



# Leadership Challenges in Biomedical Innovation in an Era of Disruptive Change, Escalating Complexity and Pervasive Uncertainty

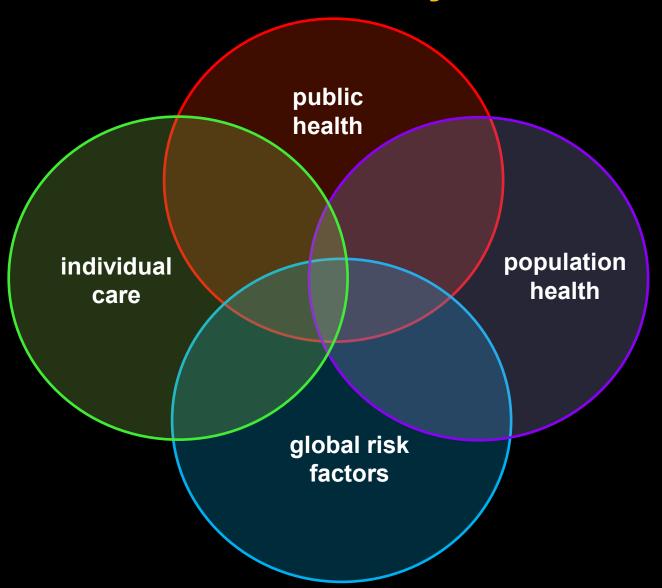
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## The Health Ecosystem



## The US Healthcare Ecosystem

- the \$4.1 trillion US health system (c. 20% GDP) is unmatched in the scale and diversity of organizations and functions
- over 450,000 entities involved in the development and delivery of highly specialized services to heterogenous populations over their lifetimes
- health ranks highest in public and political expectations regarding access, availability, affordability and quality of care

## The US Health Ecosystem

- demographics of an aging society and increased chronic disease burden
  - 50% cost incurred in last six months of life
- disturbing increase in mental illness, SUD, suicide even before the COVID pandemic
- economically and clinically unsustainable
- imbalance between care-centric (sick care) versus health-centric (wellness) expenditures
- fee-for-service incentives for providers reward volume of care versus outcomes
- imbalance in investments in population focused health initiatives versus individual care

## The US Health Ecosystem

- protracted and varied diffusion of new technologies into clinical practice
- wide variation in clinical practice
- poor coordination and continuity of care across the health/health care system
- large disparities in access to care
- inefficient integration and analysis of data to drive evidence-based/best practice protocols

## The US Health Ecosystem

- urgent societal imperative to increase access to care, reduce cost and improve clinical outcomes
- need for greater recognition of social determinants of health (SDoH) in disease risk and access/cost of care
- fragility in preparedness/resiliency for unanticipated large-scale disruption (pandemic, cyber, grid collapse, supply chains)

### The Health Ecosystem

- facing a confluence of complex events that will radically alter all aspects of biomedical research and health care delivery
  - national and global
- cross-domain technology convergence
  - biomedicine, engineering and computing
- cross-sector industry convergence `
  - diagnostics, therapeutics, data analytics, social media
- public and political expectations
  - access, availability, affordability and outcomes
  - reduce disparities and inequities

## The Health Ecosystem

 facing a confluence of complex events that will radically alter all aspects of biomedical research and health care delivery

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- cross
  - bio
- cross
  - diagnostics, therapeutics, data analytics, social media

VALUE

- public and political expectations
  - access, availability, affordability and outcomes
  - reduce disparities and inequities

## Leaders as 'Design Architects'

'Design Thinking' in an Era of Disruptive Change, Escalating Complexity and Uncertainty

## **Navigating Change**

## Complex Interactions Between Multiple Stakeholders with Different Incentives



Technical, Socio-Cultural, Economic and Political Change Drivers



Incremental Innovation Versus Disruptive (Radical) Innovation



### **Innovation**

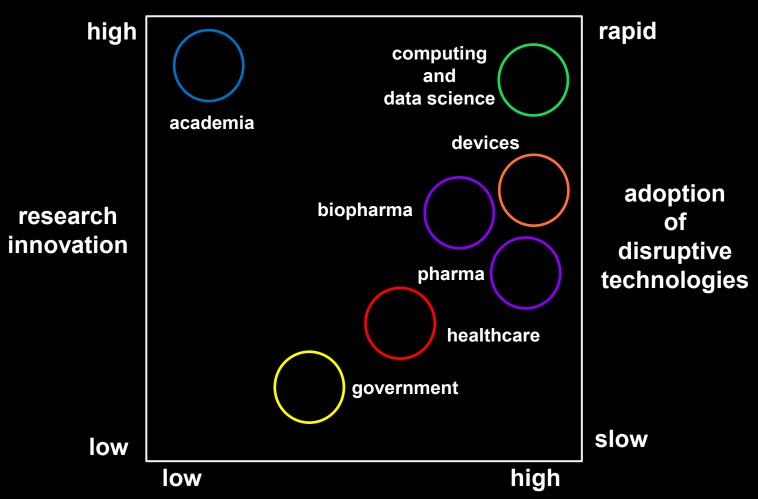
#### **Disruptive Innovation**

- new technical or commercial concepts that disrupts the status quo
- creation of entirely new markets for novel products/services
- competition on NEW VALUE PROPOSITIONS (intellectual/commercial/military)
- often unrecognized or dismissed by currently successful organizations (complacency)

#### **Incremental Innovation**

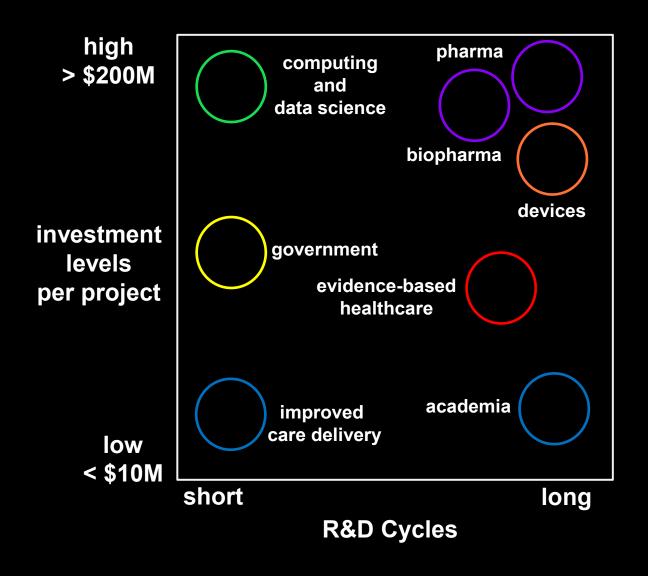
- small conceptual refinements and/or design of additional features into existing products and services
- competition on VOLUME between minimally differentiated products/services (market share)

