Big Data and the Evolution of Precision Medicine

Dr. George Poste

Chief Scientist, Complex Adaptive Systems Initiative
and Del E. Webb Chair in Health Innovation
Arizona State University
george.poste@asu.edu
www.casi.asu.edu

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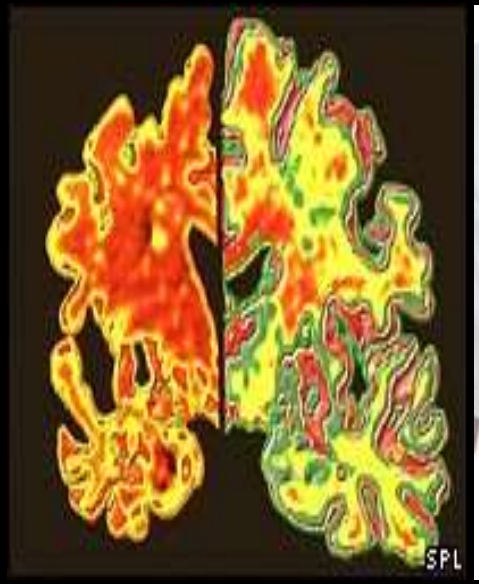
Challenges Facing US Healthcare

- Balancing Infinite Demand versus Finite Resources
- From Volume-Based FFS Care to Value-Based Care
- From Reactive, Episodic Interventions in Disease Episodes to Proactive Continuity of Care Services
- Improving Outcomes at Lower Cost and Realizing the Wellness Premium
- Technology, Innovation and New Value Propositions in Healthcare

Extending Life: Balancing Cost and Quality of Life

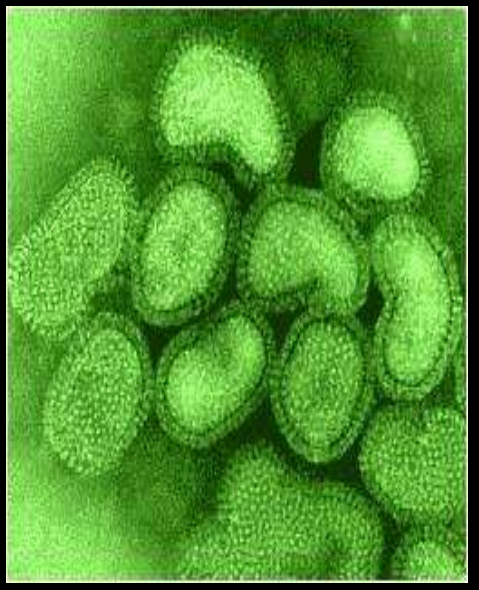
Unmet Medical Needs and Disease Burden: Confronting the Largest Economic Disruptions in Sustainable Healthcare

cancer



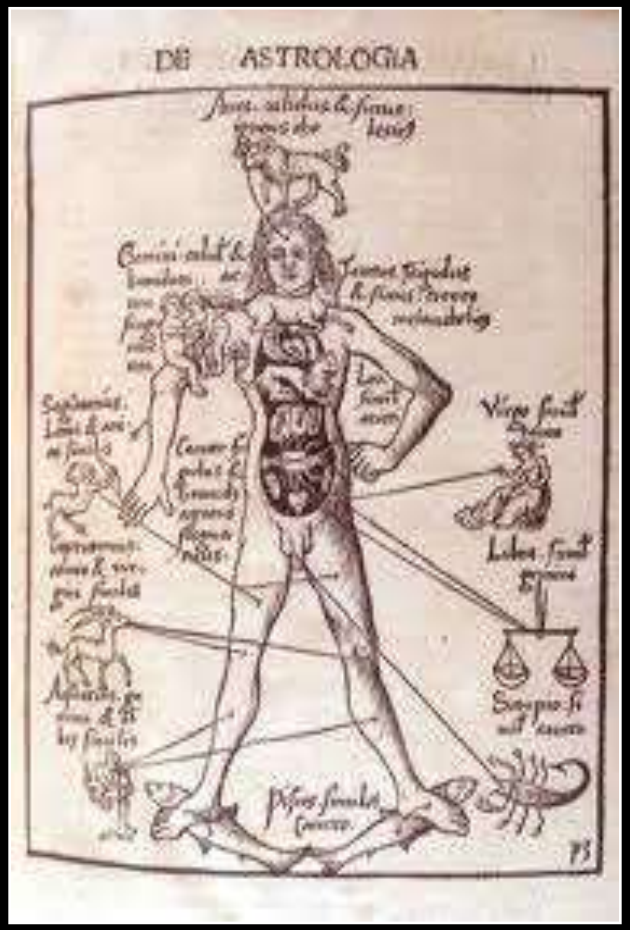
neurodegeneration

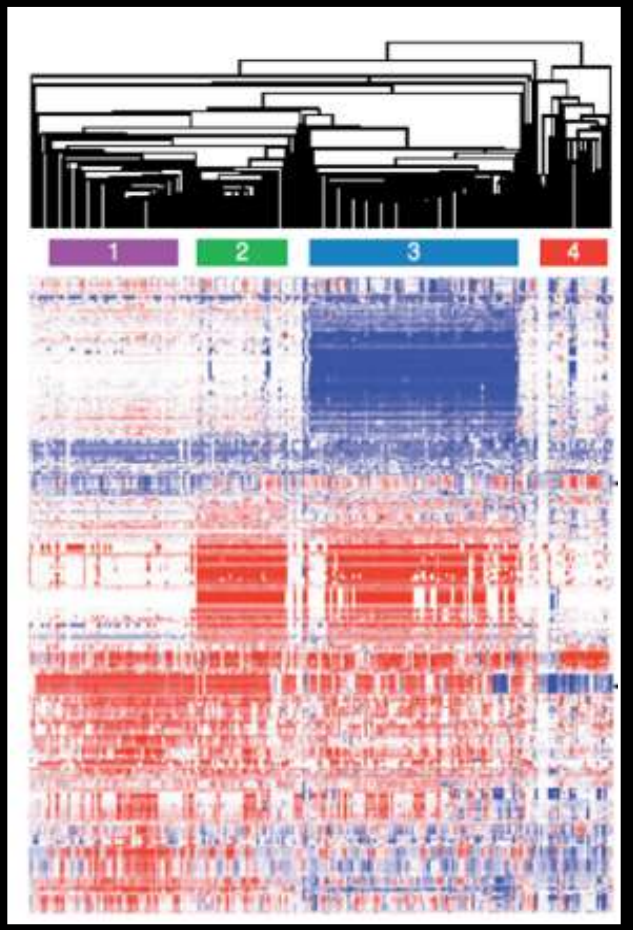
cardio-vascular/ metabolic disease



infectious disease wildcard

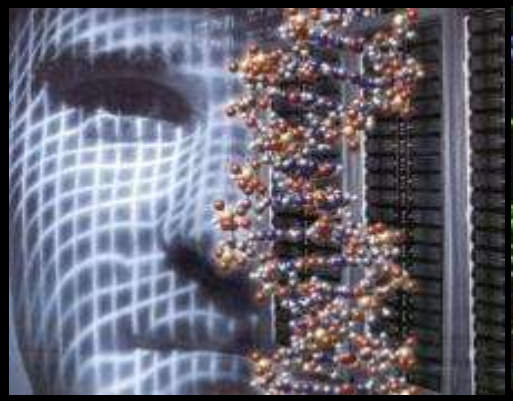
Medical Progress:
From Superstitions to Symptoms to Signatures

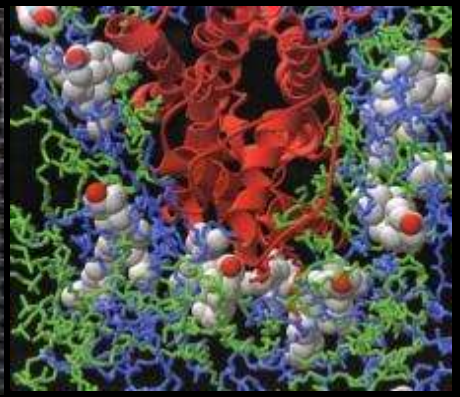


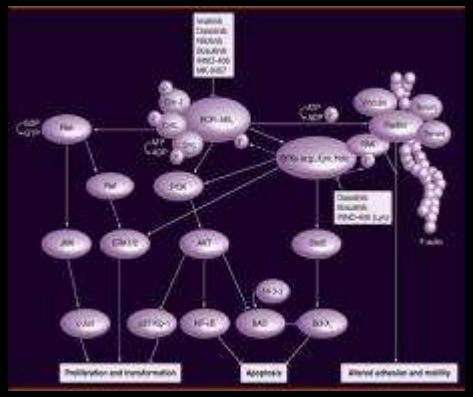


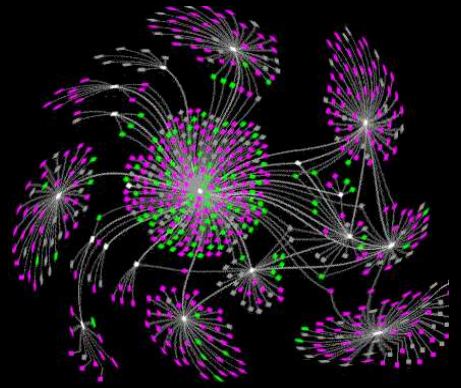
Precision Medicine: PanOmics Profiling and Mapping the Disruption of Molecular Networks in Disease

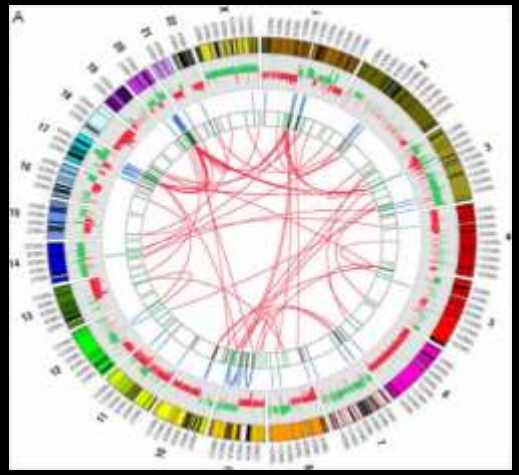
(Epi)Genomics	Proteomics	Molecular Pathways and Networks	Network Regulatory Mechanisms





