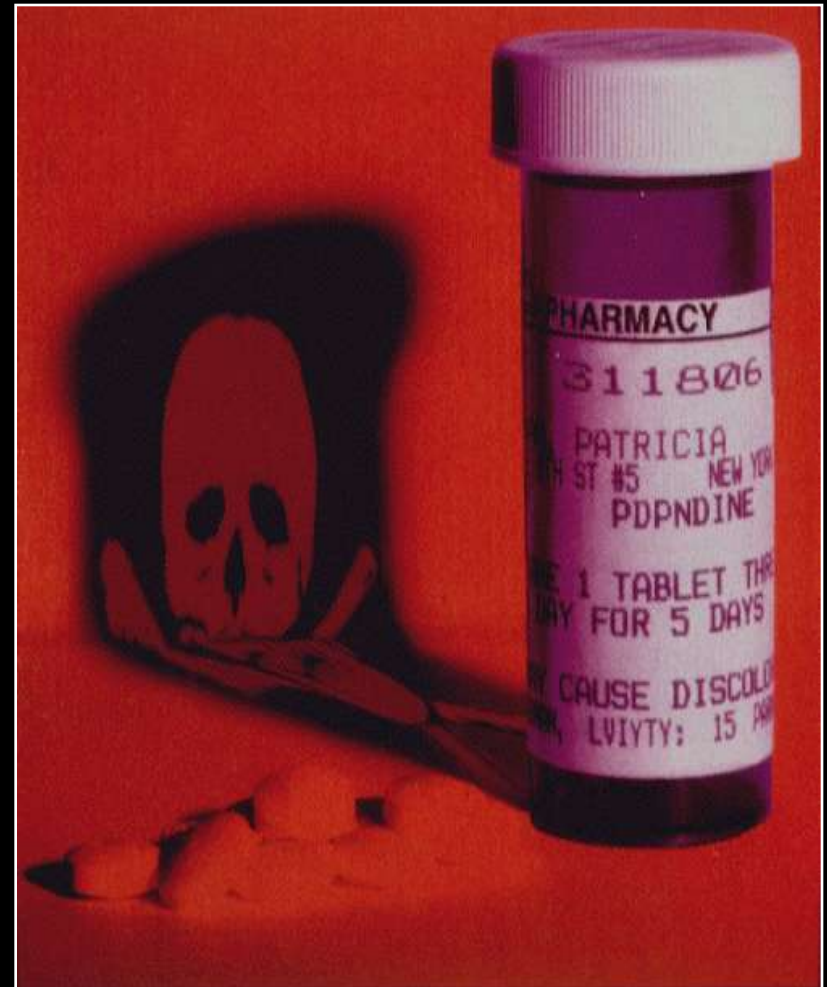
From Pharmaceuticals to Pharmasuitables

Disease Subtyping:



Right Rx for Right Disease

Individual Variation and AE risk

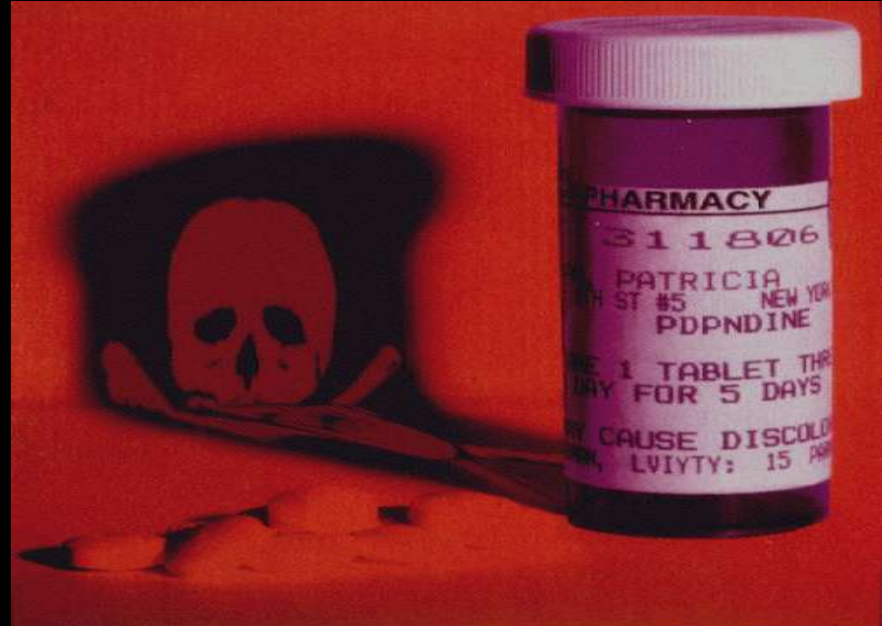


Right Rx for Right Patient

Molecular Medicine and Rational Therapeutics: Targeted Rx and Rise of Molecular Diagnostics and Patient Profiling

- **opening era in linking disease molecular pathology to rational Rx**
- **increasing payor, regulatory and public pressures for reliable ID of Rx-responsive patients**
- **demand for Dx-Rx combinations will intensify**
- **Dx-Rx combination will become an obligate element of NDA/BLA submission and product labeling**
- **development of Dx-Rx combinations as intrinsic components of R&D programs for investigational Rx**