## **Drivers of the Healthcare Innovation Ecosystem**



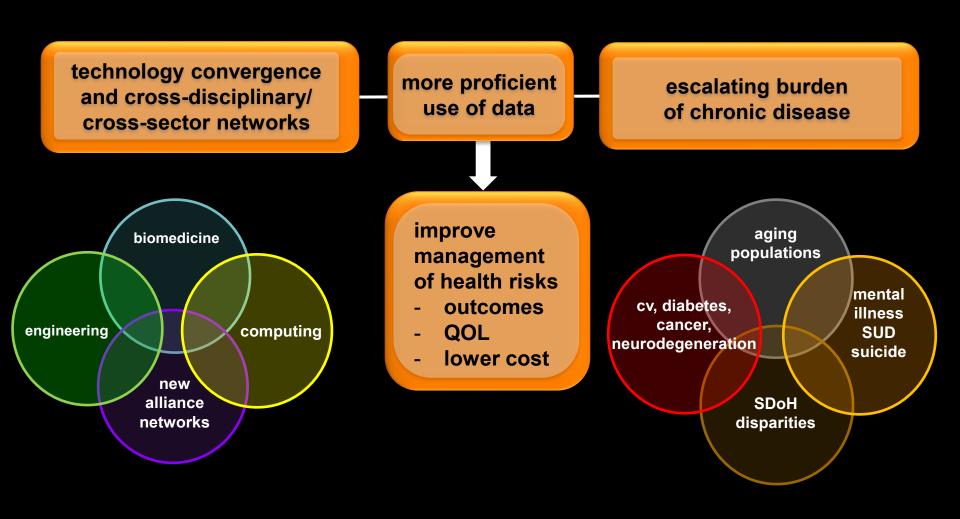
translational proficiency: scale and dependence on systems-based integration

## **Drivers of the Healthcare Innovation Ecosystem**



## Precision Health and Digital Health: Inter-dependent Strategic Drivers in the Evolution of Healthcare Policies and Priorities

#### The Strategic Landscape for Biomedical Research and Health Services

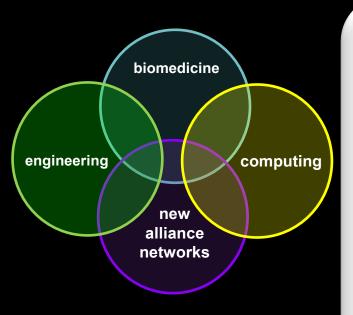


#### The Strategic Landscape for Biomedical Research and Health Services

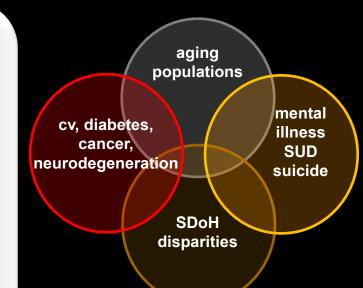
technology convergence and cross-disciplinary/ cross-sector networks

more proficient use of data

escalating burden of chronic disease



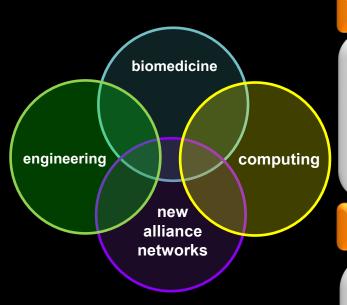
- remote health monitoring to identify/mitigate risk
- reduce (re)hospitalization
- the expanded care space and continuity of care
- SDoH and health disparities
- improve outcomes and QOL



#### The Strategic Landscape for Biomedical Research and Health Services

technology convergence

escalating chronic disease burden

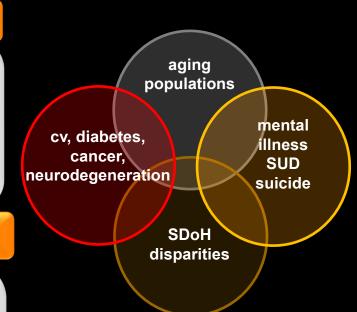


#### precision health

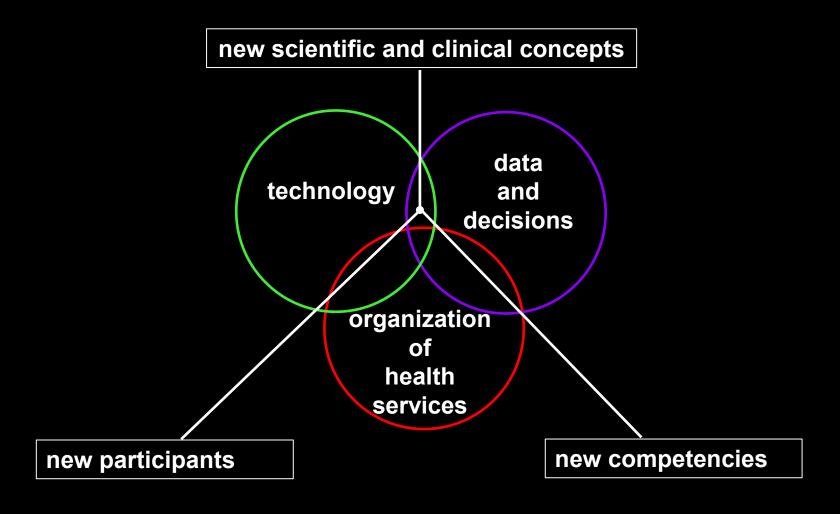
- defining disease at the molecular level
- disease subtyping and optimum treatment selection
- identify predisposition risks

#### digital health

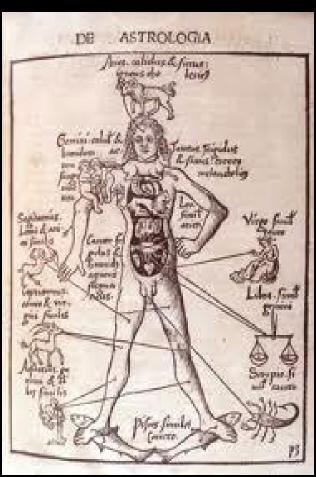
- telemedicine
- remote health monitoring
- ML/Al for large data analytics
- clinical decision support tools
- empowered patients



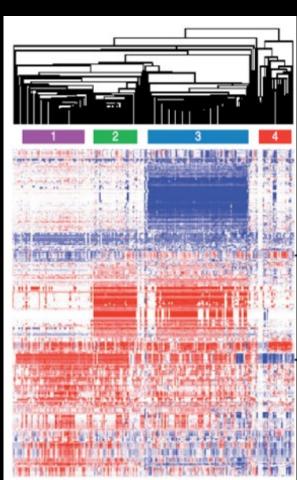
## The Evolving Systemic Landscape in Health