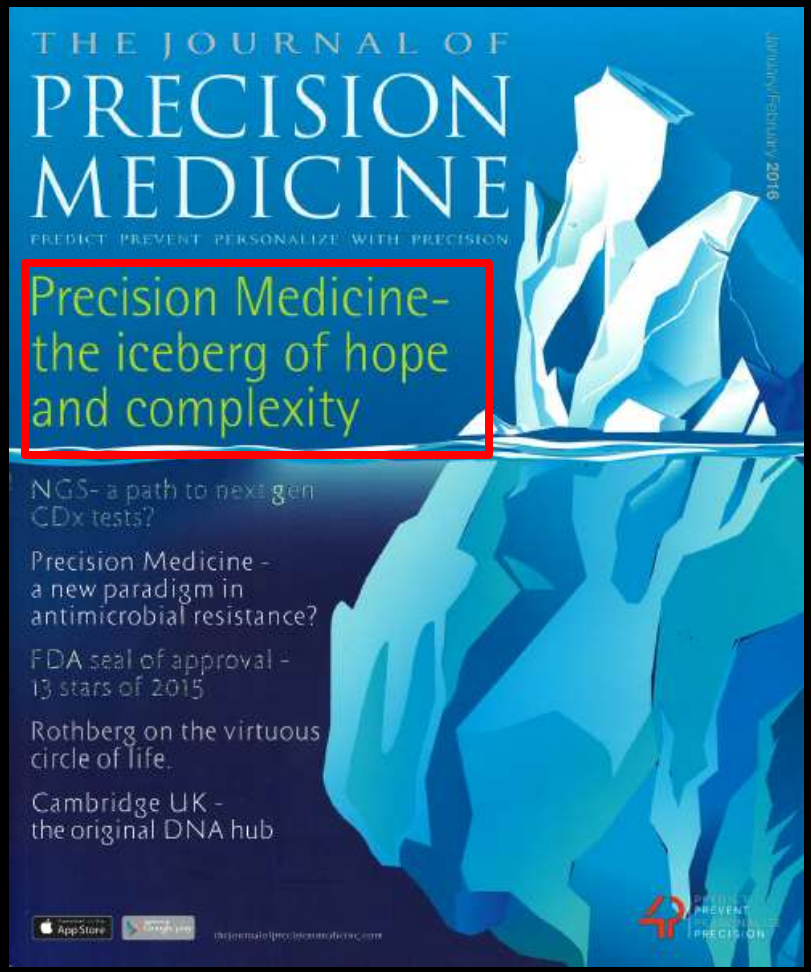






ID of Causal Relationships Between Network Perturbations and Disease	Patient-Specific Signals and Signatures of Disease or Predisposition to Disease

Precision Medicine:
Not If, But…

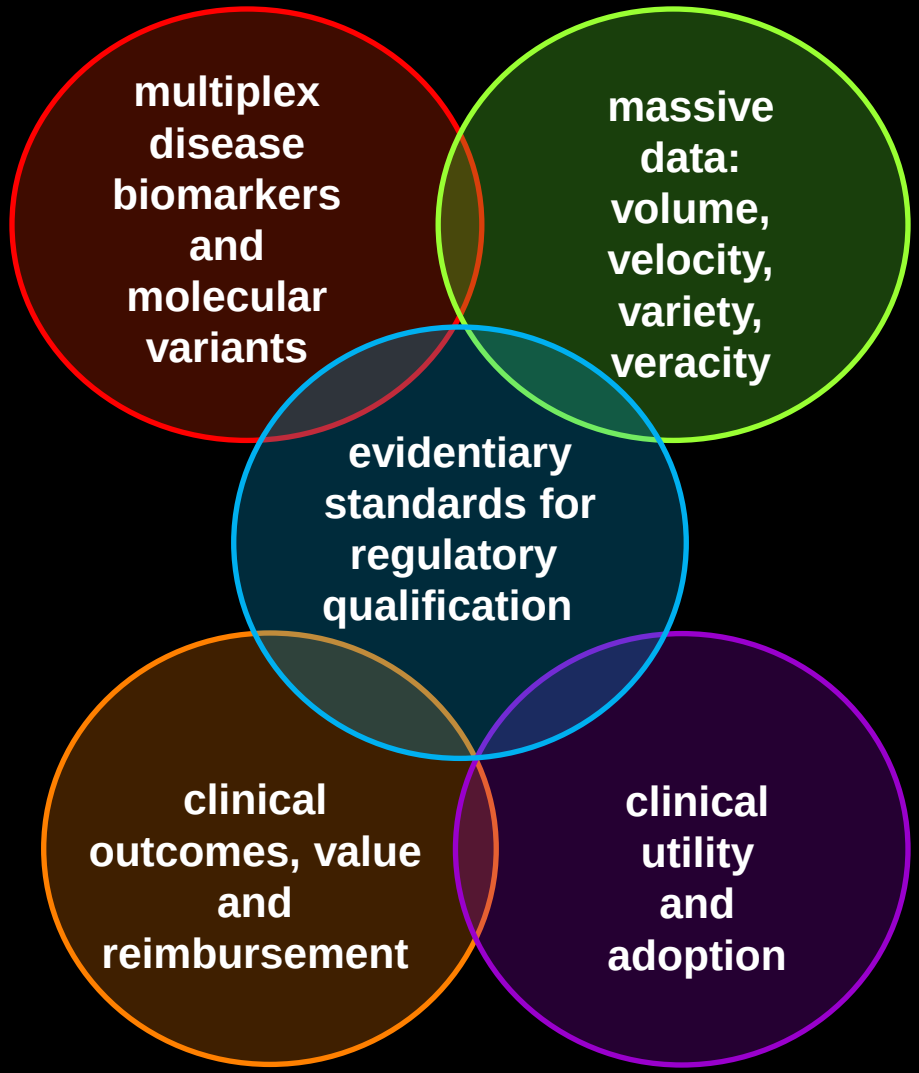


- when?
- what?
- how?
- who?
- value?

Precision Medicine

- panOmics profiling and a new molecular taxonomy of disease
- intellectual foundation for diagnostic accuracy and rational therapy
- mapping the diversity and dynamic range of disease-associated alterations in the architecture of molecular signaling (information) networks
- profiling individual variation in disease risk, patterns of disease progression and therapeutic responses
- understanding the topologies and dynamics of molecular signaling (information) networks

Analytical and Clinical Validation Protocols for the Utility of Molecular Profiling in Precision Medicine



Precision Medicine: Mapping The Signatures Of Biological Signaling (Information) Networks

- "health"
- homeostasis

- subclinical disease
- graded threshold states

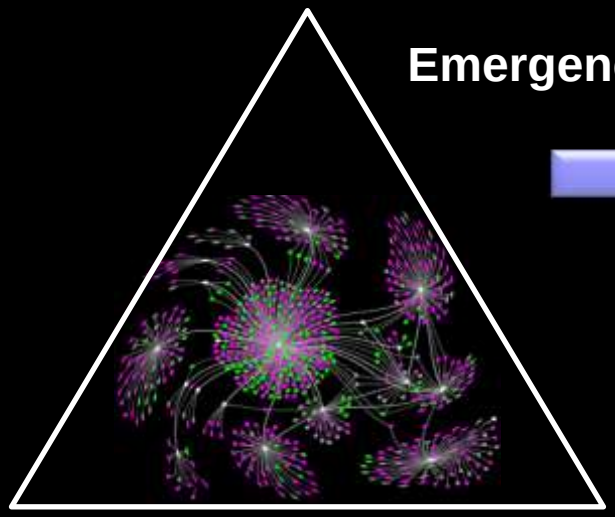
- overt clinical disease
- diverse phenomes

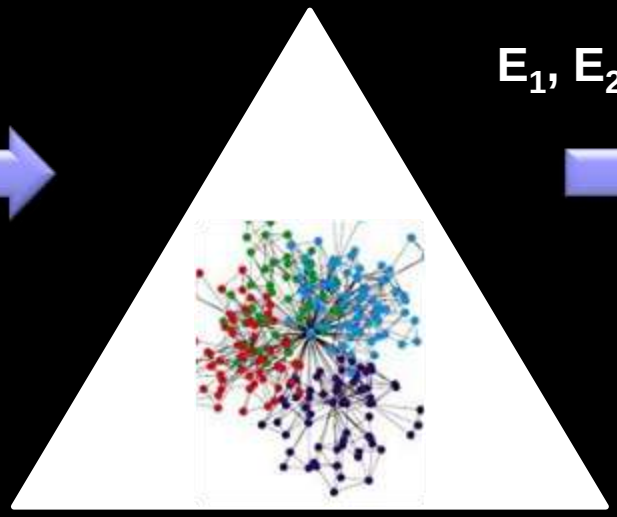
network topology

Emergence(E)

state shifts

$E_1, E_2 \ldots E_n$





Ignoring Biological Complexity

Genes For ….
The Overly Simplistic and Deterministic Dangers of a Genome-Sequence Centric Perspective

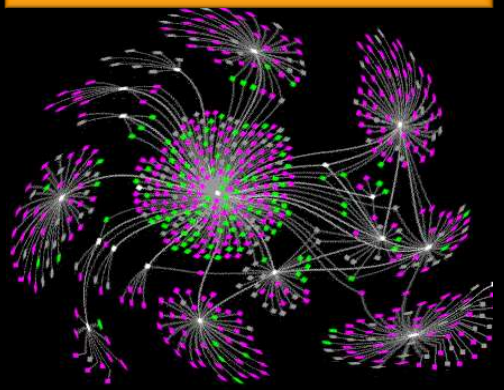
The Over-Simplified Perspective That
While Exome-and Whole Genome-Sequencing
Will Reveal the Full Etiology of Disease Pathogenesis

Individual Variation, Genome Complexity and the Challenge of Genotype-Phenotype Predictions

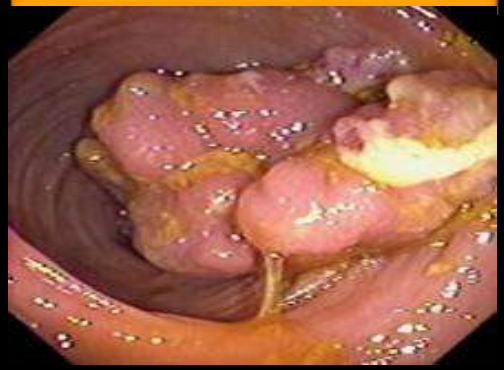
Junk No More: Pervasive Transcription

recognition of (epi)genome organizational and regulatory complexity

Cell-specific Molecular Interaction Networks



Perturbed Networks and Disease



The Reductionist, Simplistic Obsession With Genome Sequencing

(Epi)Genome Sequencing and Clinical Care

- because we can?
- because it is useful?