Pharmacogenetic Predisposition to Adverse Drug Reactions



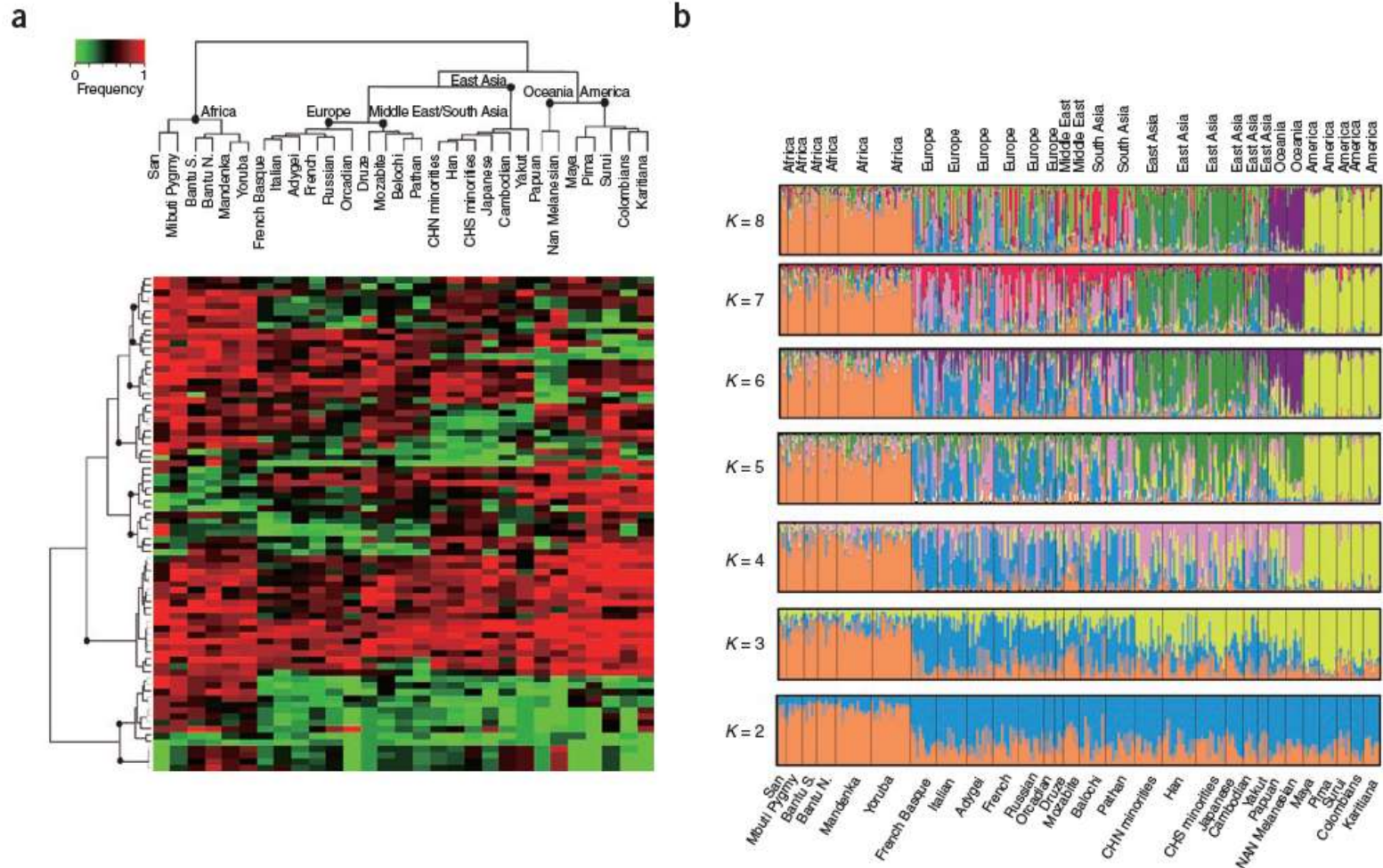
- 1.5 to 3 million annual hospitalizations (US)
- 80 to 140 thousand annual deaths (US)
- est. cost of \$30-50 billion



Molecular Diagnostics and Pharmacogenetic Profiling to Identify Individuals at Risk for Rx Adverse Events

- **broader, more complex profiling platforms than MDx assays for ID of drug targets**
- **ID of slow metabolizer genotypes**
- **unknown effects of genetic and environmental confounders in AD(M)E beyond genetic variation in drug-metabolism (I-III) repertoire**
- **complex patterns of ethnic variation and haplotype associations impose continuum of metabolic phenotypes**