## The Path to Precision Health: From Superstitions to Symptoms to (Molecular) Signatures





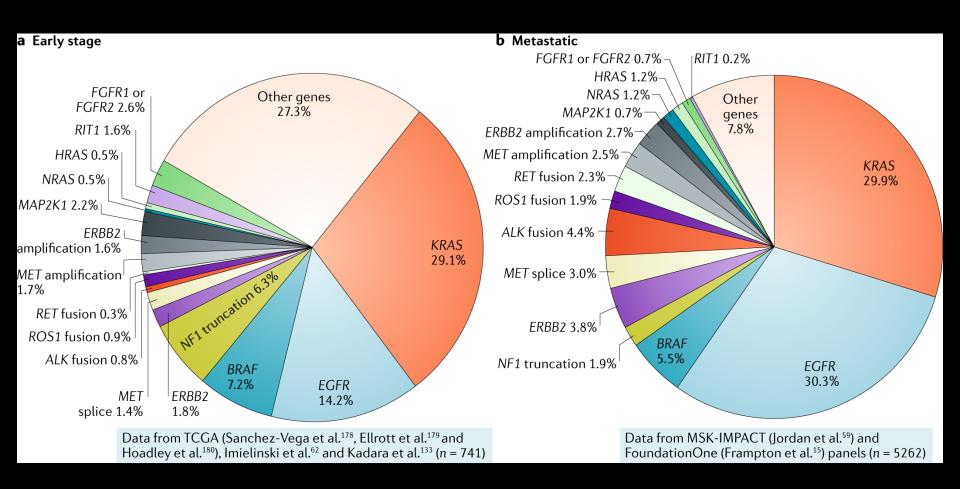


humors; astrology, shamanism, sin and divine fate

biochemistry and organ-based pathophysiology

molecular biology and multi-omics profiling

## Molecular Classification of NSCLC and Identification of Single, Largely Non-Overlapping Oncogenic Alterations

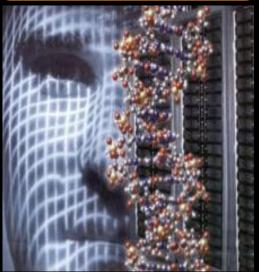


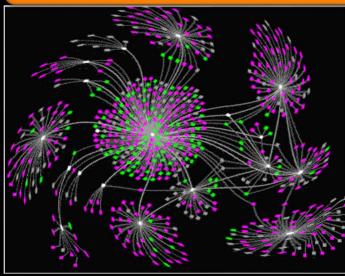
From: F. S. Koulidis and J. V. Heymach (2019) Nature Rev. Cancer 19, 495

## **Precision Health**

(Epi)Genomics and MultiOmics Profiling

Detection of Altered Molecular Signaling Networks in Disease: A New Taxonomy of Disease and Subtype Classification







MDx Signatures of Disease Predisposition and Subtyping of Overt Disease for Optimum Rx Selection

- terabytes per 100001111 individual
- zettabyte yottabyte population databases

The Challenge of Big (Messy) Data

## Deep Phenotyping: "Much More Than Omics"

From Womb to Tomb: Systematic Integration of Diverse Health Data



SDoH, Lifestyle, Environment, Health Disparities



- the majority of events that influence wellness/disease risk and treatment adherence occur outside of formal interactions with the healthcare system
- daily decisions by individuals have greater effects on their health than decisions controlled by the healthcare system

## **Expanding the "Care Space" in Healthcare**

**Healthcare Beyond The Clinic** 

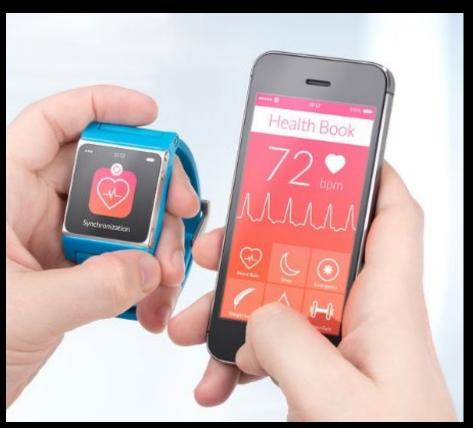
**Remote Health Status Monitoring** 

Smartphones, Wearables, Devices and Digital Services

M4: Making Medicine More Mobile

**AORTA: Always On, Real Time Access** 

## Wearables and Mobile Devices: Key Drivers in Remote Health Monitoring and Care Delivery





## **Wellness Apps for Fitness, Diet and Exercise**

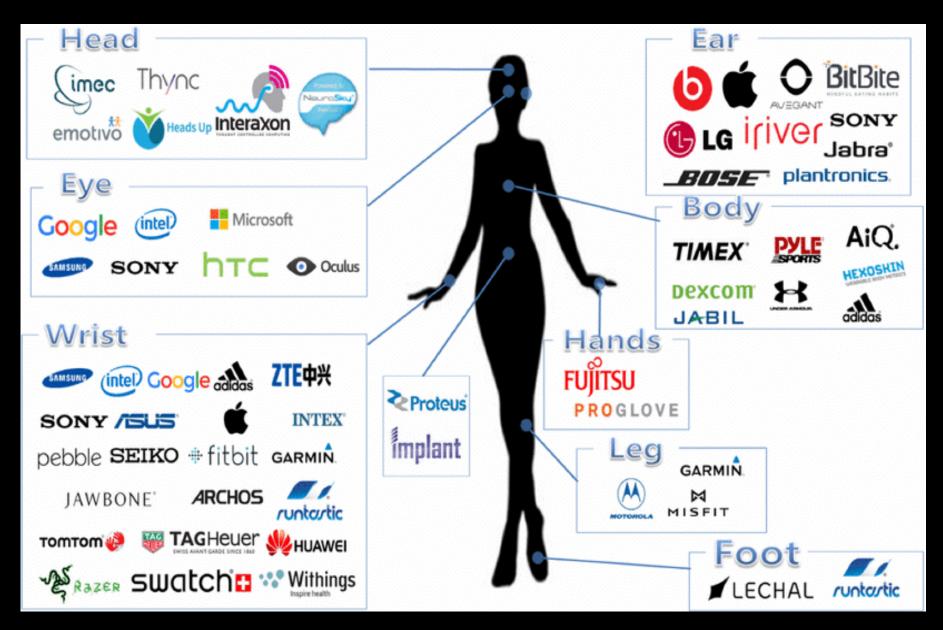








## Wearables and Remote Health Status Monitoring



## **Smart Devices for Automated Drug Delivery** and Improved Therapeutic Adherence









Propeller Health

Gecko (now Teva)