Meeting the ‘Fit-for-Purpose’ Standard

The Urgent Imperative to Define Analytical and Interpretation Standards for Clinical Grade Genome Sequencing

Standards for Genome Sequencing and Pathogenic Variant Classification*

- Comparison of BRCA1 and BRCA2 variant classification across five databases
  - Breast Cancer Information Core
  - Leiden Open Variation Database 2.0
  - UMD (INSERM)
  - ClinVar
  - Human Gene Mutation Database
- 2017 variants cataloged
  - 116 identified as pathogenic in at least one database
  - consensus on only 4 variants as pathogenic in all five dbases
- 34% of mutations in Myriad db not present in these public repositories

*P. J. Vail et al. (2015) J. Comm. Genetics 6, 351-59

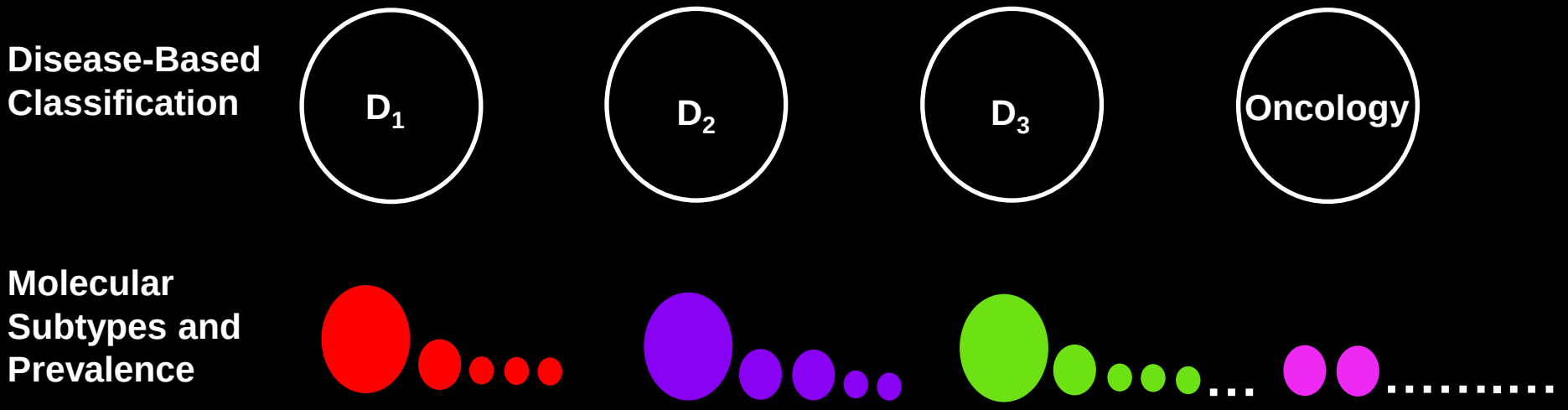
Precision Medicine: The Complexity of Genotype-Phenotype Relationships

Genome Sequencing Alone Will Not Suffice: The Need for Deep Phenotyping

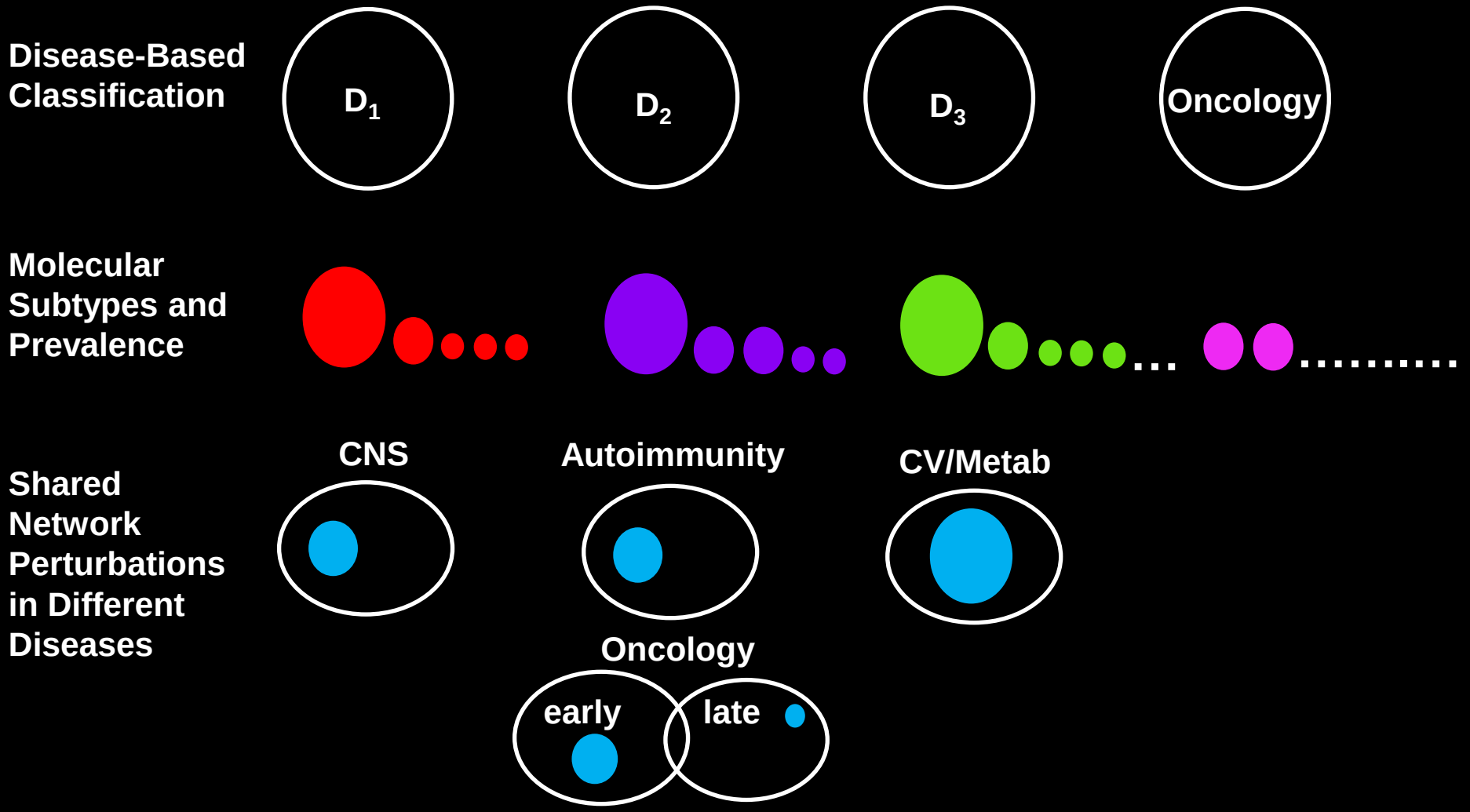
Phenome-Association Data (PheWAS): Integration of panOmics Profiling with Clinical Disease Progression and Treatment Outcomes

Understanding the Complex Interplay Between PanOmics, Environment and Behavior

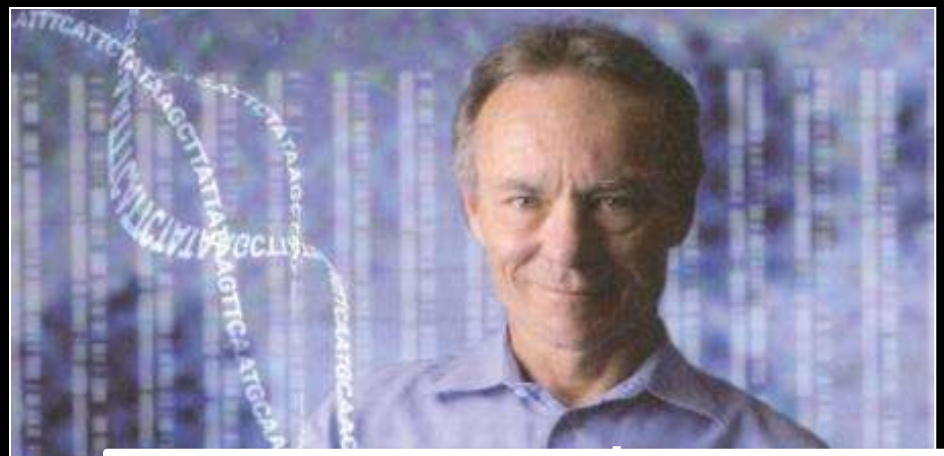
Precision Medicine: Molecular Subtypes, Endophenotypes and the Dynamic Range of Clinical Phenotypes