Identification of Ethnic Differences and Implications for Rx Efficacy and Safety



From: Ruqiang Li et al. (January 2010) Nature Biotech. Vol. 28, p. 59

Genetic Polymorphisms Influencing Responses to Antidepressants

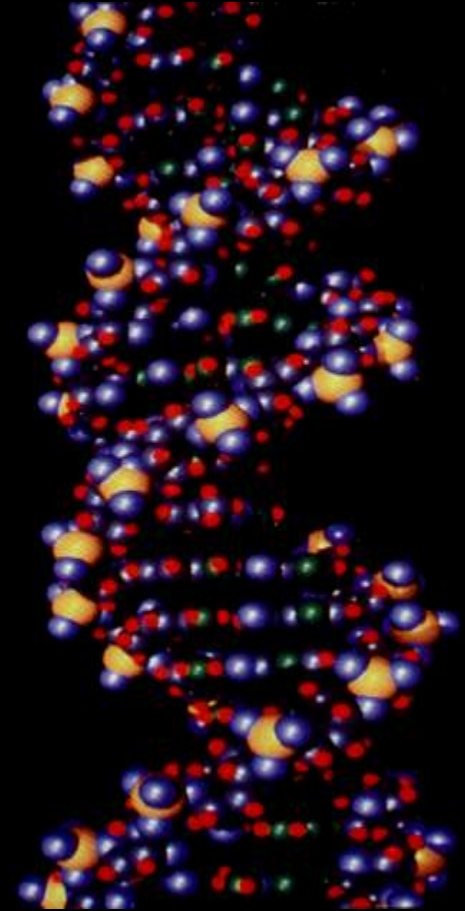
Target	Function		# of Papers on Association	
			Positive	Negative
Serotonin transporter	Serotonin transporter	5-HTTLPR	15	6
		STin2	3	6
Dopamine transporter	Dopamine transporter	VNTR	1	-
Norepinephrine transporter	Norepinephrine transporter	G1287A	2	-
		T-182C	-	1
Serotonin receptor 5-HT1A	Serotonin autoreceptor	C(-1019)G	3	3
		Gly272Asp	1	1
Serotonin receptor 5-HT1B	Serotonin autoreceptor	A-161T	-	1
Serotonin receptor 5-HT2A	Serotonin receptor located on postsynaptic neurons	-1438A/G	2	3
		C-1420T	-	1
		T102C	1	1
Serotonin receptor 5-HT3	Serotonin receptor, ligand-gated Na ⁺ and K ⁺ cation channel	178CIT	1	-
Serotonin receptor 5-HT6	Serotonin receptor	C267T	1	1
Dopamine receptor	Dopamine receptor	Ser311/Cys311, VNTR	-	1
β-adrenergic receptor	Adrenoreceptor	G1165C	1	-
Tryptophan hydroxylase	Enzyme, biosynthesis of serotonin	A218C	2	6
Monoamine oxidase	Enzyme catalyzing the catabolism of neurotransmitters	T941G		
		VNTR	2	2
		A644G	1	-
Catechol-O-methyltransferase	Enzyme catalyzing the catabolism of neurotransmitters	Val158Met	3	1

The Human Microbiome: A Barely Understood Influence in Health



- **complex meta-system**
 - host, microbes, viruses, other organisms, metabolites, xenobiotics
 - is there a core microbiome?
 - how do perturbations affect disease and vice-versa?
 - does the microbiome influence xenobiotic metabolism and the metabolite spectrum?

The Hunt for Gene Loci Associated with Complex Human Diseases



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

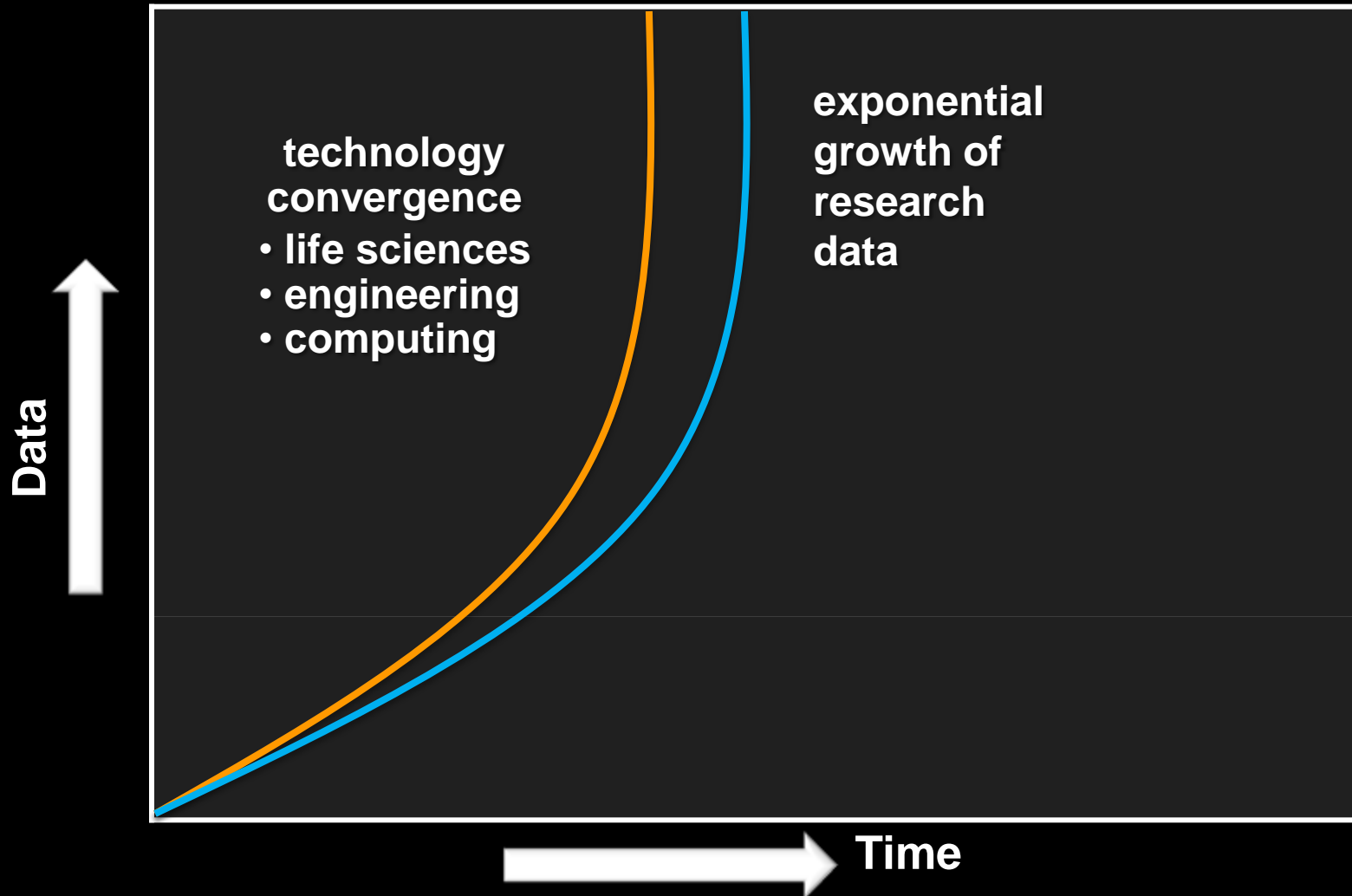
- **slower evolution than many predict**
- **Genome-Wide Association Studies (GWAS)**
 - **high cost**
 - **multiple low penetrance alleles**
- **substantial ambiguities regarding probabilistic risk of overt disease**
 - **epistasis**
 - **epigenetics**
 - **environmental confounders**
 - **source of poor replication of GWAS studies?**