CapMedic

Biocorp Inspair







## Rapid Growth in Wearables, Sensors and Devices for In-Home Remote Health Status Monitoring



### The Eldercare Gap

10,000

boomers turn 65 every day

79%

increase in boomers age 80 or older from 2010 to 2030

1%

 projected increase in number of caregivers aged 45 to 64 from 2010 to 2030

348,000

 projected number of home health aides needed in next decade

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



Rx adherence



in-home support and reduced readmissions



cognitive stimulation



reduced office visits

## **Empowered Patients:**Social Networking Sites and Their Role in Clinical Care

- logical extension to healthcare of rapid rise of web/apps in mainstream culture
- increasingly proactive and engaged consumers/patients/families
- greater access to information on treatment options, cost and provider performance
- new clinical practice tools to optimize physicianpatient relationships
- Ux and formation of senior executive level Chief Patient Experience Officer posts in large provider organizations

### **Economies of Scale and Consumer Convenience**



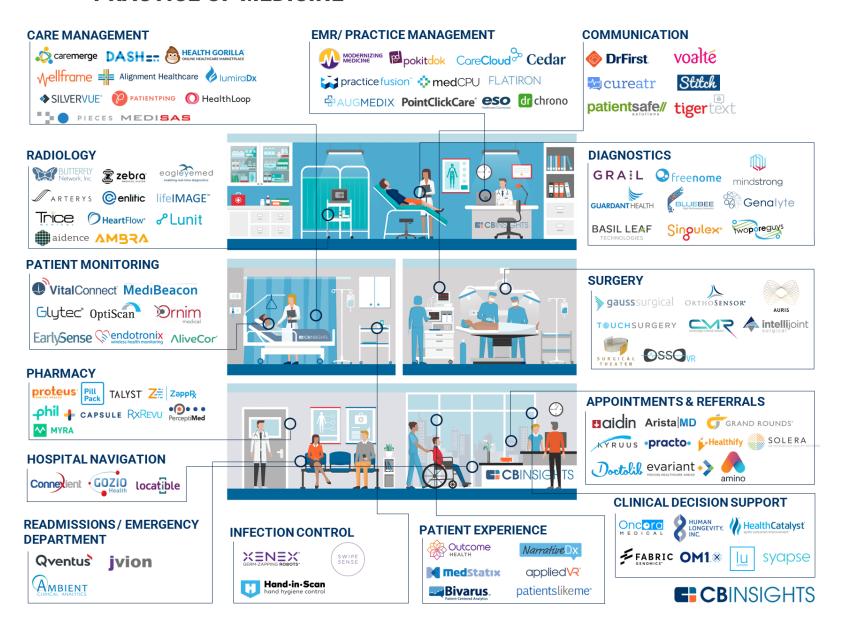


Networked Telehealth Between
Provider Organizations:
Centralized 24/7 Monitoring of
Critical Care and Expert
Consultations





## THE DIGITAL HOSPITAL: 100+ COMPANIES REINVENTING THE PRACTICE OF MEDICINE



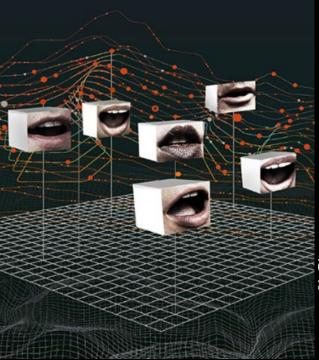
Telemedicine and Behavioral Health: Digital Psychiatry and Non-Pharmacologic Digital Therapeutics

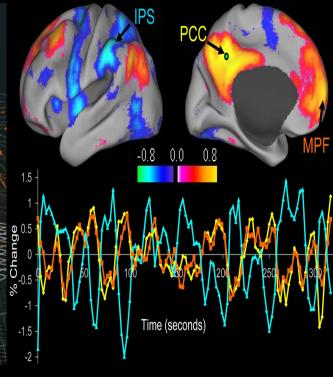
### **Increased ED Behavioral Health Emergencies**

- reported range of 8-25% of ED volume
- 70% of behavioral health patients also have one or more co-morbidities
- opioid-related visits tripled between 2005-19
- approx. 1 in 4 individuals with serious mental illness also have substance abuse disorder
- 60% of adolescents in community-based SUD treatment programs also meet diagnostic criteria for mental illness
- dramatic increase in mental health needs in COVID-19 pandemic

# Computer Vision, Facial Recognition and New Digital Psychometrics in the Evaluation of Mental Illness







- eye movements
- facial dynamics
- stimulus response reaction and interaction speeds
- speech patterns (rhythm, tone, volume)
- semantic construction
- 256 lead EEG
- brain imaging functional MRI
- altered signal pathways

ML/Al analysis of individual multiparameter responses matched to large-scale analysis of video data banks of patients with clinically validated mental disorders

## "Digiceuticals": Software as Therapy





"We envision empowering individuals with digital therapeutic solutions that address underlying motivational and technical deficits by deciphering neural pathways that support motivation, decision-making and reinforcement to prompt health."

Dr. Ben Wiegand Global Head, Janssen R&D World Without Disease Accelerator PharmaVoice 2017

#### **Digital Therapeutics Alliance**









































## **Robot–Human Directed Interactions**

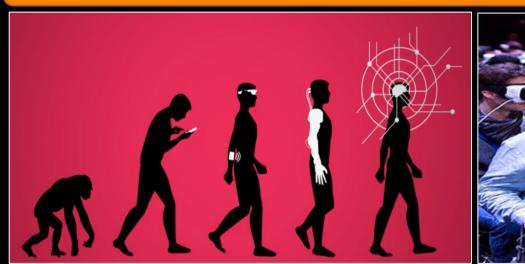








#### Co-evolution of Human-Machine Interactions, Robotics and Augmented Cognition





**VR/AR/MR** and Preparation for Complex Procedures







#### AR/VR/MR Neuromodulation in Clinical Care



- injury rehabilitation
- reduce apprehension/distraction in painful procedures
- anxiety, depression, PTSD, phobias

#### The Internet, Social Media and the Road to the Metaverse

- who knows why people do what they do?
  - the fact is that they do!
- the confessional of social media
- these actions can now be traced and measured with unprecedented precision
- with sufficient data the numbers reveal increasingly predicable behavior and individual risk patterns
- blurring of private and public spaces
- blurring of the real and the imaginary
- complex ethical and legal issues
  - consent, privacy, security, surveillance

