Complex Adaptive Systems Initiative
Arizona State University

ASU Health

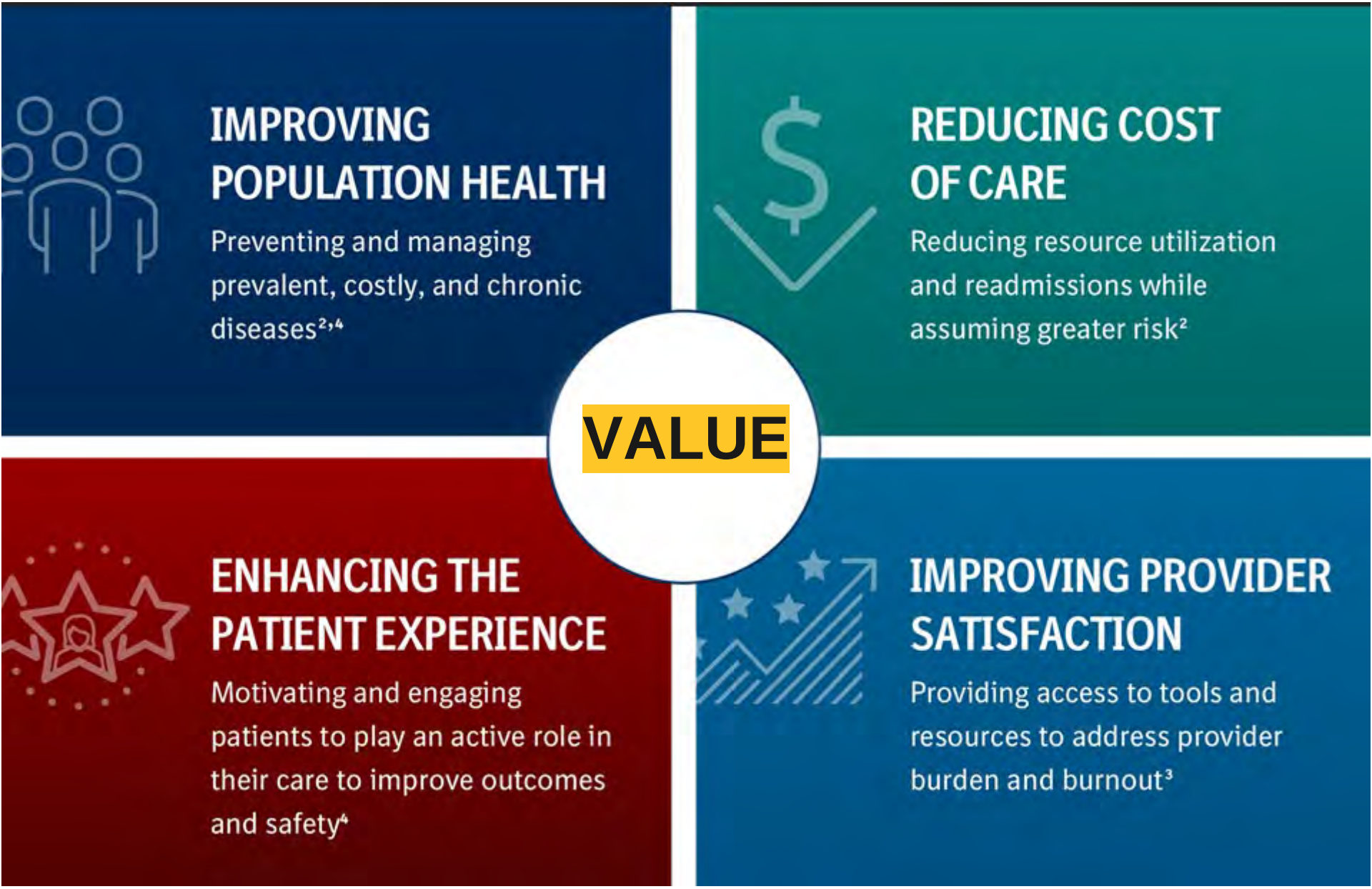
The Strategic Landscape for the Evolution of Precision Health:

Disruptive Changes in Biomedical Research, Public Health and Care Delivery

Dr. George Poste
Regents' Professor and Del E. Webb Chair in Health Innovation
george.poste@asu.edu

ASU Health: Grand Rounds, 29 January 2024
Slides Available @ http://casi.asu.edu/presentations

The Quadruple Aim



https://www.strategiesforqualitycare.com/quadruple-aim

The US Health Ecosystem

- what are the principal technical, clinical, market and regulatory forces and new value propositions that will shape the evolution of the health ecosystem?
- what are the principal vulnerabilities and inadequacies in the current health ecosystem ripe for reform?
- are biomedical research, academic medicine and MD education facing critical inflection points?
- how will new ASU Health initiatives address these challenges and opportunities

- School of Medicine and Advanced Medical Engineering
- School of Public Health Technology
- Health Observatory at ASU
- Mayo Clinic and ASU Alliance for Healthcare

The US Health Ecosystem
Fragmentation, Fragilities and Looming Disruptions

- isolated silos of expertise and care services
  - poor continuity in patient care
- cost escalation without improved outcomes
- disproportionate investment of $4.4 trillion annual expenditure on reactive management of active disease (90%) versus proactive focus on health optimization (10%)
- continued dominance of fee-for-service and volume- based acute care/hospital-centric business models
- aging society and increased chronic disease burden