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

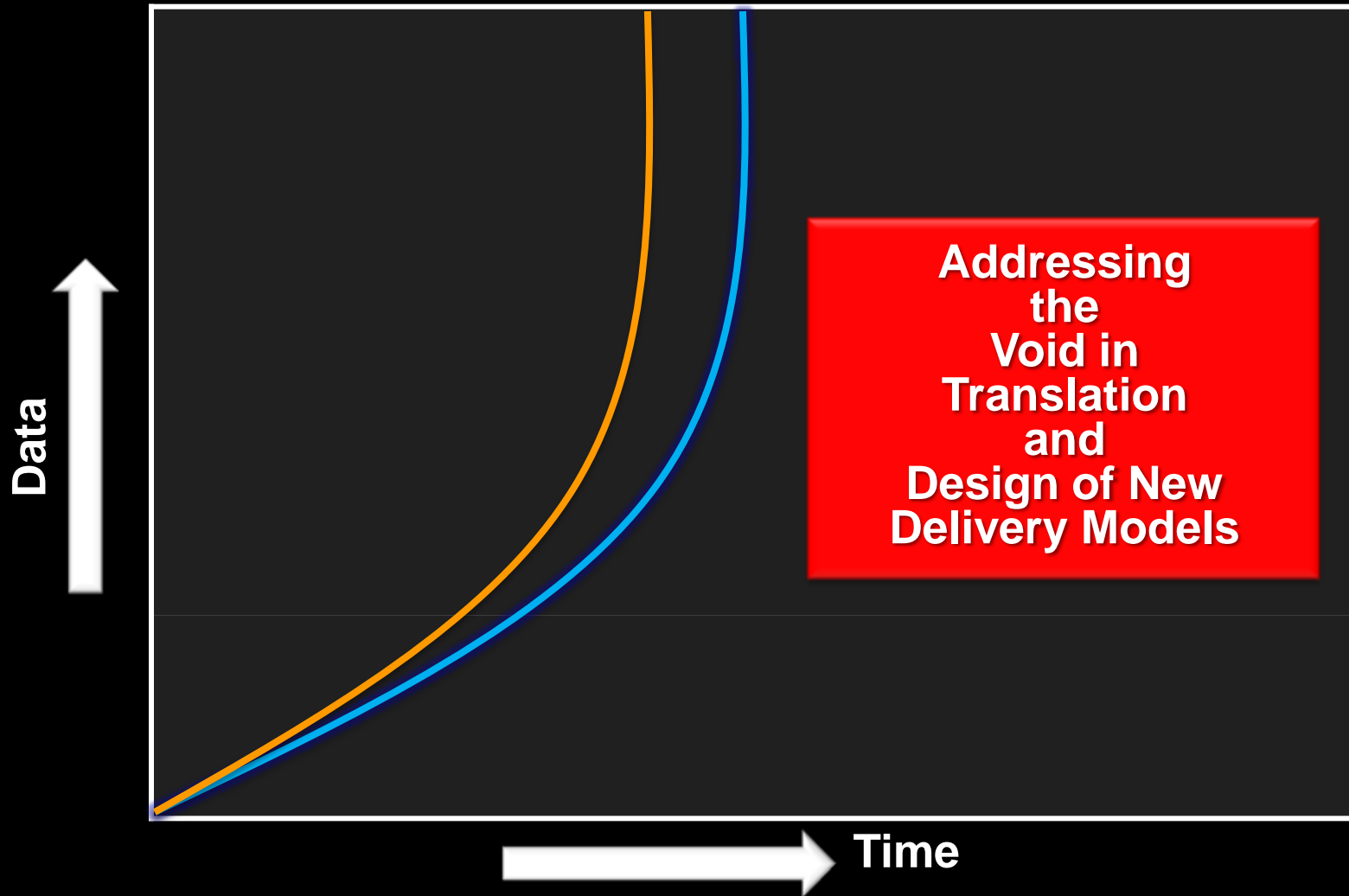
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The premature quest to provide consumer genomic testing (CGx) for future risk of major diseases