## Welcome to Avatar World: Metaverse V. 1



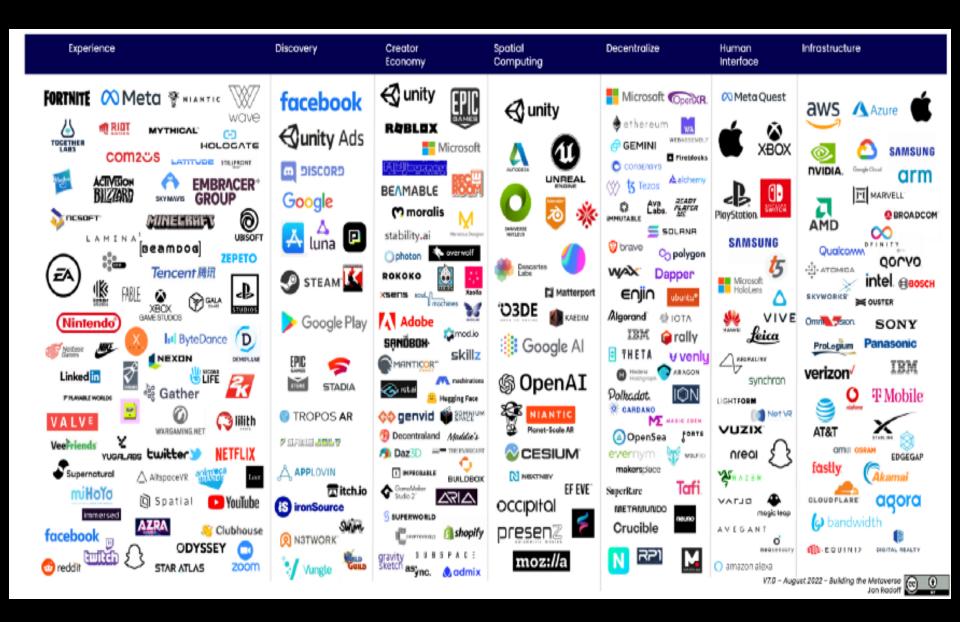




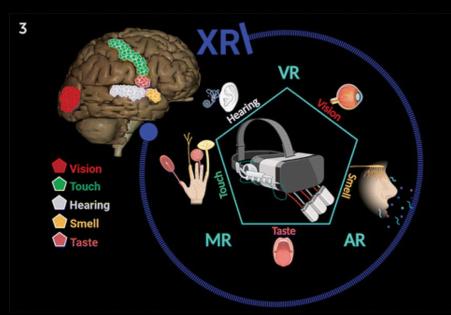
### The Road to The Immersive Metaverse



## **Metaverse Market Map**



## **Welcome to Metaverse World:**



extended reality (XR): building the virtual sensorium

new virtual experiences:
Tamagotchi babies



#### The Neurobiology of Instant, Superficial, Repeated Gratification



interactive multiplayer gaming and modulation of reward neurocircuitry

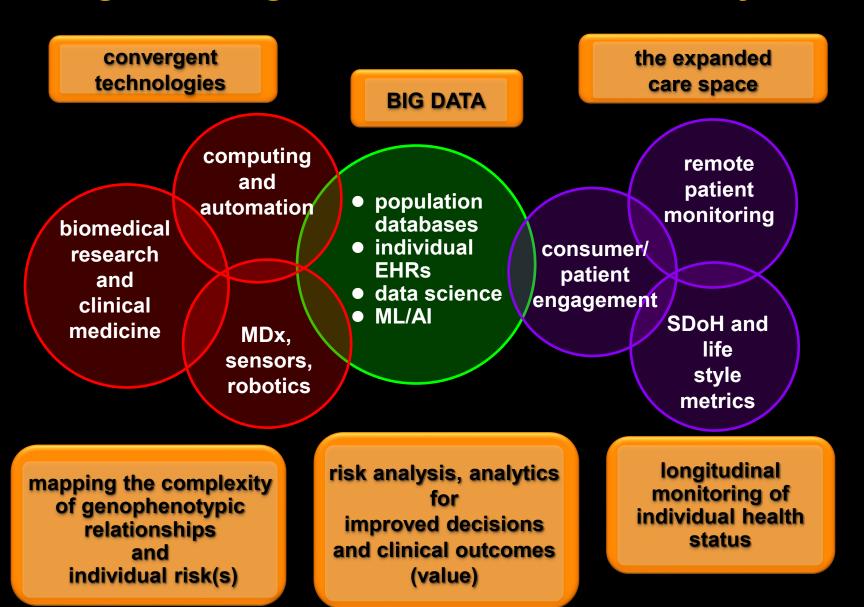
virtual immersion and education in the most plastic phase in the development of human analytical skills and socialization



# Health Effects of Ubiquitous Immersion and Dependencies in Digital Environments

- unknown long term socio-cultural implications of new sensory, cognitive and behavior patterns positively reinforced in digital ecosystems
  - individuals, institutions, society
  - the new evolutionary selection pressure?
     (digital Darwinian fitness)

# The Co-Evolution of Precision Health, Digital Health: Building Learning Healthcare Information Systems



### **Now Comes the Hard Part!**

Driving Precision Health and Large Scale

Data Analytics into Routine Clinical Practice

**New Incentives and New Delivery Models** 

**New Participants and New Business Models** 

## More Than Just Technology

- integration of new work processes
- no risk to income(HCPs), profitability(private sector)
- continuing training curricula and CME

Clinical-Centric (Caregiver)Needs Centric Needs

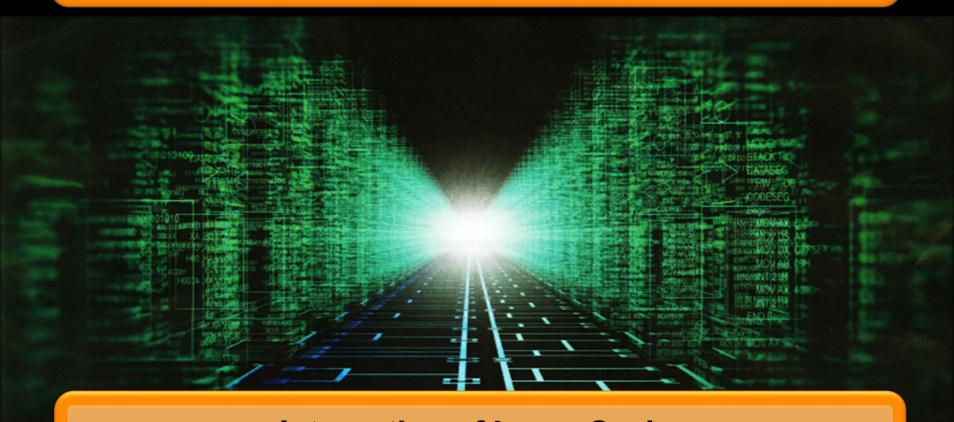
Payor Needs

- increased convenience, acceptance and adherence treatment
- telemedicine and interactive systems
- empowerment

- the bottom line and margins
- reduce direct care costs
- optimize use of finite and expensive resources (Facilities, Equipment, Personnel, Training)