The US Health Ecosystem
Fragmentation, Fragilities and Looming Disruptions

- inefficient integration and analysis of data to drive evidence-based best practice and care decisions
- myriad embedded inefficiencies
  - duplication, waste, error
- neglect of social determinants of health and adverse impact on minority/marginalized communities
- disparities in access and affordability of care
- fragilities and fault lines revealed and amplified by COVID-19 pandemic

The US Health Ecosystem

- facing a confluence of complex events with the potential to radically alter all aspects of biomedical education, research and health care delivery
  - national and global
- cross-domain technology convergence
  - biomedicine, engineering and computing
- cross-sector industry convergence
  - diagnostics, therapeutics, devices, robotics, imaging, big data analytics and AI
- economies of scale will drive increased vertical and horizontal consolidation
- new organizational models and site(s) for care delivery

Precision Health

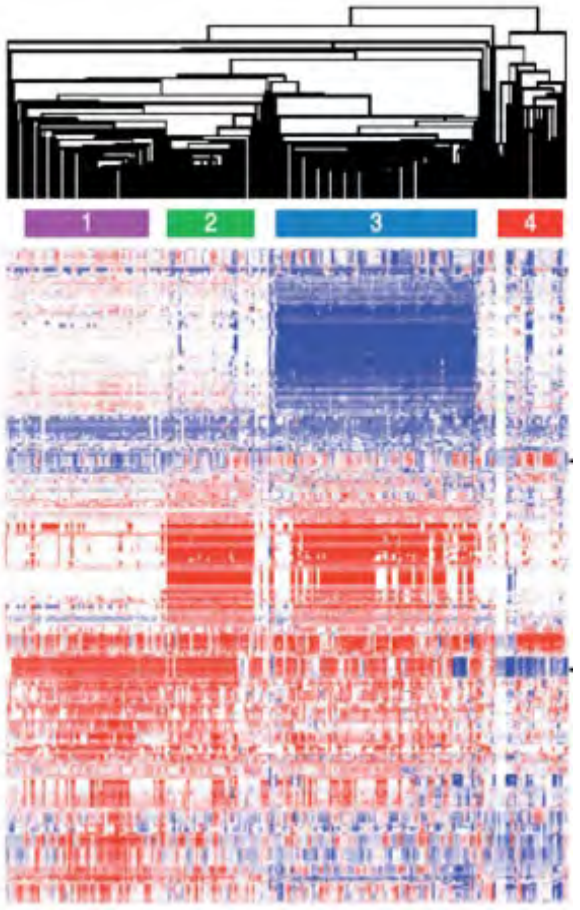
- **optimize the health of populations and individuals by improved precision in the identification and mitigation of health risks across the life span**

multiple elements of the organization, capabilities, incentives and deliverables of the current health ecosystem are misaligned with this strategic aspiration

The Evolution of Precision Health: Improved Identification and Mitigation of Health Risk

- increasingly rational public health and clinical care interventions to optimize health based on features unique to specific individuals/population cohorts
- shift societal burden from current predominant demands of treating advanced chronic disease to management of earlier stage disease and disease prevention
- strengthen proactive surveillance, preparedness and resilience to disruptive external threats to health
  - emerging infectious diseases, climate, cyber-risks

The Path to Precision Health:
From Superstitions to Symptoms to Molecular Signatures of Health Risk



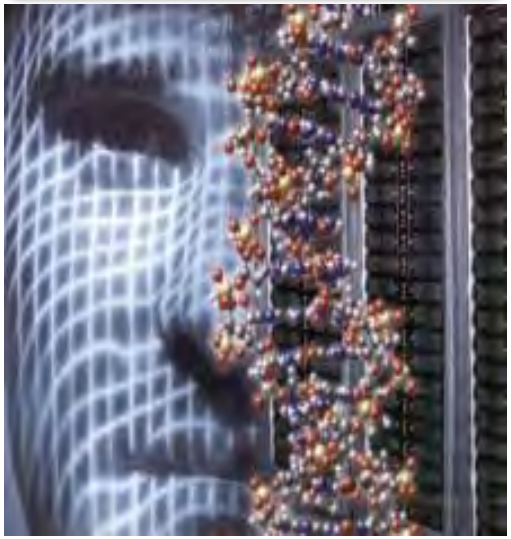
humors; astrology, shamanism, sin and divine fate

biochemistry and organ-based pathophysiology

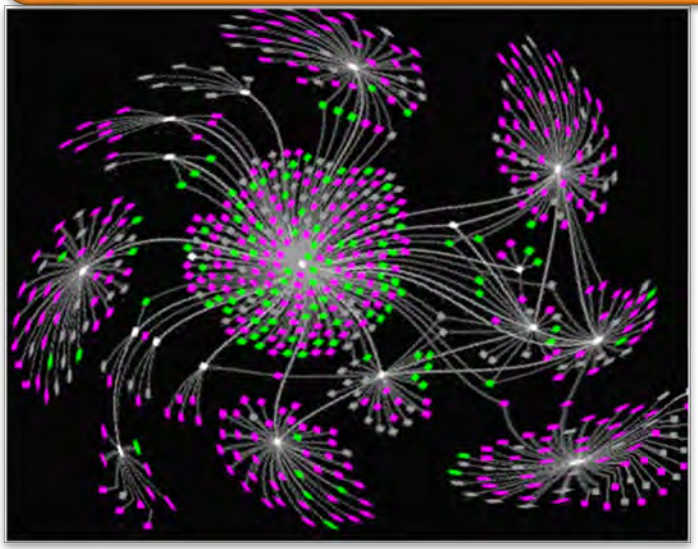
molecular biology and multi-omics profiling