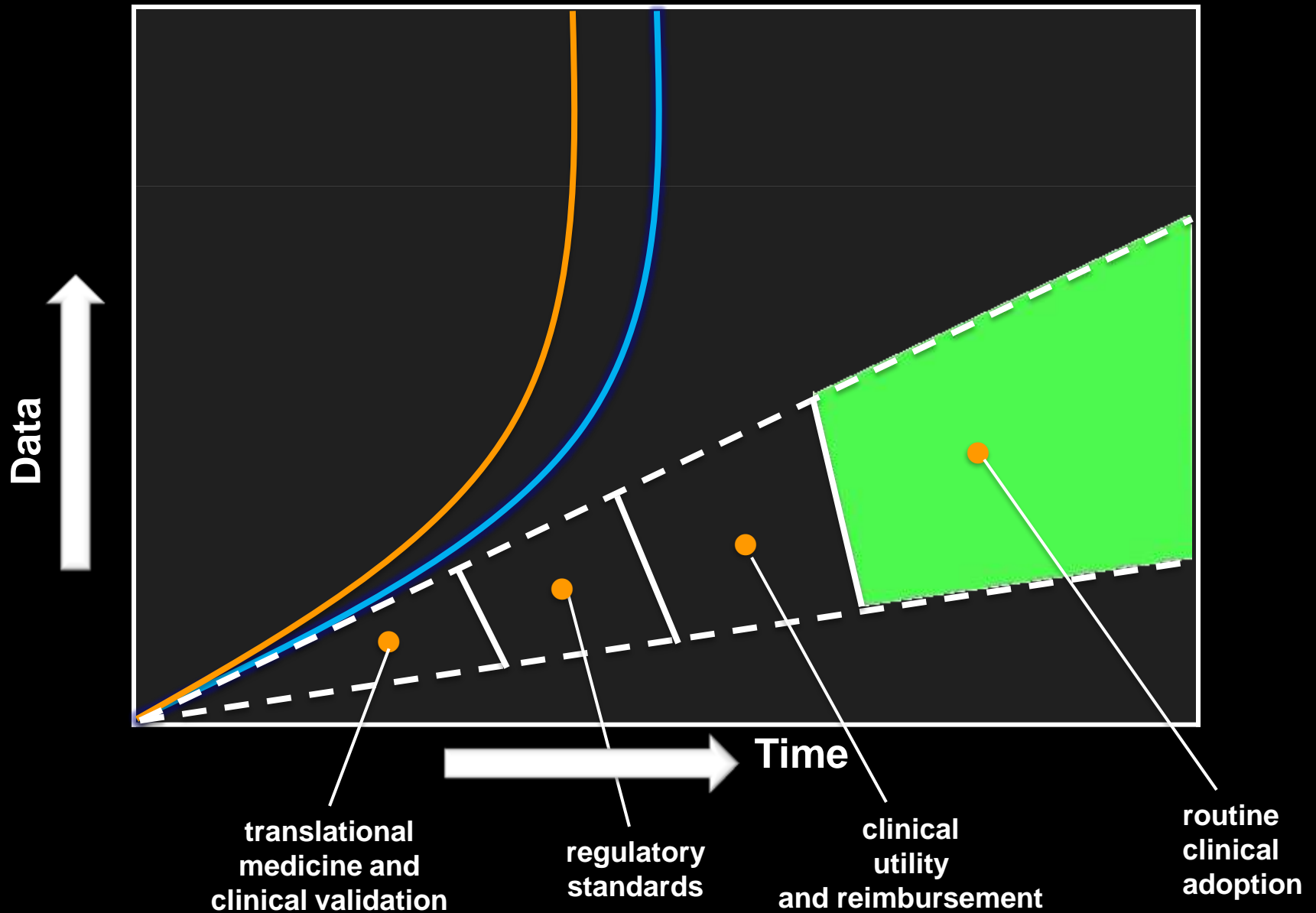
The Trajectories for Molecular Medicine



The Trajectories for Molecular Medicine



The Trajectories for Molecular Medicine



Deriving Value from “-Omics”

- **useful only when correlated with additional parameters**
 - **clinical outcomes**
 - **clinical utility**
 - **actionable information**
 - **demonstrable economic value**

Disease-Associated Biomarkers and Validation of New Molecular Diagnostic for Personalized Medicine

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

Increased Legislative Interest in Standards, Oversights and Regulation of Molecular Diagnostic Testing



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



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



- (2009) Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions



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



- (2009) SB 42: Post-CLIA Bioinformatics Services

Reimbursement for Diagnostic Tests

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

- **inadequate US Medicare coding and payment mechanisms**
 - **out moded, out-dated, lacking in transparency, inconsistently applied**
- **inappropriate assignment of existing CPT codes to new tests**
- **engagement of third party payers who derive economic/clinical value from new Dx**

K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy



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



clinical guidelines



- regulatory endorsement in product labeling



- payor adoption

Protracted Adoption of Science/Evidence-Driven Guidelines Cultural Arrogance or Defensive Denial?