## Big Biology and Biomedicine Meets Big Data

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

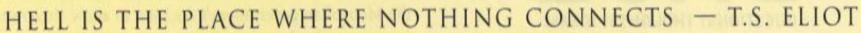


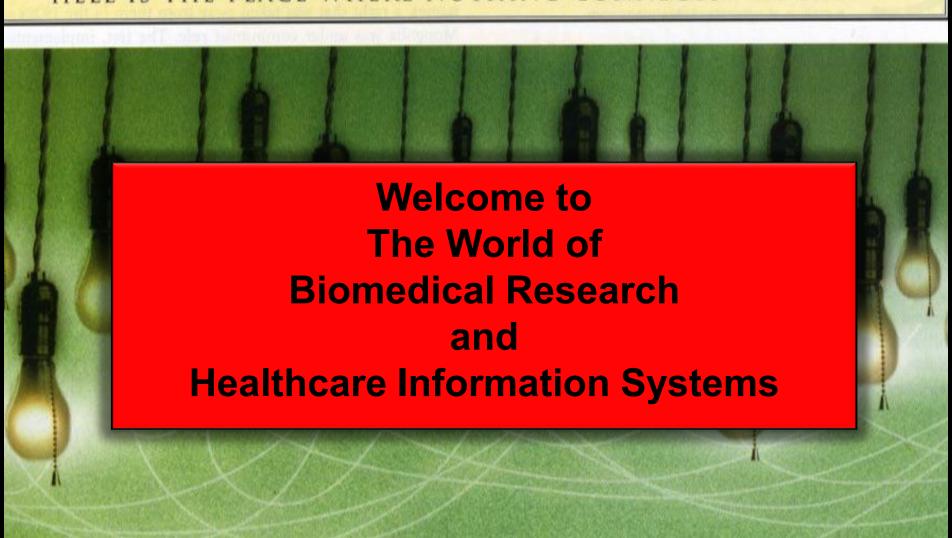
**Integration of Large Scale, Multi-Disciplinary Datasets** 

## Managing Big Data in Biomedicine Will Not Be a Simple Extrapolation from Current Practices



Co-Evolution of Professional Competencies With Advanced Computing and Automated Clinical Decision Systems





#### Biomedical Data: Vast, Growing Rapidly but Poorly Used

- inadequate standardization
- fragmented, incomplete, inaccurate data and uncertain provenance
- incompatible data formats as barrier to data integration and sharing
- static, episodic snap shots of individual health status versus integrated longitudinal health history
- obstacles to EHR integration of new data classes multi-Omics; wearables; IoMT; RHM
- legislative barriers to data transfer based on well intentioned privacy protections (HIPAA)
- organizational, economic and cultural barriers to open data sharing
- major impediments to research productivity, optimum clinical decisions and continuity-of-care for patients

# Data Security and Protection of Health Information



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



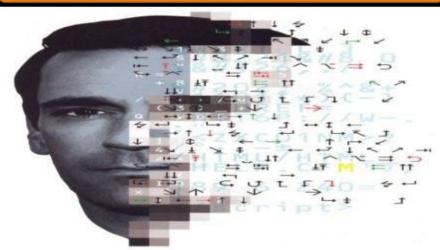
- limits to individual expertise
- limits to our multi-dimensionality
- limits to our sensory systems
- limits to our cognitive experiences and perceptions
- limits to our objective decision-making

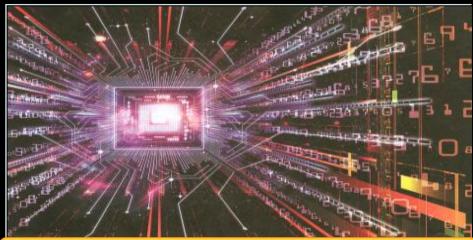
# Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Medical Education

#### **Data Deluge**



#### **Cognitive Bandwidth Limits**



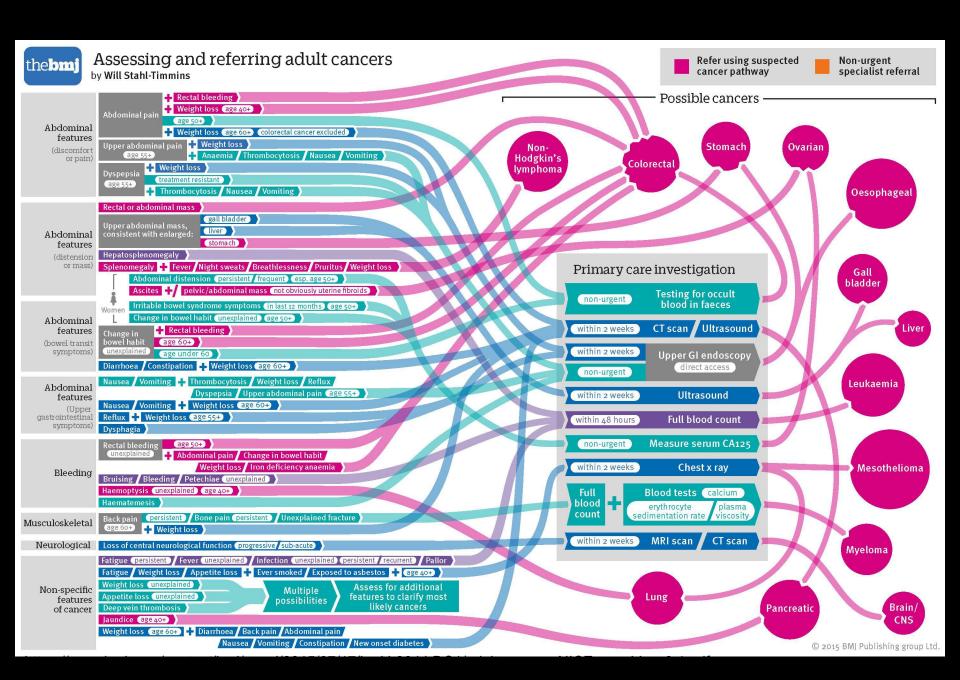






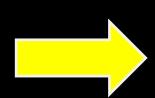
**Automated Analytics and Decision Support** 

**Facile Formats for Actionable Decisions** 



# Precision Health and Digital Health: Building a Learning Health System

qualitative,
descriptive
information of
variable quality and
provenance



quantitative data of known provenance and validated quality

complex ecosystem
of largely
unconnected
data sources

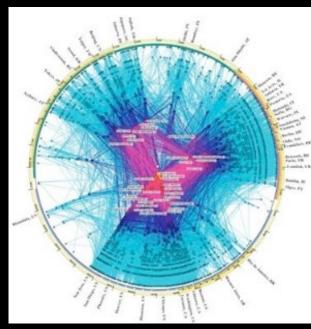


evolving,
inter-connected
networks of data
sources for robust
decisions and
improved care