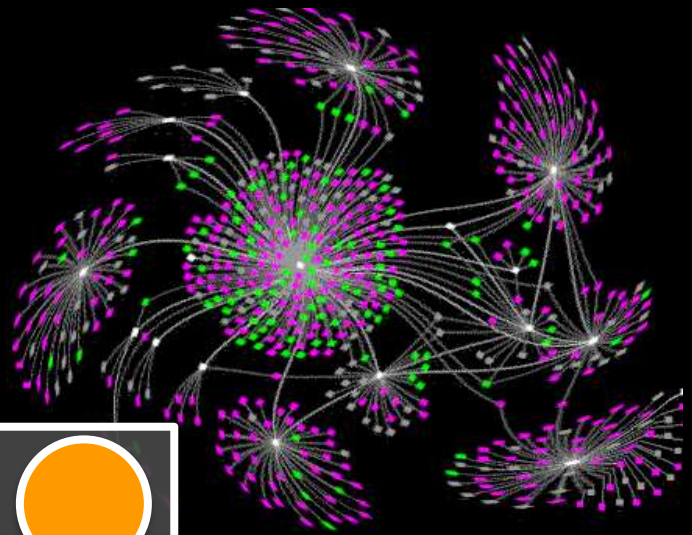


Precision Medicine: Molecular Subtypes, Endophenotypes and the Dynamic Range of Clinical Phenotypes



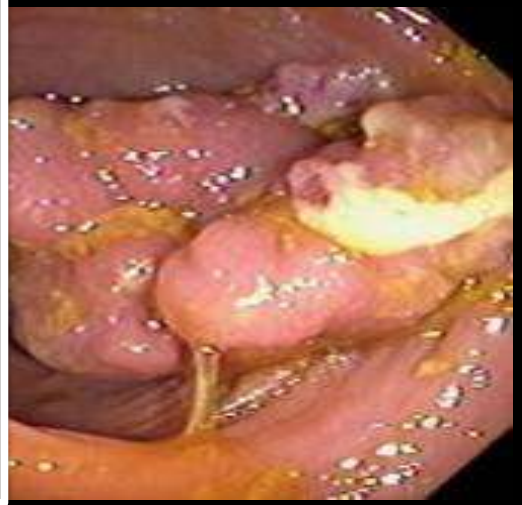
The Challenge of Translation of Burgeoning panOmics Data Into Clinically Relevant (Actionable) Knowledge





- Data
- Reliability and Robustness
- Biological Insight
- Clinical Utility

?



Invasion of the Body Trackers: Changing The Touch Points in Healthcare Delivery

Individual Biosignature Profiling Via On Body:In Body (OBIB) Sensors and Devices

Remote Health Status Monitoring

M4: Making Medicine More Mobile

Mobile Devices, Wearables, Sensors and Remote Health Status Monitoring: The Changing 'Care Space' and Improved Continuity in Care Provision

- from fixed, tethered, compartmentalized, provider-centric facilities

to

- distributed- and virtual-architectures linking multiple providers, home, work and the internet

expanded 'points-of-touch' with the health systems

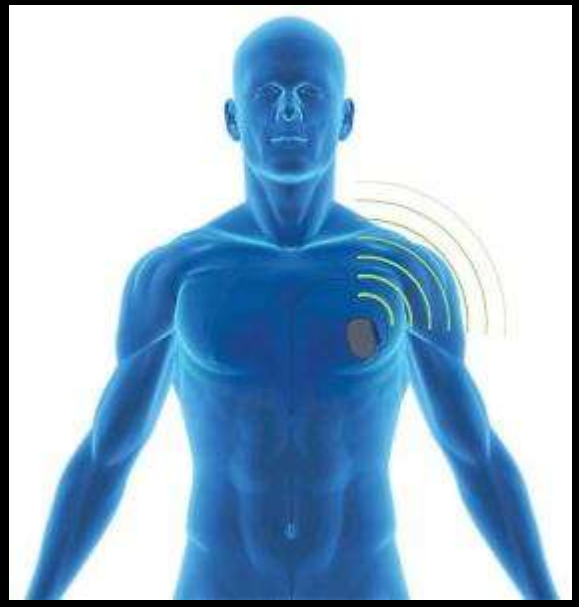
- from reactive, incident-centric, poorly coordinated and sequential referrals and inefficient post-incident follow-up(s)

to

- pervasive, persistent monitoring of health status for pre-emptive risk mitigation, improved compliance and personal stewardship of health

improved continuity of care and data integration

m.Health



Real Time Remote Health Monitoring and Chronic Disease Management

Lifestyle and Fitness

Information for Proactive Health Awareness (Wellness)

“Medical Selfies”: The Proliferation of Mobile Devices in Healthcare

Robotics: Telemedicine and Home Healthcare

Gray Technologies and Aging in Place: Independent But Monitored Living for Aging Populations

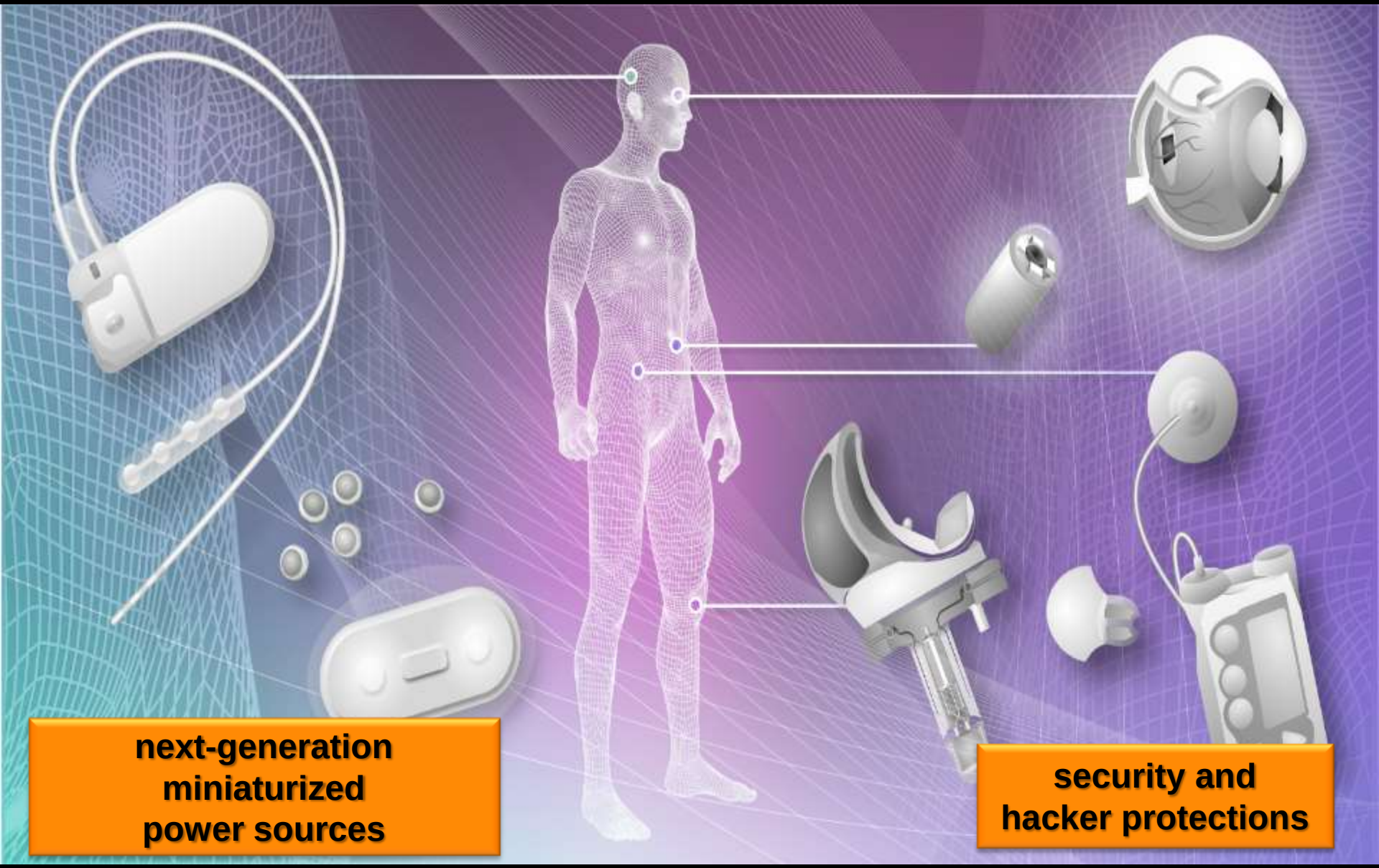
Rx compliance

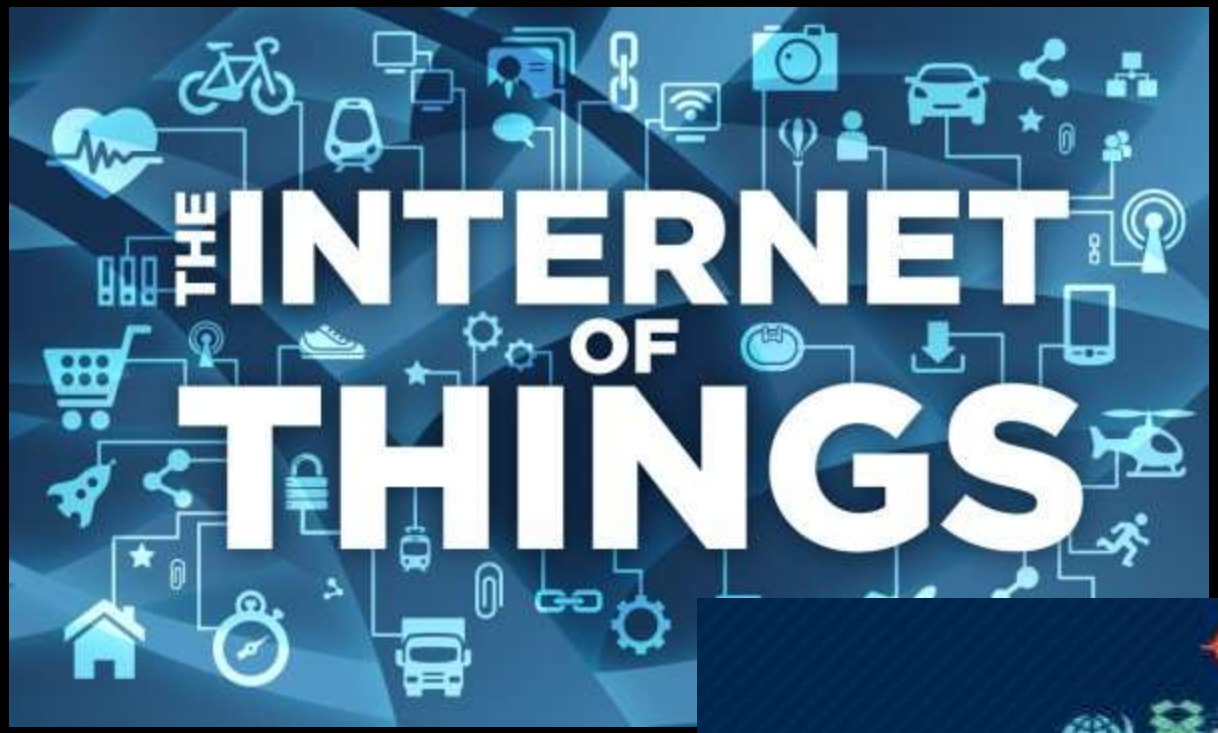
cognitive stimulation

in home support and reduced readmissions

reduced office visits

Implantable Devices and Wireless Monitoring (and Modulation)