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

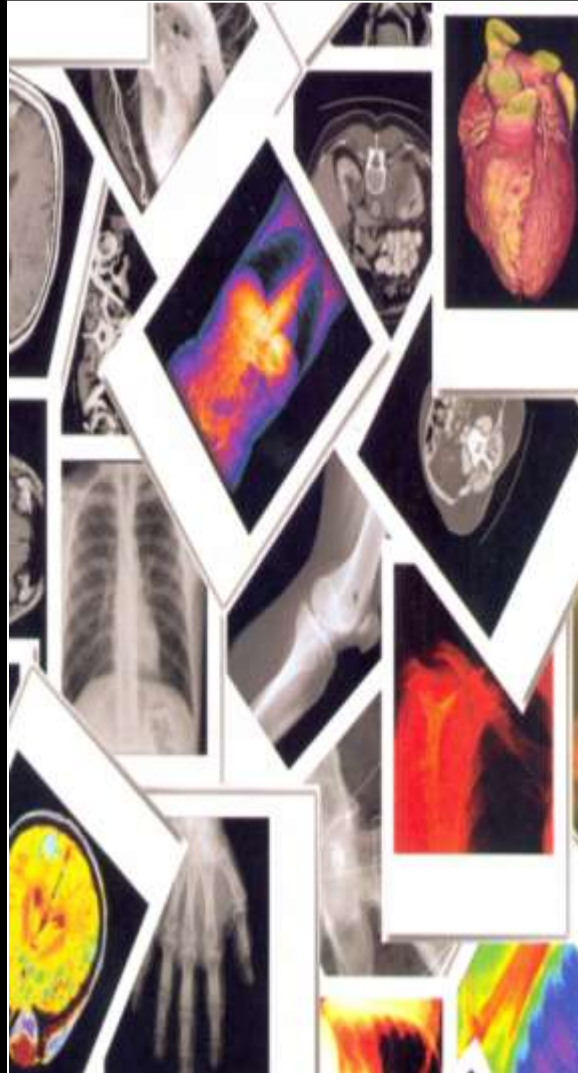
**Dr. Lee Newcomer
Head, Oncology Services
United Healthcare
Health Affairs (2008) 27, 41**

DHHS Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) Task Force (Oct. 2009)

**“The Task Force found that patents
are not “powerful” incentives for
conducting genetics research
disclosing genetic discoveries or
investing in development of genetic tests
but that they limit access to genetic tests”**

**Dr. James Evans,
Chair, SACGHS**

How Much New Technology Can We Afford?





INITIAL NATIONAL PRIORITIES FOR

COMPARATIVE EFFECTIVENESS RESEARCH

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES



The NEW ENGLAND JOURNAL of MEDICINE

(2009) 360, 1925

Does Comparative-Effectiveness Research Threaten
Personalized Medicine?

Alan M. Garber, M.D., Ph.D., and Sean R. Tunis, M.D.

- selection of comparators
- shortcomings in clinical phenotyping/outcomes classification
- retrospective data and meta-analyses versus cost/complexity of prospective studies

UK National Institute for Health and Clinical Excellence (NICE)



Nice Gets Nasty (or Rational?)



Personalized Medicine: Consumer-Centric Healthcare: A Key Driver

- **structural shift in healthcare delivery from encounter-/procedure-driven to incentives for integrated disease management**
- **clinical and economic benefits of coordinated care of complex chronic conditions**
- **cost-shifting to consumers**
- **lifestyle and disease risk mitigation**
- **new information intermediaries**
- **cost-driven transitions from ‘passive patient’ to ‘engaged consumer’**

The Costs of Non-Compliance with Rx Regimens



- **\$177 billion projected cost**
- **20 million workdays/year lost (IHPM)**
- **40% of nursing home admissions**
- **projected 45-75% non-compliance (WHO)**
- **50-60% depressed patients (IHPM)**
- **50% chronic care Rx (WHO)**

On Body: In Body Sensors and Devices

Objective

- remote monitoring of health status



Applications

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



Deloitte.

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

cast 
Center for Aging Services Technologies

Audit. Tax. Consulting. Financial Advisory.