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





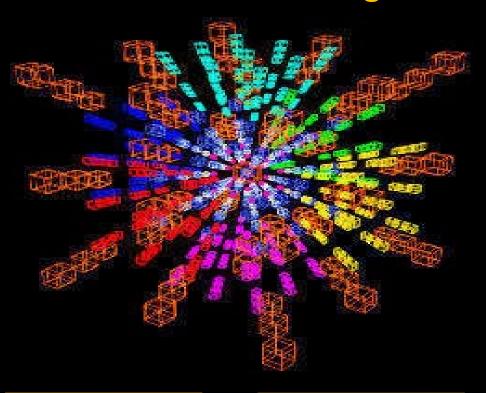


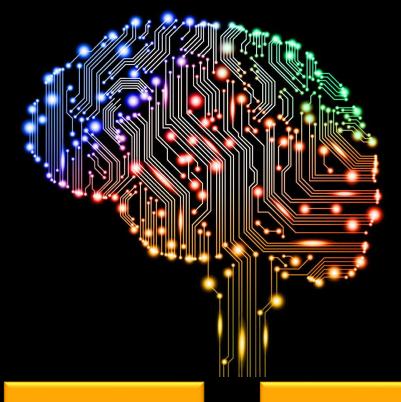
Isolated Data

Complex Networked Data

Complex Computational Data

# **Automated Context: Data Finding Data** "Intelligence at Ingestion"





Feature
Extraction
and
Classification



**Context Analysis** 



Persistent Context



• Relevance
Mapping

Learning Systems



 Situational Awareness

Rapid,
Robust
Decisions

# Machine Learning (ML) and Artificial Intelligence (AI) and the Analysis of Large Scale Heterogenous Health Data

The Future of 'Automated Search' and 'Retrieval'

**Deep Understanding of Content and Context** 

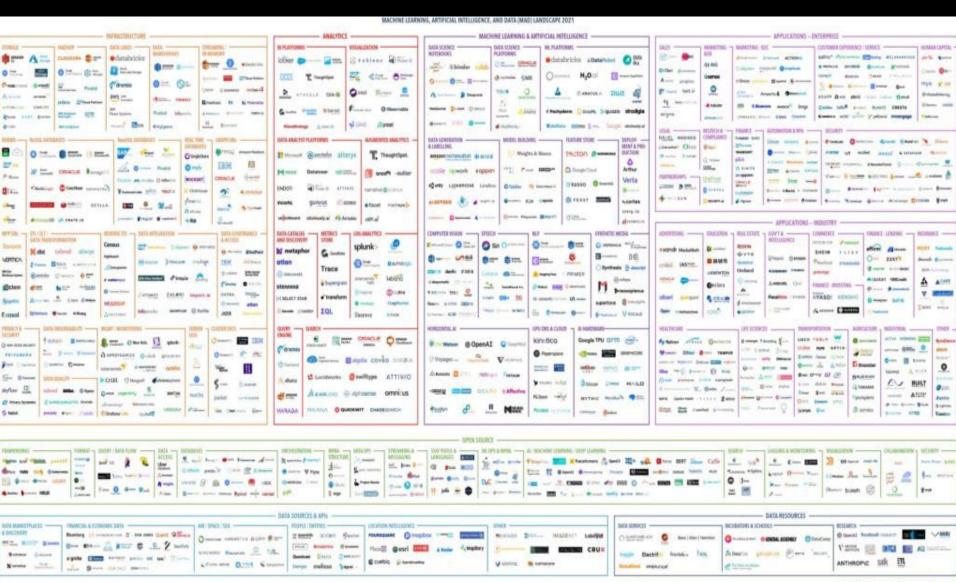
Collapse Time to Decision: Intelligence at Ingestion

Automated and Proactive Analytics:
Why Wait for the Slow Brain to Catch Up to the Fast Machine

#### Machine Learning (ML) and Artificial Intelligence (AI):

#### Massive Infusion of Private-Sector Funding and Entrepreneurial Activities

https://mattturck.com/data2021/



#### **Just What the Data Ordered**

### Machine Intelligence and Algorithms for Clinical Diagnosis and Treatment Decisions

**Black Box Medicine?** 

### The ML Adoption of Al Platforms in Clinical Medicine

 from current applications in image analysis to comprehensive assembly and interpretation of multifactorial "deep phenotyping" data to build 'signatures' of individual health status and risk

# Precision Health and Digital Health: Evolving Inter-Dependencies

#### **Individual Data**

#### **Population Data**



and analysis of large-scale diverse data Montral delphis sington

Wirginia Beach

Exabyte

and zettabyte data tsunami

#### **Deep Phenotyping:**

- multiOmics clinical history- EHR/PHR
- remote health monitoring
- socio-behavioral data
   environmental exposures

# **Building Personalized 'Digital Twins': Matching Individual Deep Phenotypes to 'Best Fit' Cohorts**

#### **Individual Data**

#### **Population Databanks**

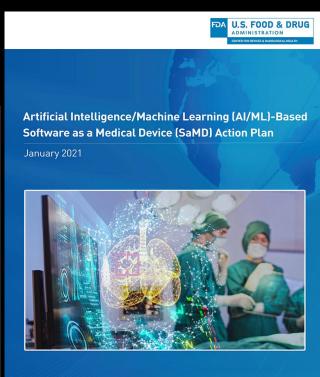


- 'digital twins and siblings' and imputed phenotypes
- risk predisposition and disease prevention
- selection of optimum treatment regimen for overt disease
- improved outcomes and QOL

# How Will Healthcare ML-Al Algorithms/Decision Analytics Be Validated and Regulated?







## Validation of 'Black Box' ML/Al Algorithms

- regulatory frameworks for ML/Al platforms used for clinical decisions for patient care
  - 'software as medical device'
- "interpretable AI"
  - uncoupling of learned intermediary from comprehension of how the output(s) for decision opinion(s) were derived
- getting ready for "primetime"?
  - generative adversarial networks and transformer platforms
- general artificial intelligence (GAI)
  - ChatGPT, RYTR, and DALL-E

## ChatGPT Generative AI Passed All Three Parts of the US Medical Licensing Examination (Dec. 2022) Without Prior Training on Medical Dataset







Performance of ChatGPT on USMLE: Potential for AI-Assisted Medical Education Using Large Language Models

Tiffany H. Kung, Morgan Cheatham, ChatGPT, Arielle Medenilla, Czarina Sillos, Lorie De Leon, Camille Elepaño,

Maria Madriaga, Rimel Aggabao, Giezel Diaz-Candido, James Maningo, Victor Tseng

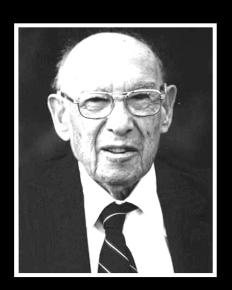
doi: https://doi.org/10.1101/2022.12.19.22283643



# Machine Learning (ML), Artificial Intelligence (AI) and Healthcare

- which clinical specialties/processes will be at risk of replacement by ML-Al and when?
- how will professional competencies in using ML-AI decision-support tools be developed and sustained?
  - MD curriculum, CME
  - non-medical data science professionals
- how will ML-AI platforms alter payment schemes?
- what new malpractice liabilities will emerge by failure to use/interpret ML-Al platforms?