THE INTERNET OF THINGS

An Apps-Based Information Economy in Healthcare

- wearables and continuous sensors (individual, environmental)
- theoretical rationale but integration of data with EHR platforms poses numerous challenges
  - lack of developer access to high quality healthcare data to validate app platforms
  - cross-platform standardization and application programming interfaces (APIs)
  - regulation: accuracy, reliability, security and privacy regulation compliance
  - reimbursement
- FDA focus on apps that transform phone/tablet into a regulated medical device
- renewed FTC interest on apps making unsubstantiated claims

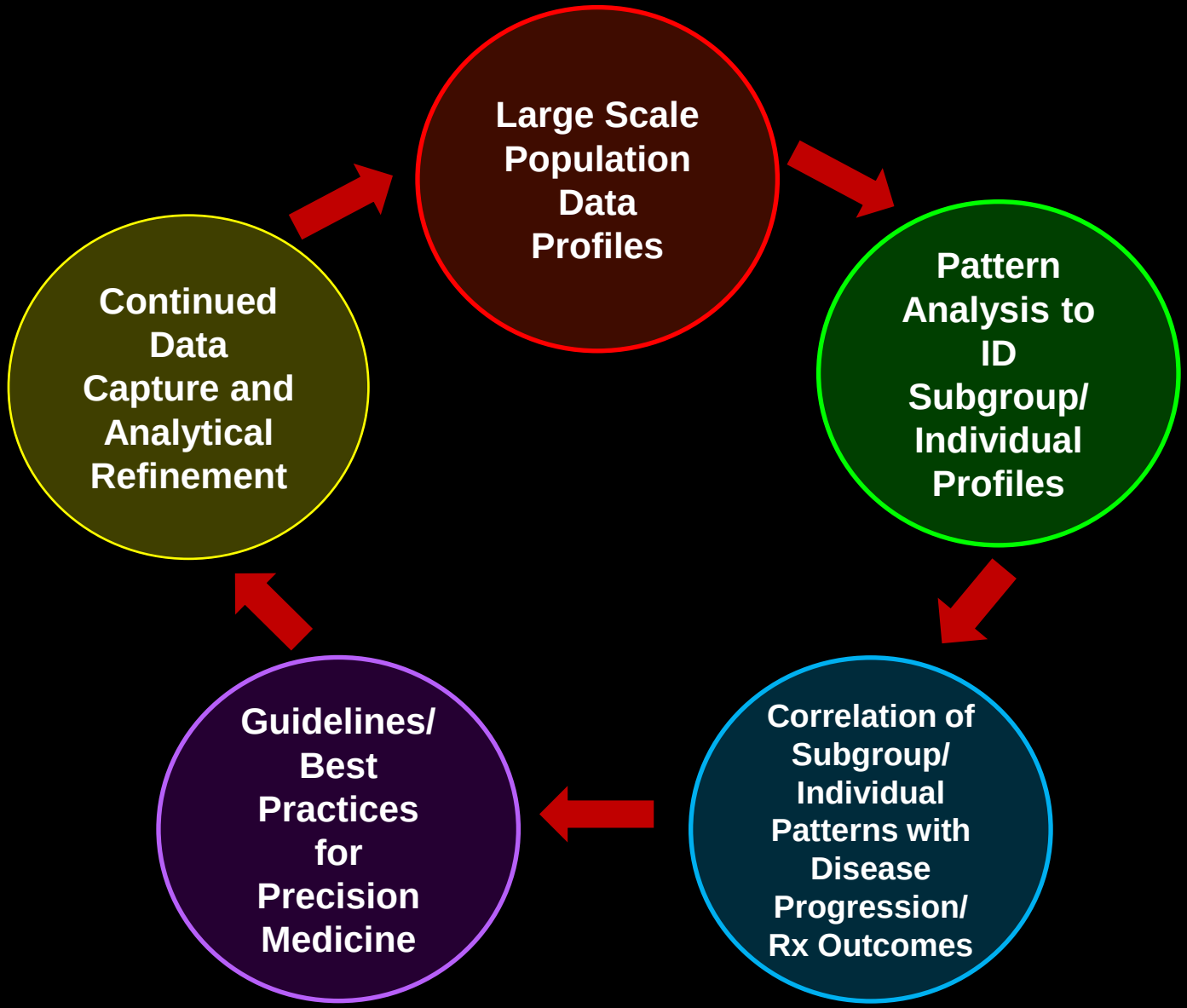
Social Spaces Become Quantifiable

- who knows why people do what they do?
  - the fact is that they do!
- these actions can now be traced and measured with unprecedented precision
- with sufficient data, the numbers reveal increasingly predictable behavior individual risk patterns
- new business opportunities in multiple sectors including healthcare
- new ethical and legal issues
  - consent, privacy, surveillance, security

Population Health Research and Precision Medicine: Blurring the Boundaries Between Research and Clinical Care

- every encounter (clinical and non-clinical) is a data point
- every individual is a data node
- every individual is a research asset

The Virtuous Circle of Data on Population Health and Individuals in Driving Precision Medicine

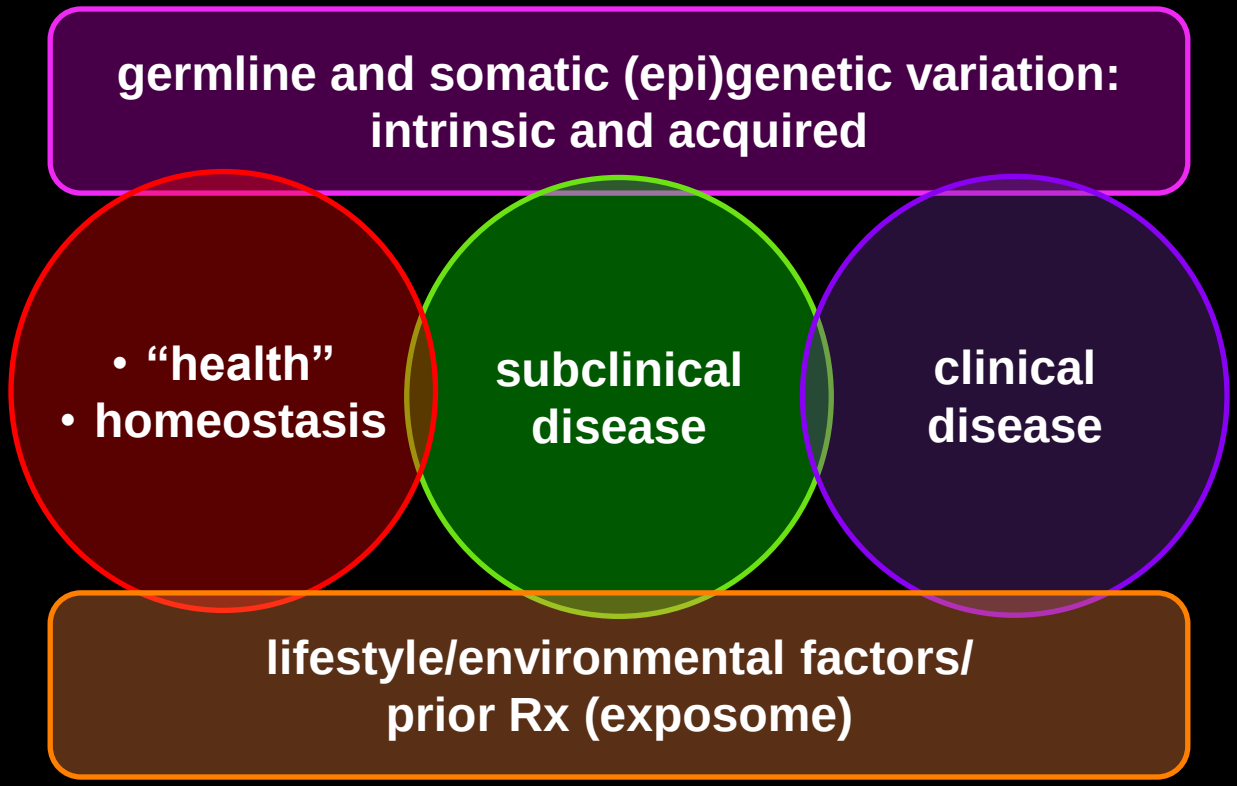


Integration of Large Scale Genomic and Clinical Information (PheWAS)

- 4 April 2016
- BioVu data base
  - de-identified DNA database of 215K genetic samples and 2.5 million clinical records

- 6 April 2016
- Million Veterans Program
- Hybrid Cloud for Genotype-Phenotype Graph Analysis Engine

Precision Medicine



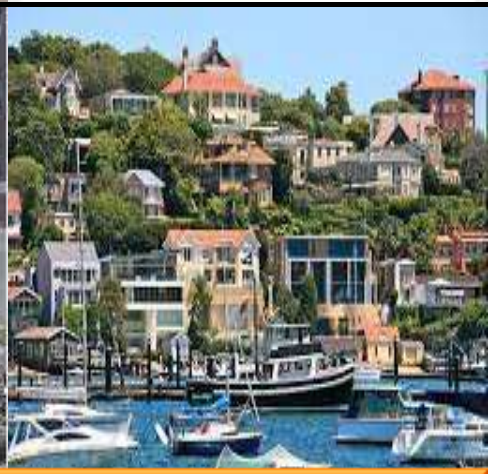
The Evolution of a Data-Driven Health Ecosystem: Systematic Integration of Diverse Data Sets for Population Health Analytics

Continuity of Care Record: From Womb to Tomb







Behavior

Environment

Mobile Apps, Wearables, Sensors and Continuous Monitoring

- who sets the standards?
- who integrates and interprets the data?
- who pays?
- who consents?
- who owns the data?