The Infocosm: Emerging Networks of Global Connectivity



Wireless Technologies: Consumer and Clinical Markets Converge



iPhone Apps for Your Health and Fitness

Gym Buddy



8 months, 2 weeks ago



WebMD Mobile



8 months, 4 weeks ago



Happiness



9 months ago



Calorie Calculator



11 months, 2 weeks ago



Indice de masa



11 months, 2 weeks ago



Gym Technik



11 months, 4 weeks ago



Pocket Workout



9 months ago



Shake Jump



9 months, 1 week ago



iFitness



9 months, 1 week ago



8h2o



1 year ago



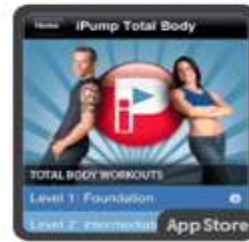
Track'n Trail



1 year ago



iPump Total Body



1 year ago



Steps



9 months, 2 weeks ago



CareConnector



9 months, 3 weeks ago



GottaKickit



9 months, 3 weeks ago



Total Coach



1 year ago



Anatomy Flash



1 year ago



Workout Buddy



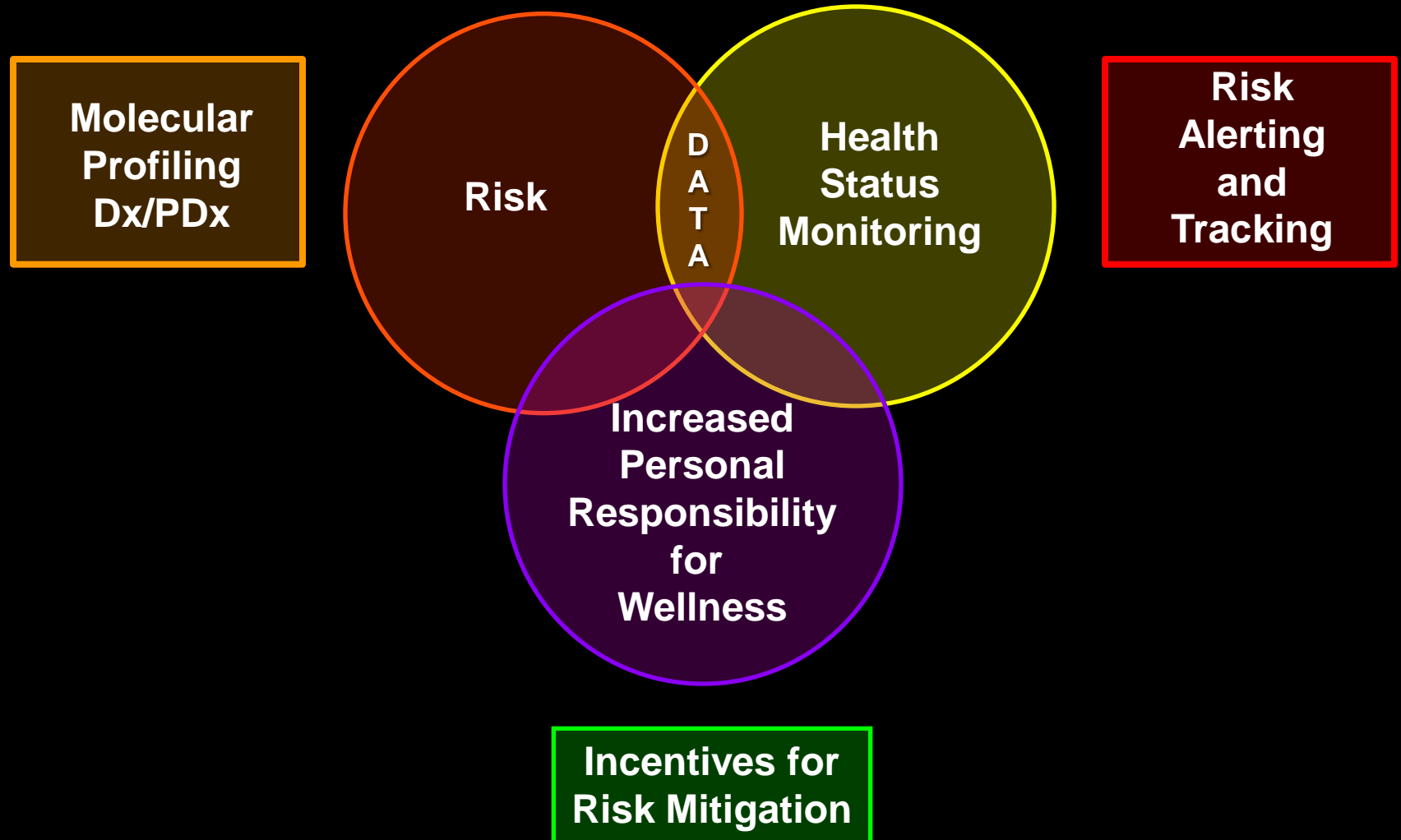
1 year ago



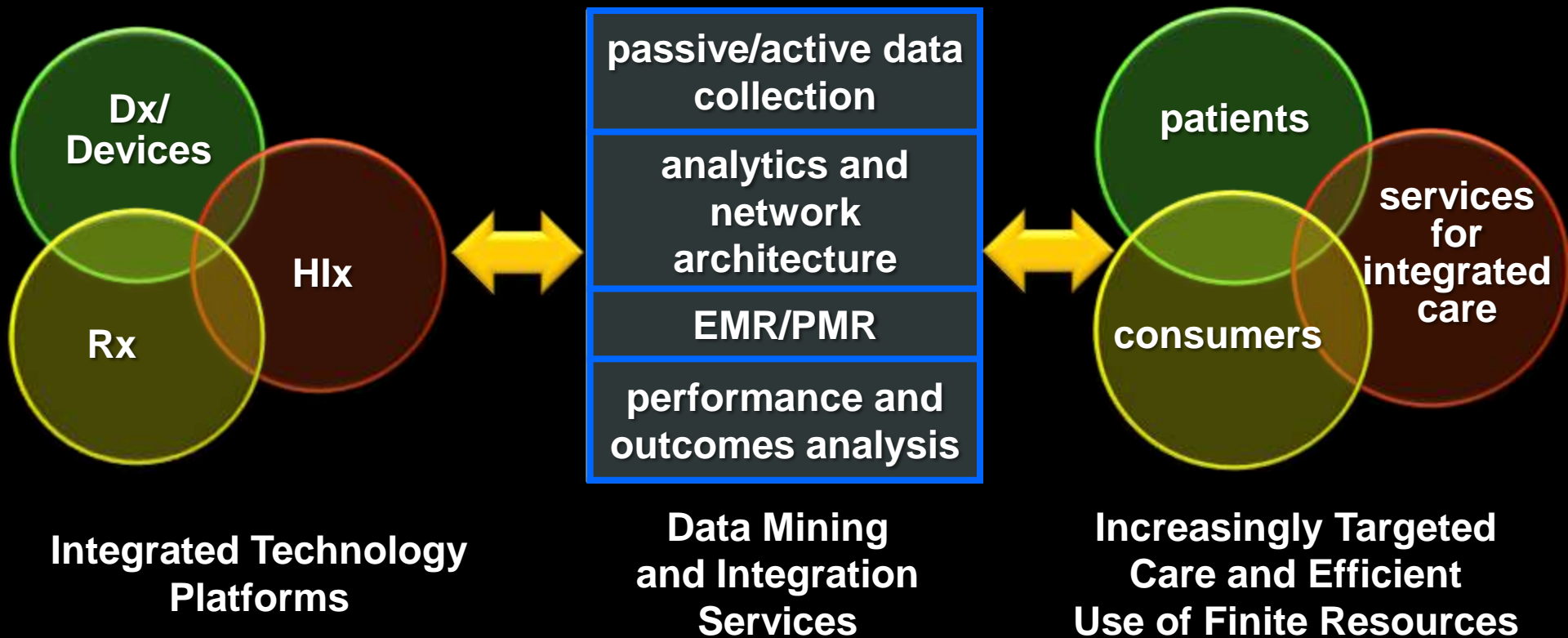
Pharma and Healthcare Social Media (Non-Brand Sponsored) Patient Communities