Precision Health

(Epi)Genomics and MultiOmics Profiling



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

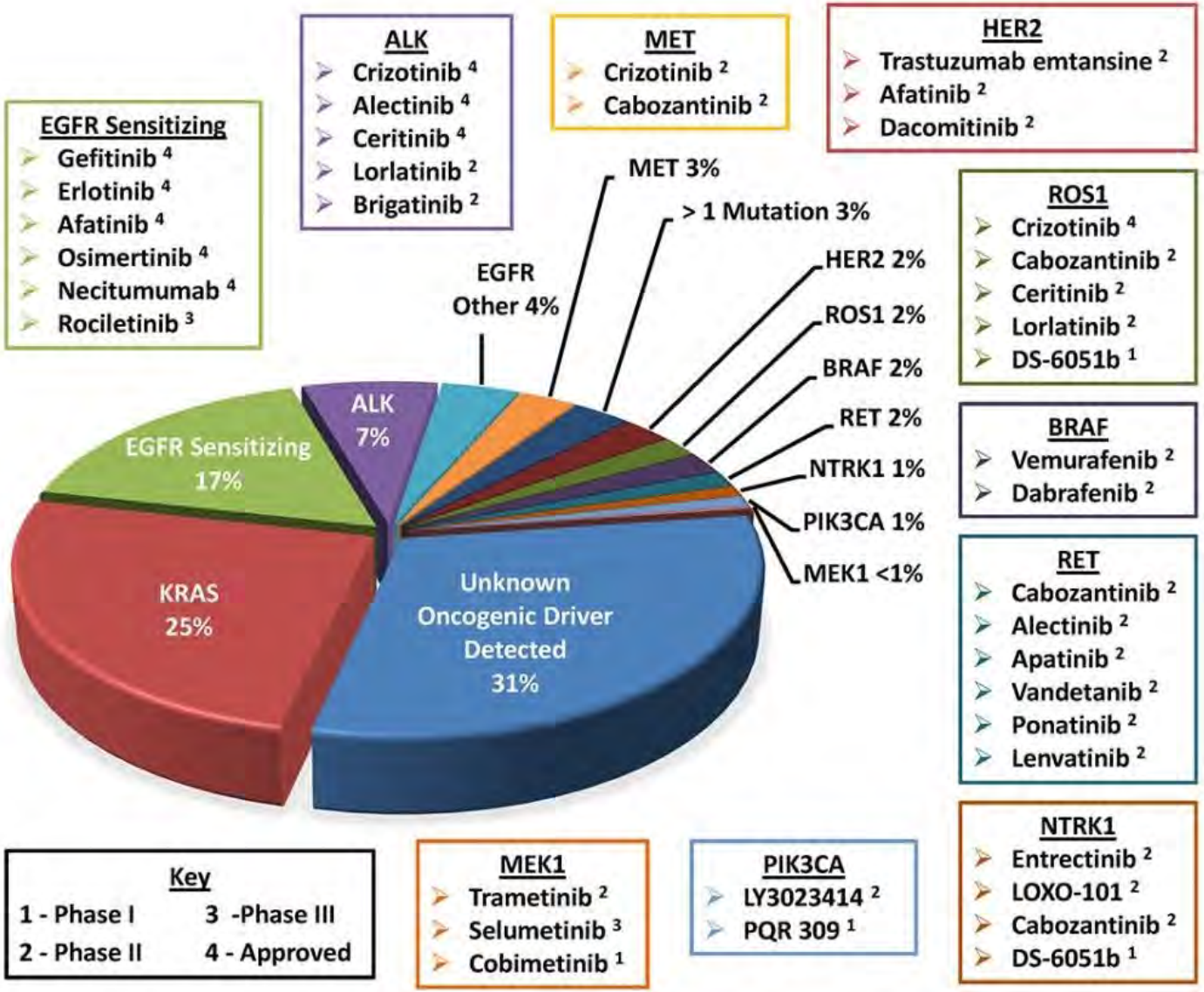


- terabytes per individual
- zettabyte – yottabyte population databases

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

The Challenge of Big (Messy) Data

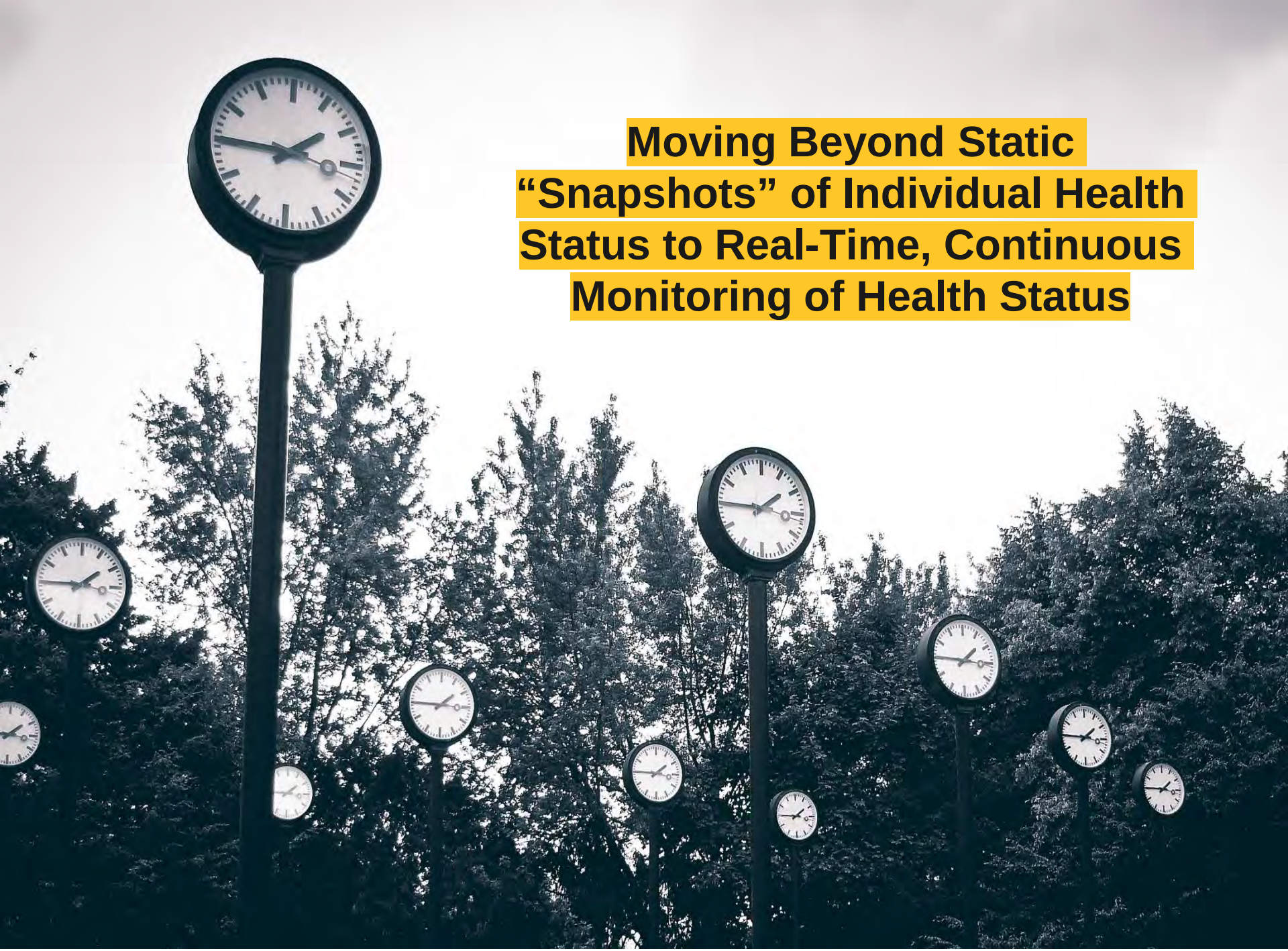
Molecular Classification of Non-Small Cell Lung Cancer



https://www.iaslc.org/

Precision Health: New Concepts and Methods for More Proficient Identification and Mitigation of Health Risks

- “signatures” of health risk (individuals and populations)
  - disease predisposition, early disease detection