"Do you solemely swear to have no involvement in your own care?"

The Wellness Premium

Greater Engagement and Incentivization of Consumers/Patients in Care Decisions and Sustaining Wellness

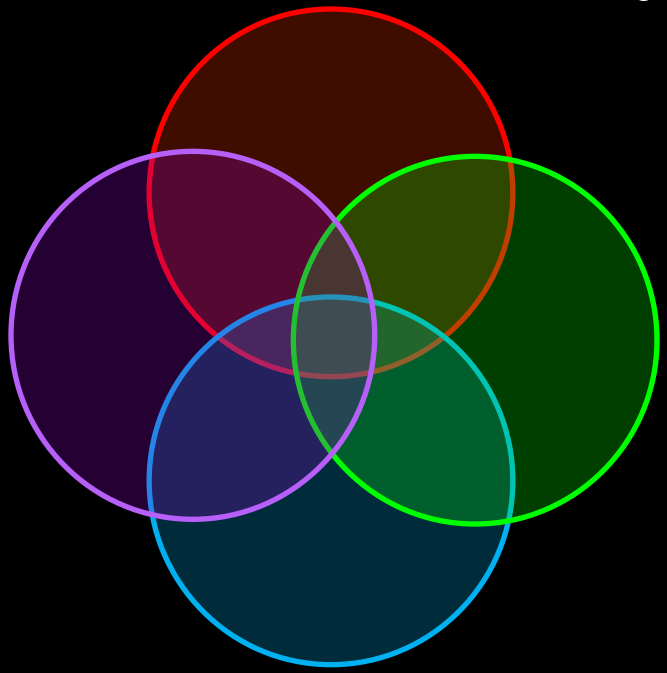
“Patient-Centric Healthcare” Without Patient Engagement Is An Illusion

The Principal Forces Shaping The Evolution of Precision Medicine

engineering and device-based medicine

- wearables
- sensors
- smart implants

- remote health monitoring
- telemedicine
- robotics



molecular (precision) medicine

- panOmics profiling
- analysis of disruption in biological networks

information-based healthcare

- m.health/e.health
- data- and evidence-based decisions and Rx selection

BIG DATA

outcomes-based healthcare and sustainable health

new value propositions, new business models and services

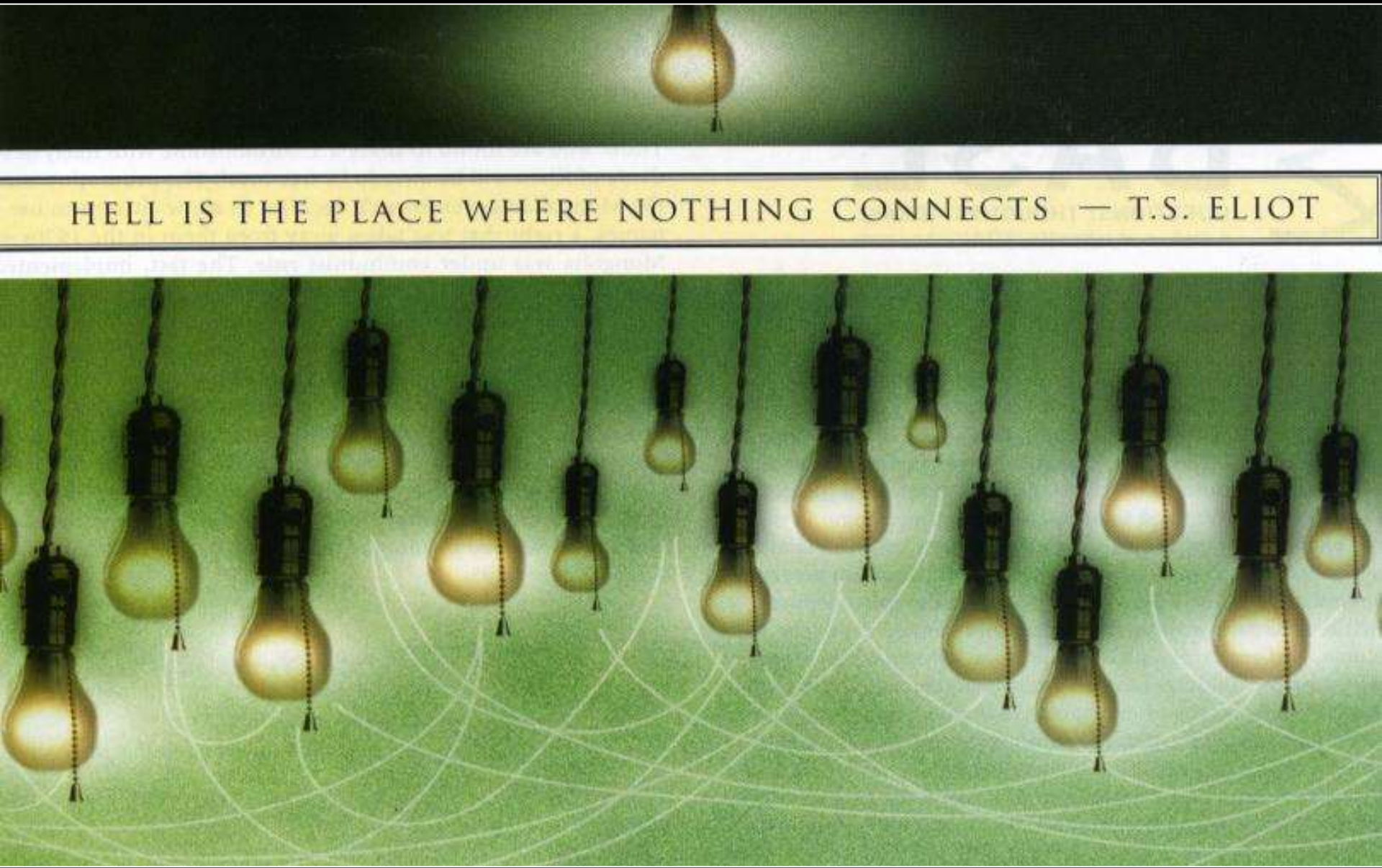
Now Comes the Hard Part!

Driving Precision Medicine and Data Analytics Capabilities into Routine Clinical Practice

Integration of Rapidly Expanding and Increasingly Diverse Datasets for Longitudinal Observational Profiling and Continuity in Care Delivery

New Incentives and New Delivery Models

New Participants and New Business Models


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

Silos Subvert Solutions:
Protecting Turf and Sustaining the Status Quo

The Worst Supply Chain in Society: The Health Information Supply Chain

- no area of the economy (15-20% GDP) generates as much information as the health sector yet uses it so poorly
- fragmented, disconnected data
- incompatible data formats as barrier to data integration
- incomplete and inaccurate data
- slow transition from paper to electronic systems
- inadequate information on behavioral and environmental influences
- legislative barriers to data transfer based on well intentioned privacy protections

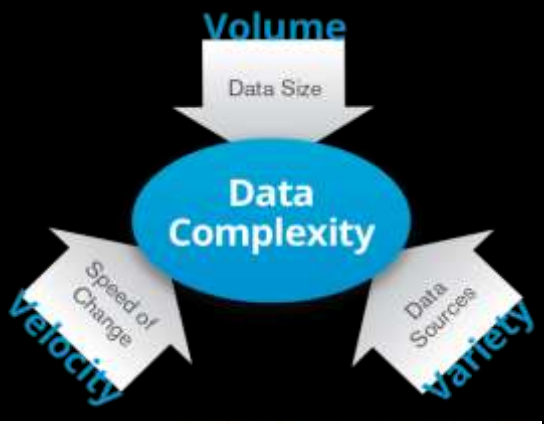
The Pending Zettabyte Era
1,000,000,000,000,000,000,000

Managing Big Data in Biomedicine is Not a Simple Extrapolation from Current Practices

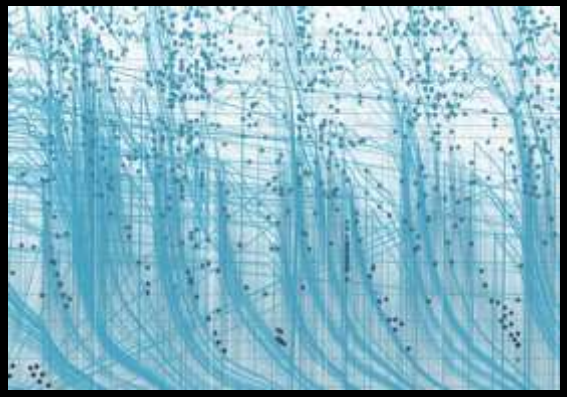
Current Institutional Structures and Competencies Are Ill-Prepared for Pending Disruptive Change