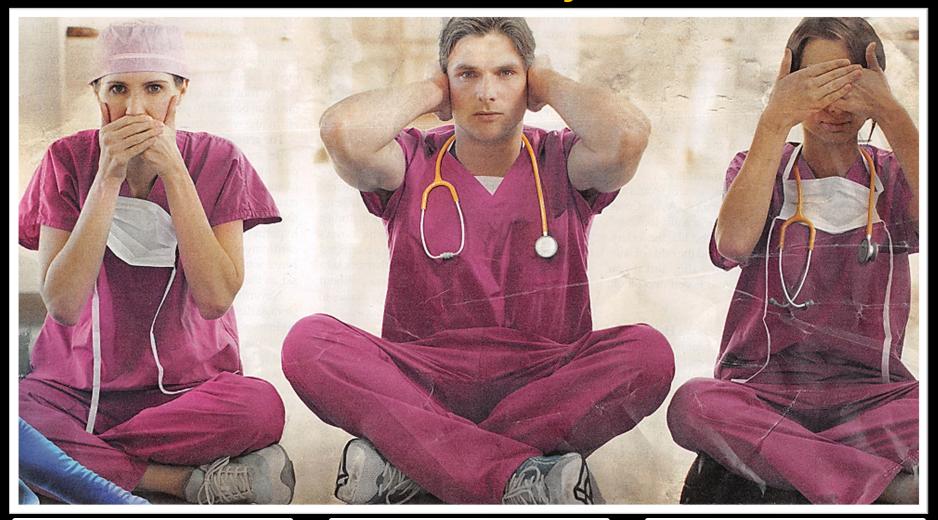
### **Unidimensional "Quick Fixes"**



"The greatest danger in times of turbulence, is not the turbulence, it is to act with yesterday's logic."

- Peter Drucker

# DNR: Is the Current Healthcare System Terminal?



**Denial** 

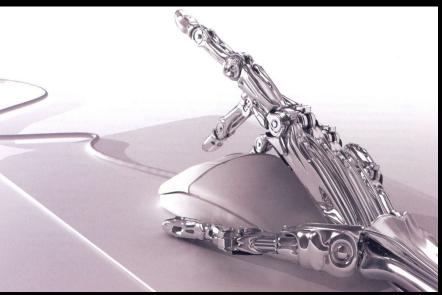
**Negativity** 

Resistance

### **Living In The Infocosm**

**Burgeoning Information and An Expanding Metaverse** 



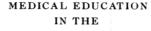


- boundaries between traditional expertise domains increasingly blurred
- entirely new domains emerge, dissolve and re-emerge in reconfigured form at ever faster rates
- escalating complexity of mapping, multi-dimensional strategic spaces
- ML/Al platforms embedded in all aspects of healthcare

# "Digital Darwinism": A Looming Digital Divide

- understanding data structure and its productive application/customization for improved decisions and clinical outcomes will become a critical institutional competency
- major skill gaps and personnel shortages in biomedicine
- training of a new cadre of data scientists (medical and non-medical)
- institutions lacking adequate computational infrastructure and critical mass in data analytics will suffer 'cognitive starvation' and relegation to competitive irrelevance

### **Major Transitions in Medical Education and Healthcare**



UNITED STATES AND CANADA

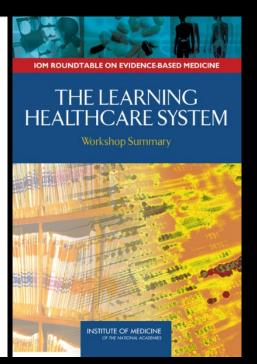
A REPORT TO
THE CARNEGIE FOUNDATION
FOR THE ADVANCEMENT OF TEACHING

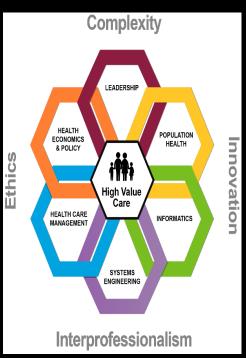
BY ABRAHAM FLEXNER

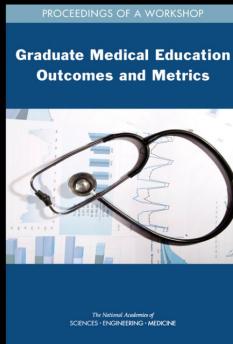
WITH AN INTRODUCTION BY HENRY S. PRITCHETT

BULLETIN NUMBER FOUR (1910) (Reproduced in 1960) (Reproduced in 1972)

> 437 MADISON AVENUE NEW YORK CITY 10022







1910 - present

2000 - present

2015 - ?

(science-centric)

healthcare as a learning system (data-centric)

mastery of escalating complexity and massive data (network-centric)

## **New Patterns of Learning**





# Asleep at the Wheel: Ignoring Healthcare Challenges of Increasing Complexity and Urgency



- dysfunctional national governance, lack of bipartisanship and legislative paralysis
- ideological extremism
- the rise of anti-science, anti-expert populism
- legislative technical illiteracy and the retreat from complexity
- the corrosive role of social media in fueling social and political division
- the myopia of short-term, cosmetic quick fixes and kicking the problem down the road

# Asleep at the Wheel: Ignoring Healthcare Challenges of Increasing Complexity and Urgency



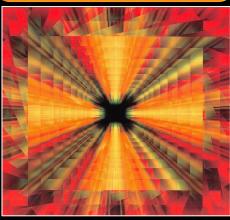


- aging demographics and the chronic disease burden cost access, availability and affordability
- mental health
- SUD and lack of border security
- cybersecurity and data protection
- preparedness for highly disruptive biosecurity events (pandemics) or other major disasters
- novel threats from dual-use technologies and complex ethical and legal issues

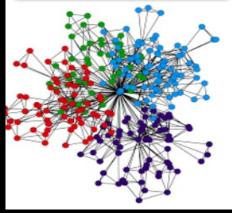
#### **The Evolution of Data-Intensive Precision Medicine**

Technology Convergence and Acceleration Mapping Geno-Phenotype Complexity Topology of Biological Information Networks

**Big Data** 



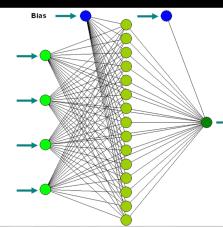














Data Security and Privacy

**Robotics and Human Machine Interactions** 

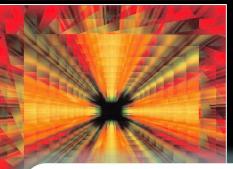
Artificial Intelligence and Decision Support

Public Policy: Ethics, Risk and Regulation

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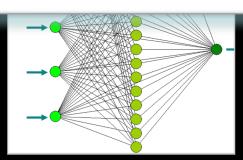




### Slides Available @ http://casi.asu.edu/presentations









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