  - disease subtyping, staging and prognosis
  - treatment selection based on specific disease features in individuals
  - prediction of Rx response, resistance and adverse events
  - faster alert of clinical deterioration due to treatment non-adherence and reduce high cost rehospitalizaiton
  - tracking social determinants of health and exposure to environmental hazards

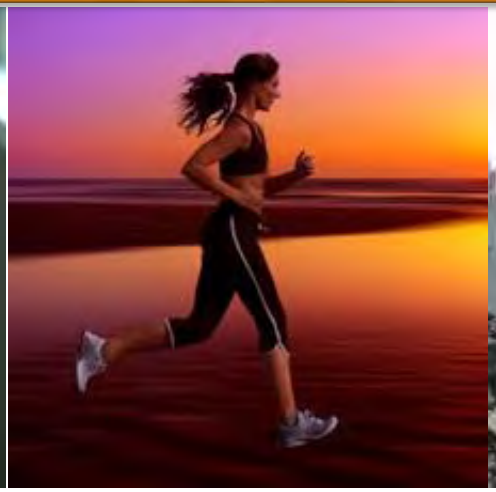

Moving Beyond Static
“Snapshots” of Individual Health
Status to Real-Time, Continuous
Monitoring of Health Status

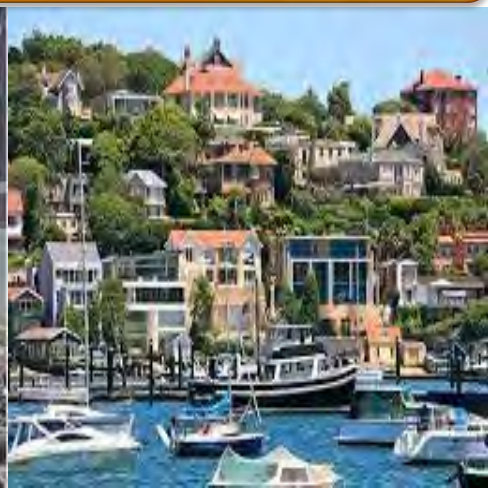
Deep Phenotyping:

From Womb to Tomb:
Systematic Longitudinal Integration of Multi-modal Data to identify Health Risk(s)