The Unavoidable Data-Intensive Evolution of Healthcare: Major Challenges Ahead

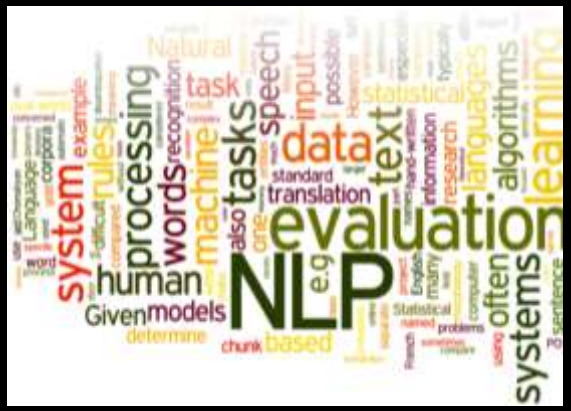
PB and TB Data Streams



Ontologies and Formats for Data Integration



Longitudinal Data Migration and Inter-operable Dbases



New Data Analytics, Machine Learning, NLP Methods

Infrastructure, Storage and Privacy

Data Science and Data Scientists

Data Privacy, Security and Ownership

- HIPAA provisions insufficient in an era of massive electronic connectivity
- ID of disease burden and potential future risk by peoples' movements and purchasing practices via location-based services
- health data in the cloud
  - increasing need/value for shared data
  - big data collaboratories and meta-analytics
  - provenance validation, access control
  - global server networks and routine data movement beyond sovereign boundaries

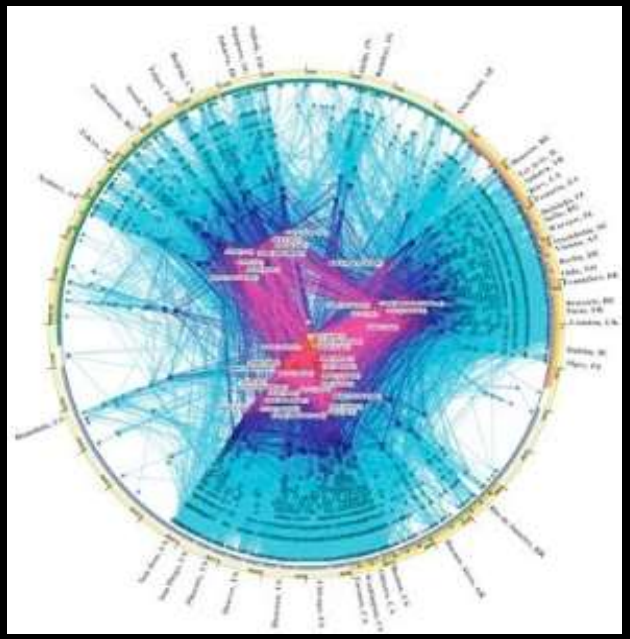
Data Brokers

- HIPAA applies only to information shared with healthcare providers, medical facilities, pharmacies and insurers
- information revealed to third parties outside of healthcare has no HIPAA protection
- over 1400 companies sell consumer data
- corporations spent over $7 billion in 2012 for access

Expanding the Concept of Consent in an Era of Molecular Profiling and Digital Health

- individual right to control use and reuse of personal information
- primacy of use of data for individual's care
- simultaneous data generation for mining for multiple purposes for research and improved care for larger populations

The Emergence of Big Data Changes the Questions That Can Be Asked



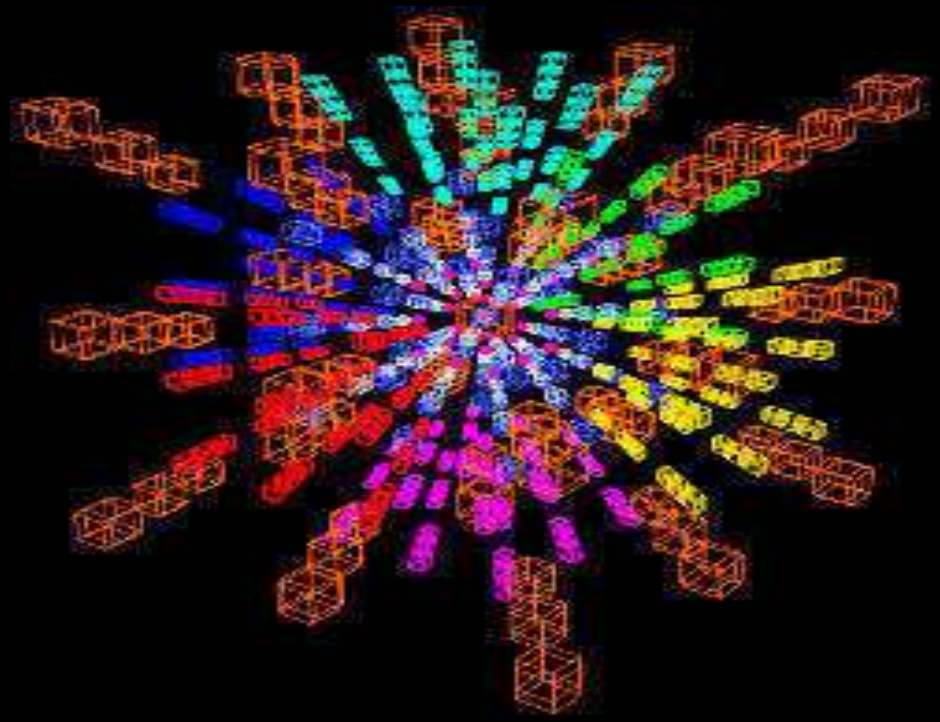
Isolated Data	Complex Networked Data	Complex Computational Data

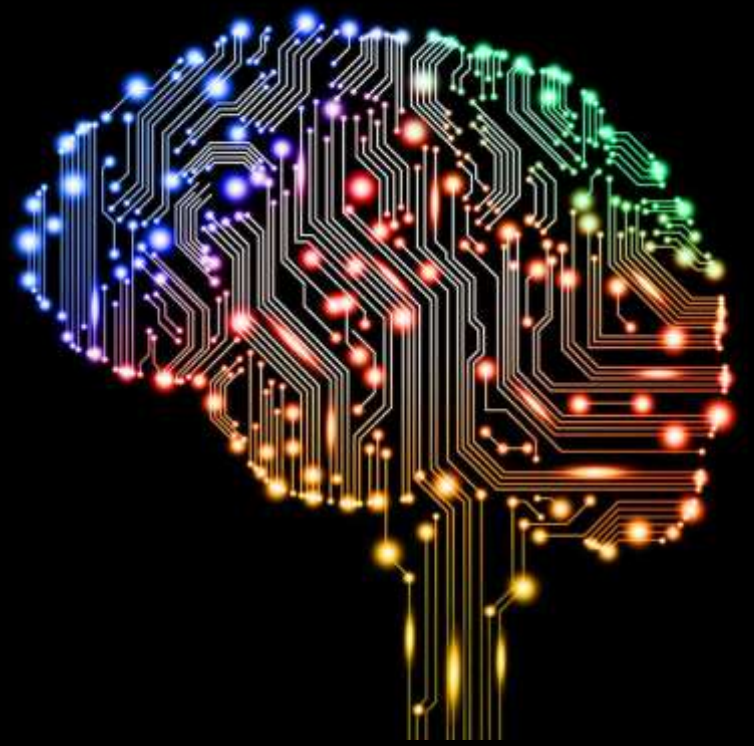
The Pending Era of Cognitive Computing and Decision-Support Systems: Overcoming the "Bandwidth" Limits of Human Individuals

- limits to individual expertise
- limits to our multi-dimensionality
- limits to our sensory systems
- limits to our experiences and perceptions
- limits to our objective decision-making

Advanced Computing and Artificial Intelligence: The Rise of 'Learning Machines' in the Analysis of Massive Datasets and Decision Algorithms

Automated Context: Data Finding Data
"Intelligence at Ingestion"





Feature Extraction and Classification

Context Analysis

Persistent Context

- **Relevance Detection**
- **Situational Awareness**
- **Intelligence**

Rapid, Informed Decisions

Computational Rationality

- convergence of analytics for ‘intelligence’ in brains, minds and machines
- representation and procedures for large scale probabilistic inference
- identification of decisions with maximum expected utility (MUE)
- inferential processes for learning, reasoning and predicting under uncertainty and incomplete data

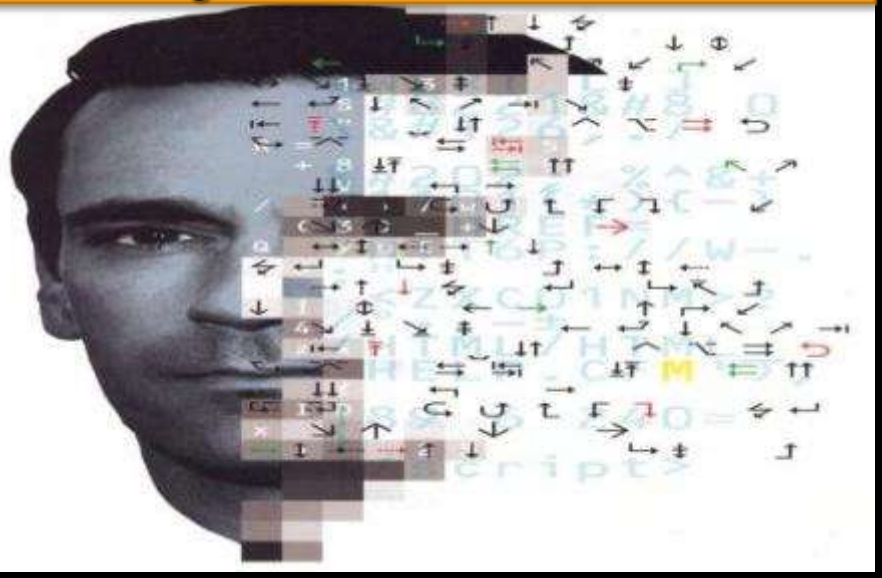
Data-Driven Knowledge, Intelligence and Actionable Decisions