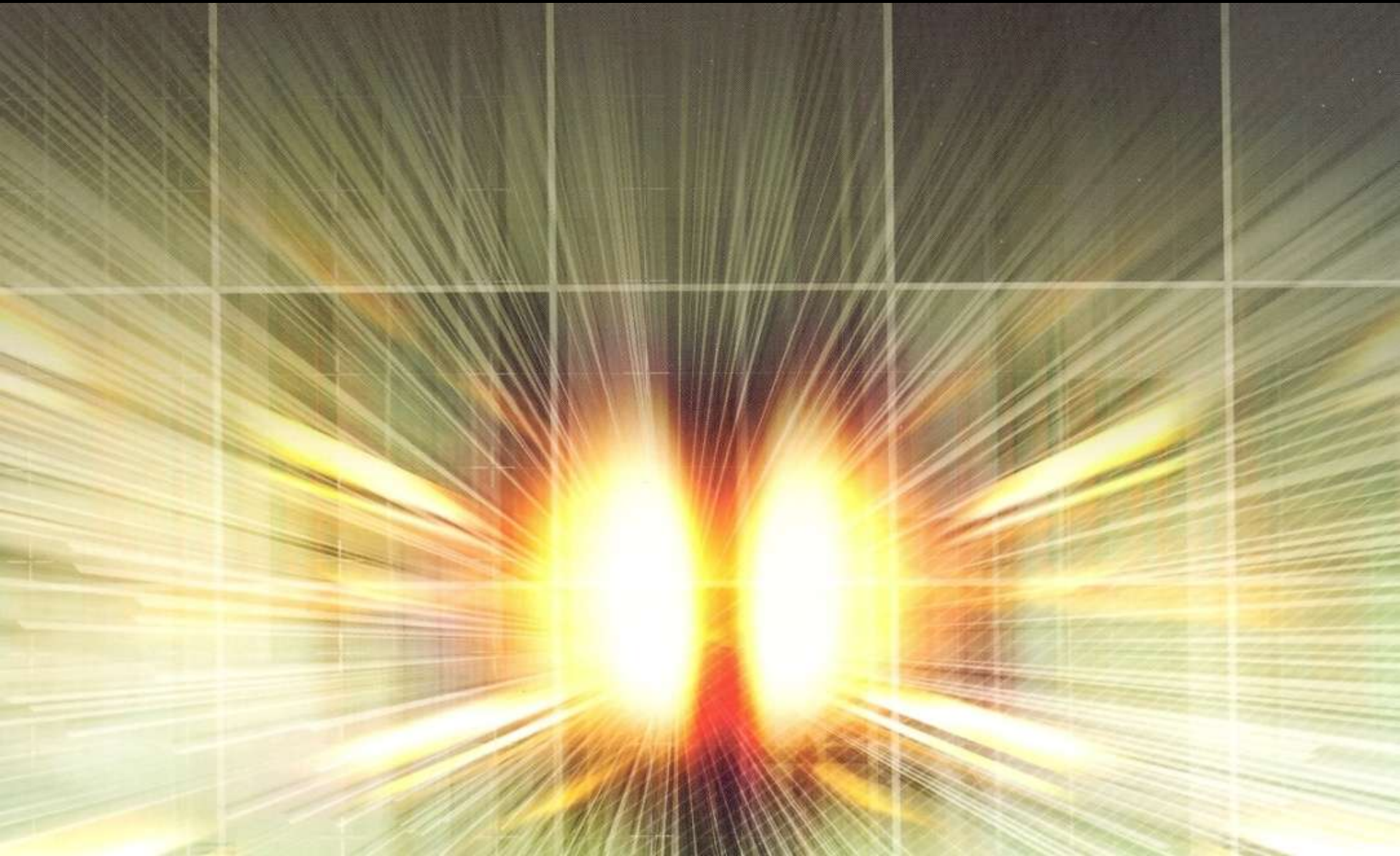
Molecular Diagnostics as a Key Element in the Evolution of Integrated Healthcare Delivery



A New Healthcare Ecosystem Arising From Technology and Market Convergence



Technology Acceleration and Convergence in Healthcare Delivery



Technology Convergence and Implications for Healthcare Delivery

Technologies

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

Clinical Practice

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

Realigned Incentives

- integrated care for complex chronic diseases
- earlier disease detection and risk reduction
- wellness versus illness
- remote health status monitoring

Technology Convergence and Implications for Healthcare Delivery

Consumers

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

Connectivity

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