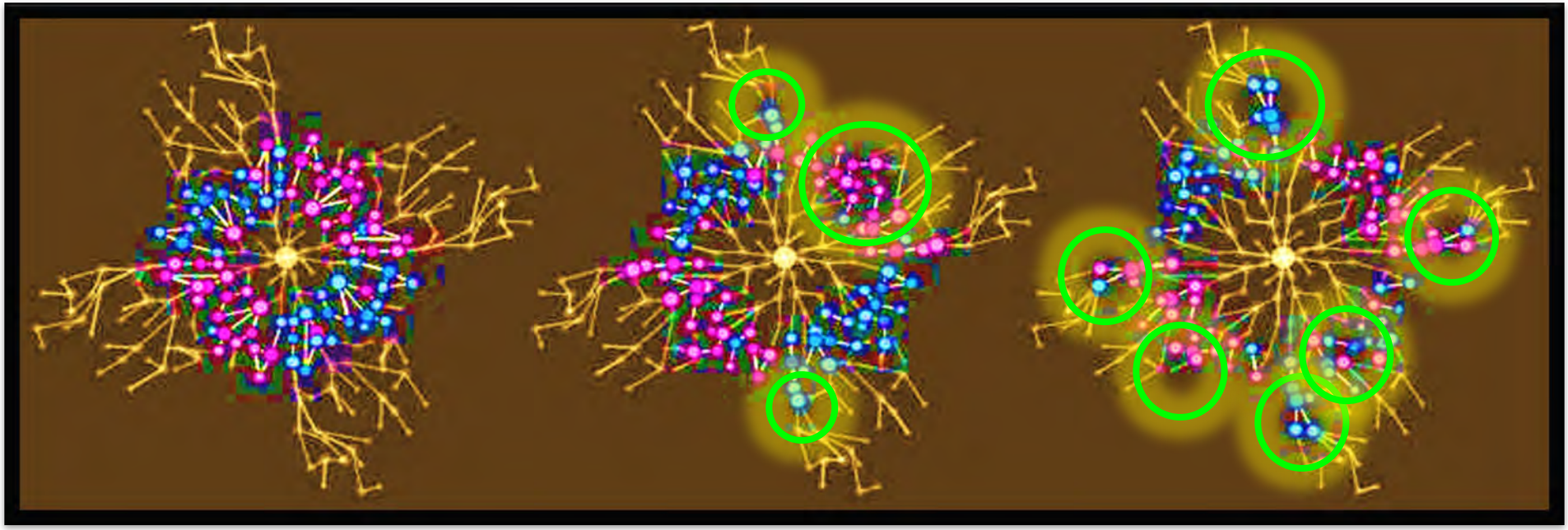



SDoH, Lifestyle, Health Disparities, Environmental Hazards (Exposome)



The Health Observatory: Mapping Individual and Community Interaction Networks and Population Health Patterns



$T_{1(n)}$	$T_{2(n)}$	$T_{3(n)}$
baseline health demographics	identification of risk foci: SDoH, disparities, EIDs	new patterns of disease prevalence and distribution

Expanding the ‘Care Space’ in Healthcare

- 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

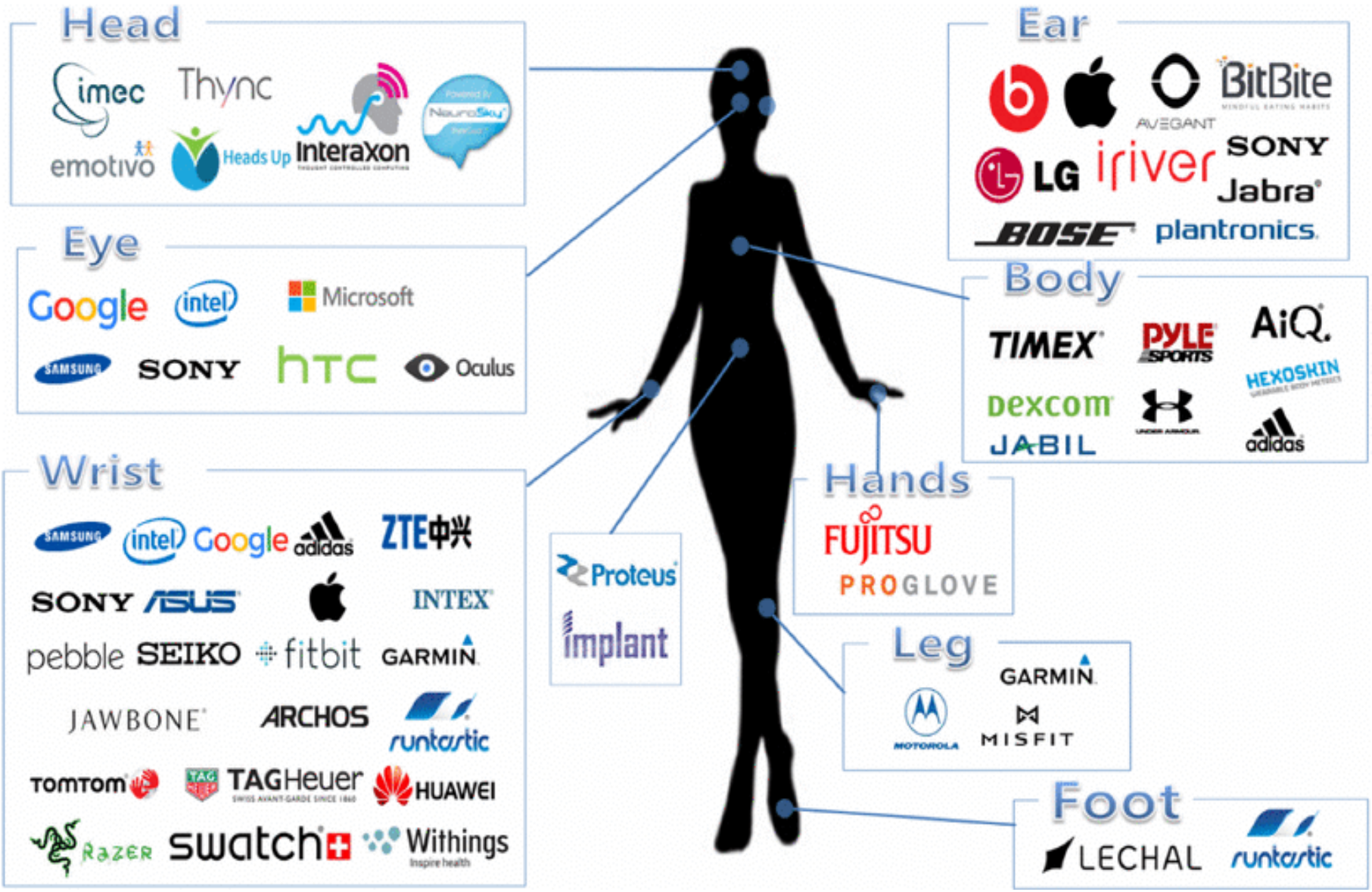
- rapid evolution of new technologies for real time remote monitoring of health status in non-clinical settings
  - Internet-of-Medical Things (IoMT)
  - longitudinal continuous tracking vs. episodic ‘static snapshots’ of health status
  - every population cohort/individual becomes their own control (tracking the Delta)