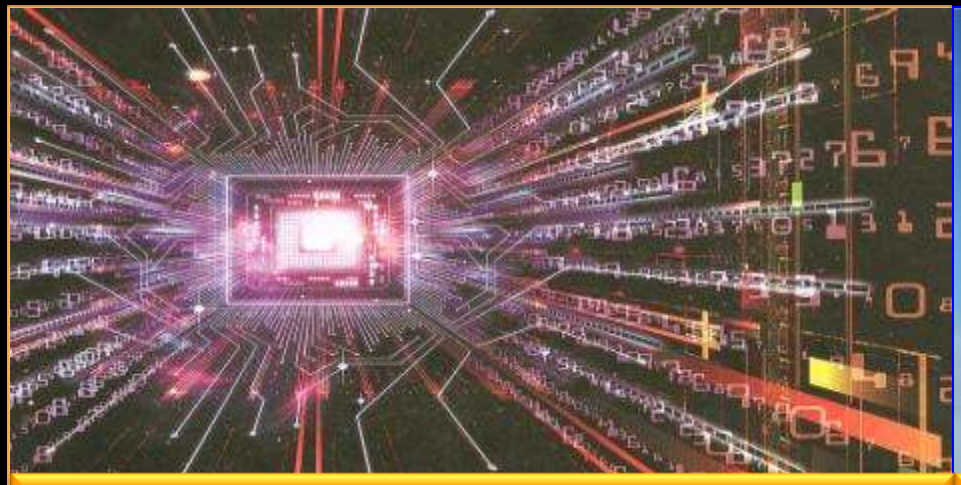
- changing the nature of discovery
  - hypothesis-driven versus unbiased analytics of large datasets (patterns, rules)
- changing the cultural process of knowledge acquisition
  - large scale collaboration networks, open systems versus individual investigators and siloed data
- changing knowledge application
  - increased quantification, big data analytics and decision-support systems
- changing the cognitive and intellectual competencies for knowledge-intensive competitiveness in multiple domains
- changing education, training, research and care delivery

Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Medical Education Curricula

Data Deluge

Cognitive Bandwidth Limits





Automated Analytics and Decision Support

Facile Formats for Actionable Decisions

Precision Medicine: Implications for Future Medical Education, CME and New Skills for Healthcare Professionals

- molecular medicine and deep phenotyping (panOmics)
- engineering-based medicine (sensors, robotics)
- data-intensive healthcare (data science)
- automated big data analytics (machine intelligence, decision science)
- consumer-engaged healthcare (UX)

Precision Medicine: Implications for Future Medical Education, CME and New Skills for Healthcare Professionals

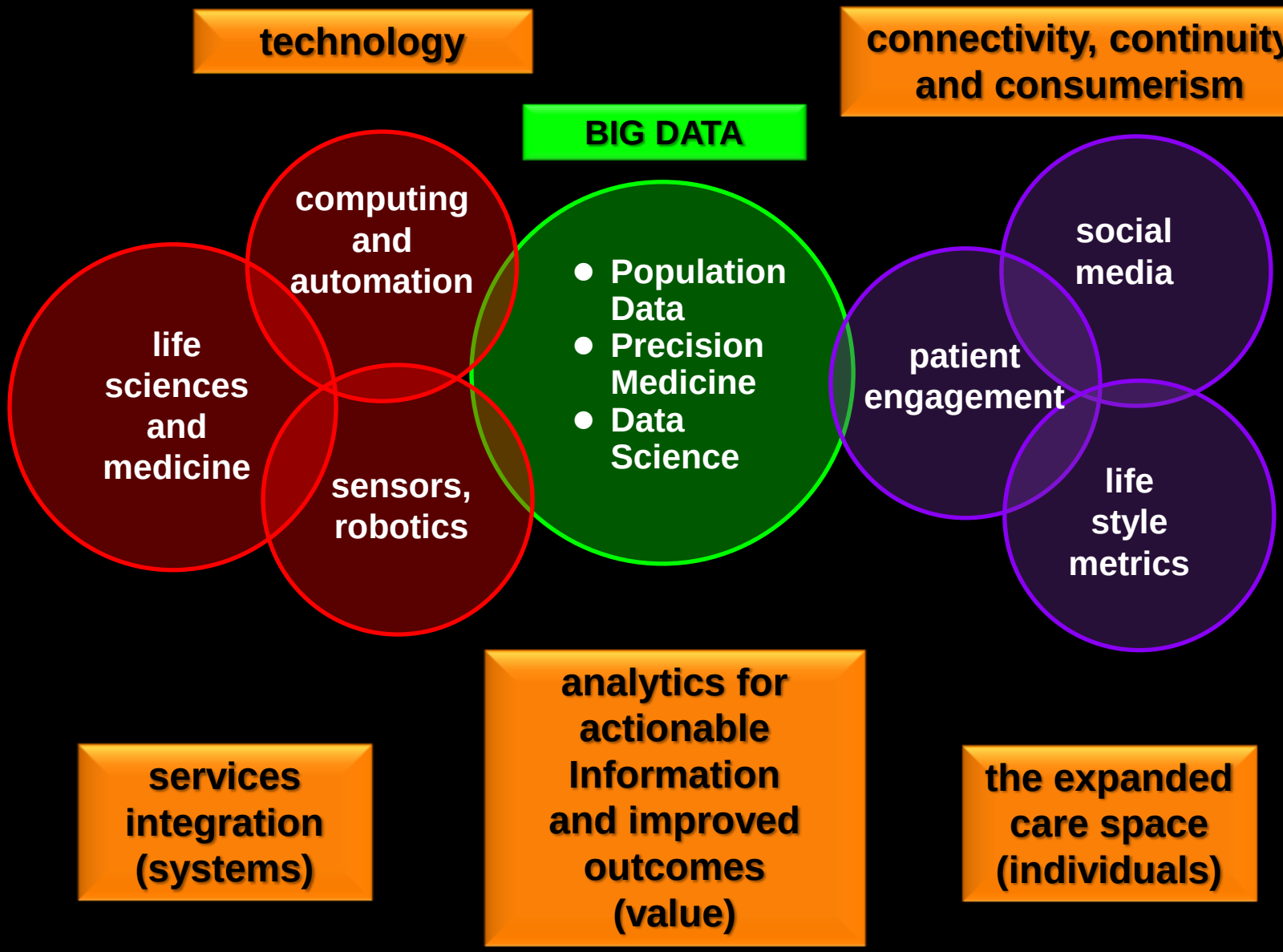
- recalibration of the primacy of MD-centric decisions in many facets of care delivery
- integrated team based care delivery
- advanced diagnostics (panOmics) and computational decision support systems

“I Can’t Let You Do That Dave”

Living in a World Where the Data Analytics and Interpretation Algorithms Are Obscure to the End User

- ceding decision authority to computerized support systems
- culturally alien to professionals in their expertise domain but they accept in all other aspects of their lives
- who will have the responsibility for validation and oversight of critical assumptions used in decision tree analytics for big data?
  - regulatory agencies and professional societies (humans)?
  - machines?

Convergence



“DNR”

- Denial
- Negativity
- Resistance

Enduring Themes in the History of Science and Technology: The Poverty of Imagination

- the recurrent myopia of individuals and institutions in recognizing new disruptive technologies
  - arrogance, complacency, denial
  - risk avoidance, investor timidity
  - indecisive, sclerotic hierarchies/cultures
- disruptive technologies
  - created disproportionately by individuals/enterprises operating at the mainstream margins or at the convergent interstices of previously separate disciplines/domains

Incrementalism

versus

Disruptive Innovation

Yes

No

Defining the Future Role of Clinical Pathology and Laboratory Medicine

- the changing analytical and data ‘spaces’ for clinical pathology and laboratory services
- role as knowledge integrators in making precision medicine a reality?

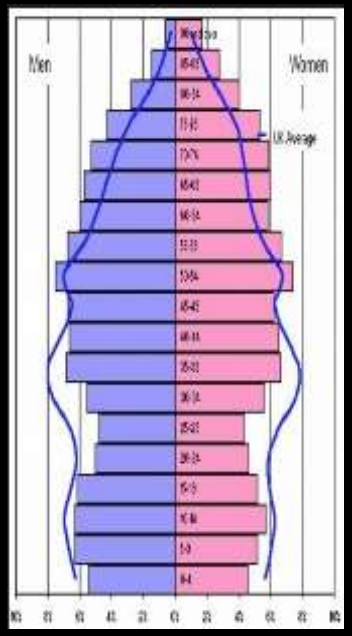
or

- Darwinian (Schumpterian) eclipse by new entrants and new service/business models?

“Strategic Spaces” in Biomedical R.D and Healthcare Delivery

Precision Medicine

Population Demographics and Disease Burden



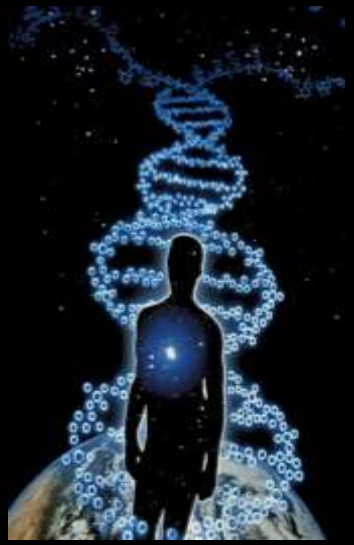
IoT: Ubiquitous Sensing and Sensor Networks

Big Data Analytics, Machine Learning

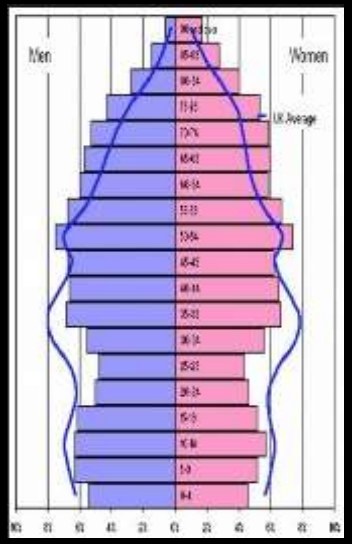
Escalating Complexity

“Strategic Spaces” in Biomedical R.D and Healthcare Delivery

Precision Medicine



Population Demographics and Disease Burden



IoT: Ubiquitous Sensing and Sensor Networks

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Escalating Complexity

New Patterns of Technology Convergence, Evolution and Adoption

New Knowledge Networks

New Participants

New Organizational Models

Opportunity Space

Slides available @ http://casi.asu.edu/