Expanding the ‘Care Space’ in the Health Ecosystem

- private sector participants will become increasingly influential in research innovation from leverage of technology convergence
  - faster mobilization and scale of inter-disciplinary capabilities
  - expertise in translational science and regulatory approval
- new opportunities for ASU-industry collaborations at multiple points in the health ecosystem

Rapid Growth in Telemedicine, Wearables, Sensors and Devices for Remote Health Status Monitoring

Wearables and Remote Health Status Monitoring



https://www.researchgate.net/figure/Development-status-of-wearable-devices-for-digital-individual-healthcare_fig1_320595358

Smart Devices for Automated Drug Delivery and Improved Therapeutic Adherence

Propeller Health

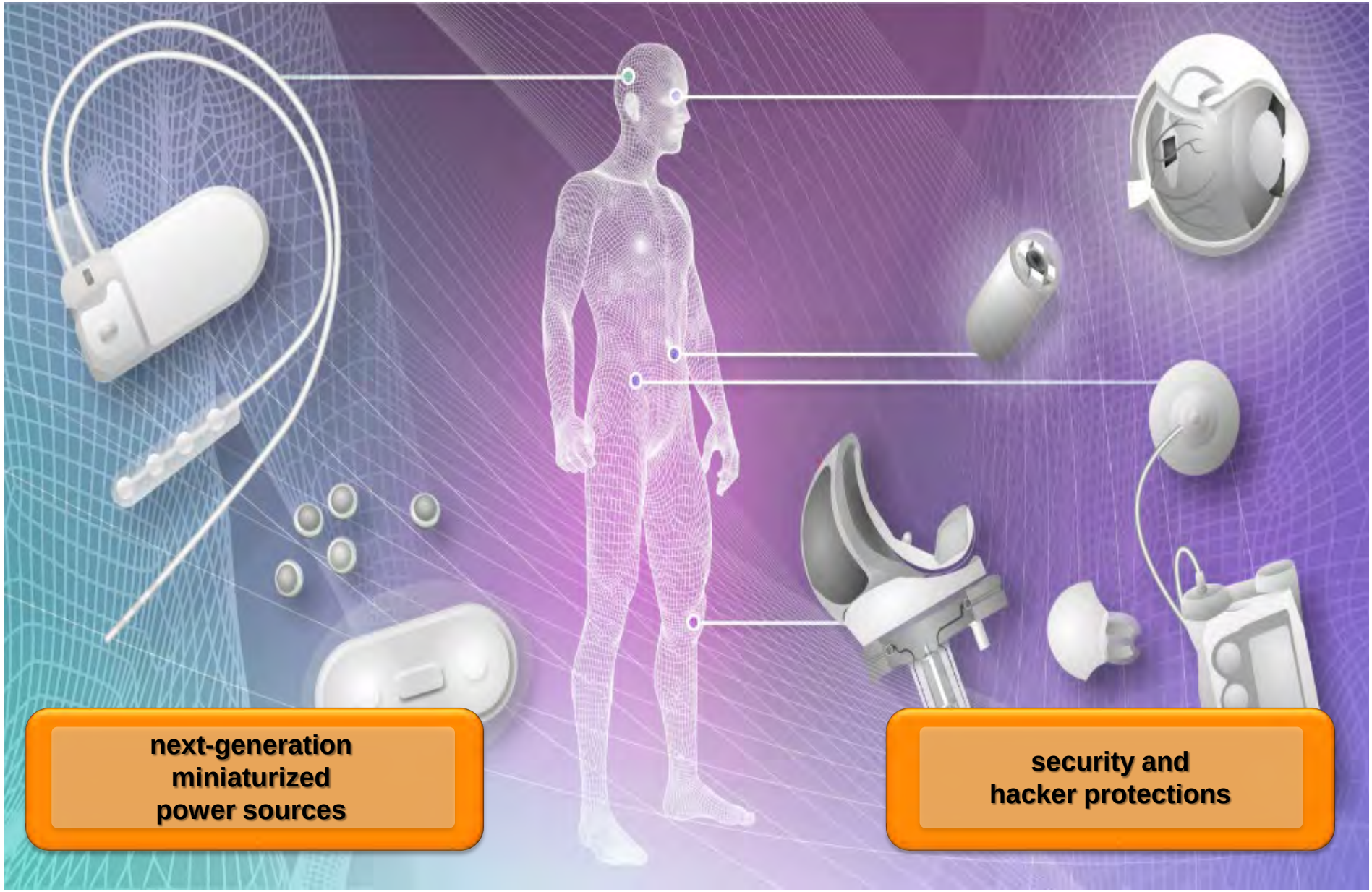
Gecko (now Teva)

CapMedic

Biocorp Inspair

Aterica
Veta
EpiPen

Implantable Devices and Wireless Monitoring (and Modulation)



The Eldercare Gap

10,000

- boomers turn 65 every day

79%

- increase in boomers age 80 or older from 2010 to 2030

348,000

- projected number of home health aides needed in next decade

5

- average number of prescription drugs taken by individuals 65 or older due to disease co-morbidities

The Demographics of an Aging Society: Clinical and Economic Challenges

wellness with longevity and high QOL

OR

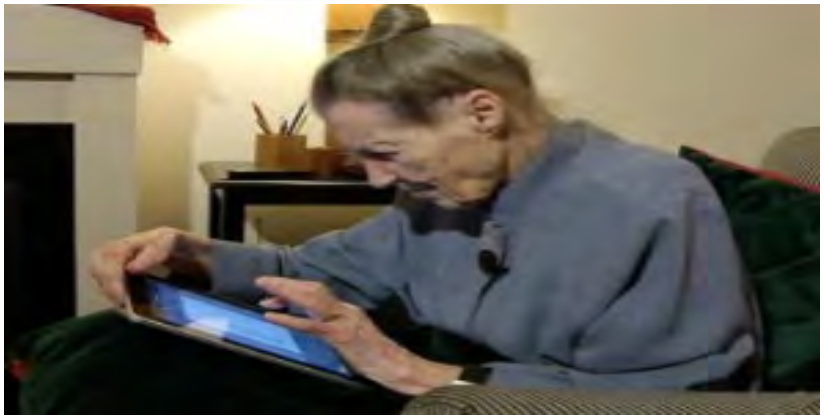
multiple co-morbidities and low QOL

?

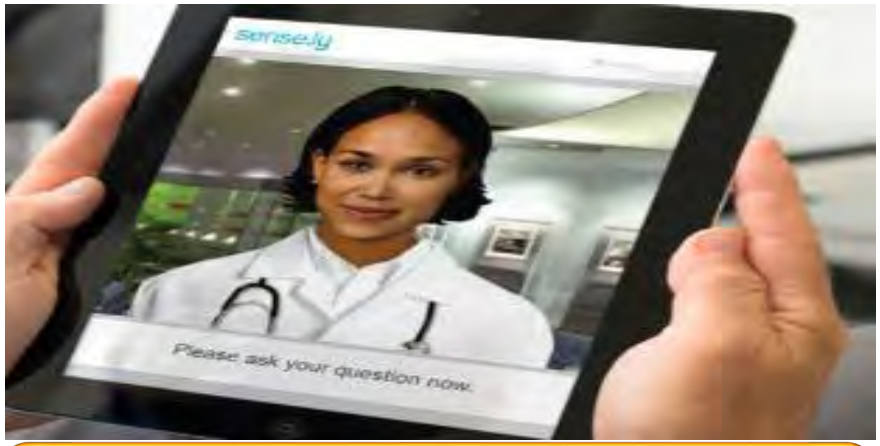
?

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

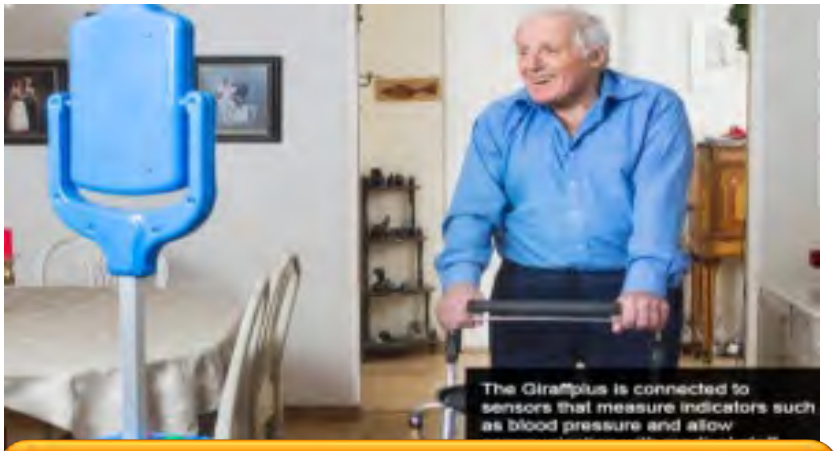
Rx adherence



cognitive stimulation



in-home support and reduced readmissions



reduced office visits

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

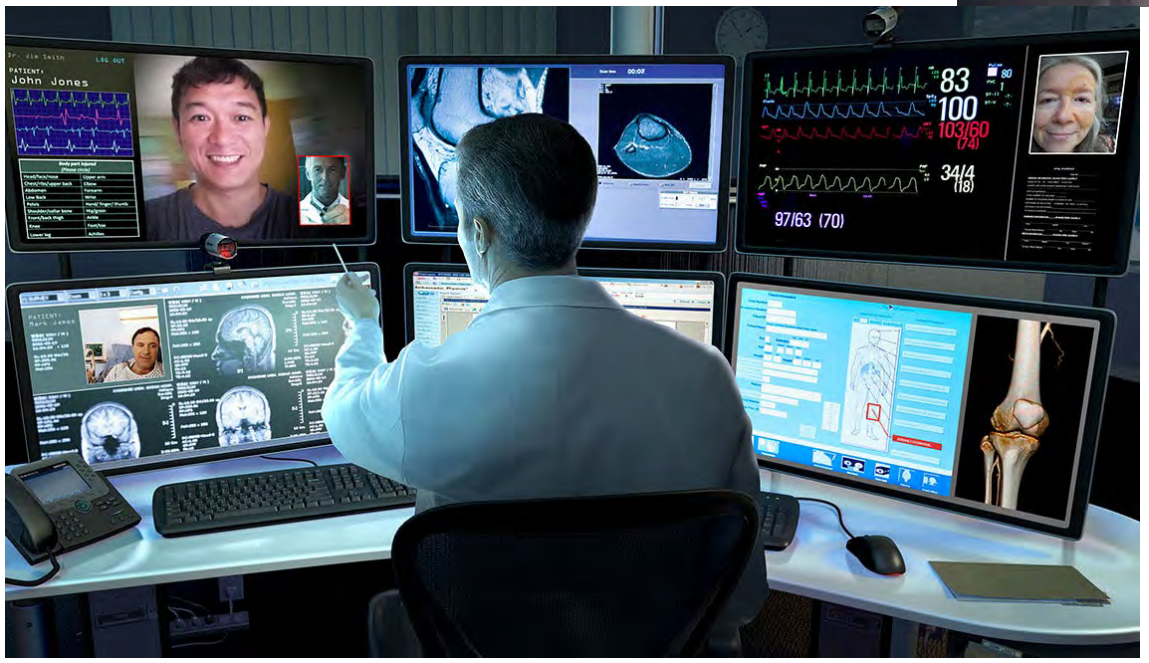
- logical extension to healthcare of rapid growth of web/apps in mainstream culture
- increasingly proactive and engaged consumers/ patients/families
- greater access to information on treatment options, cost and provider performance
- new clinical practice tools to optimize HCP-patient communication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

New Sites for Primary Care Delivery: Economies of Scale and Consumer Convenience

- ‘one stop’ shopping and telemedicine
  - disease prevention/ screening
  - primary care
  - pharmacy
  - discounted pricing

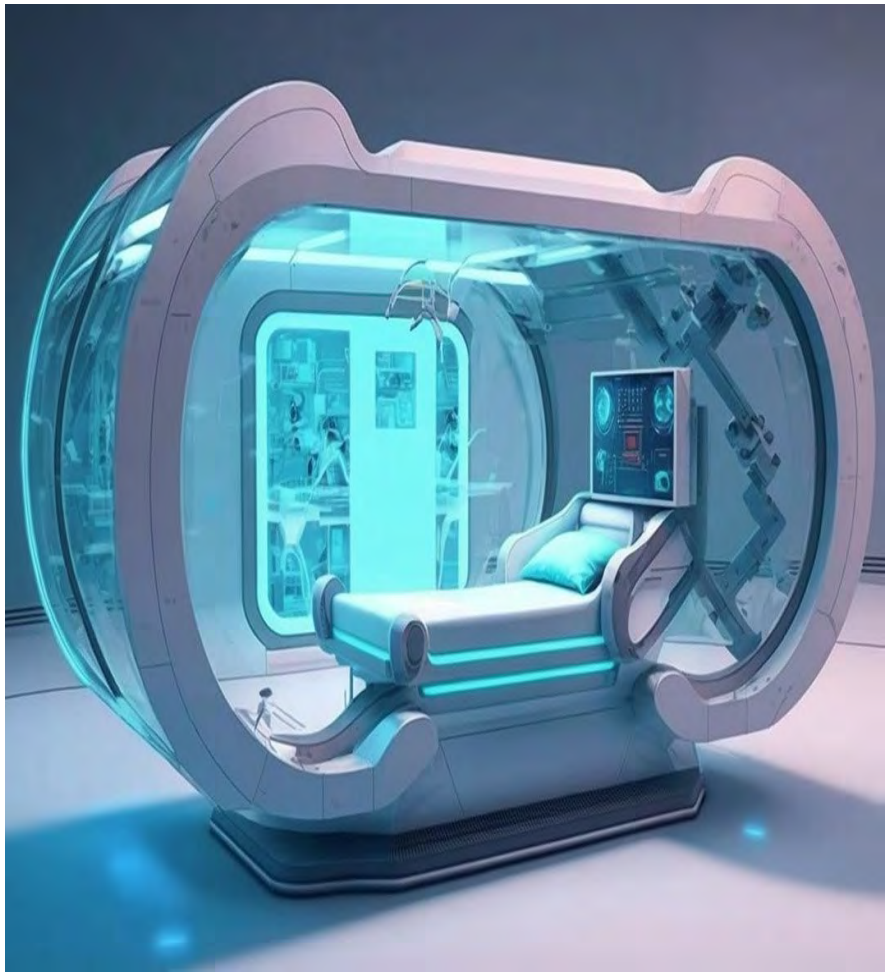
- projected expansion of NP/PA in primary care
- personalized/customized services for improved treatment adherence

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



Improved Use of Specialized Resources and Access to Expert Consultations

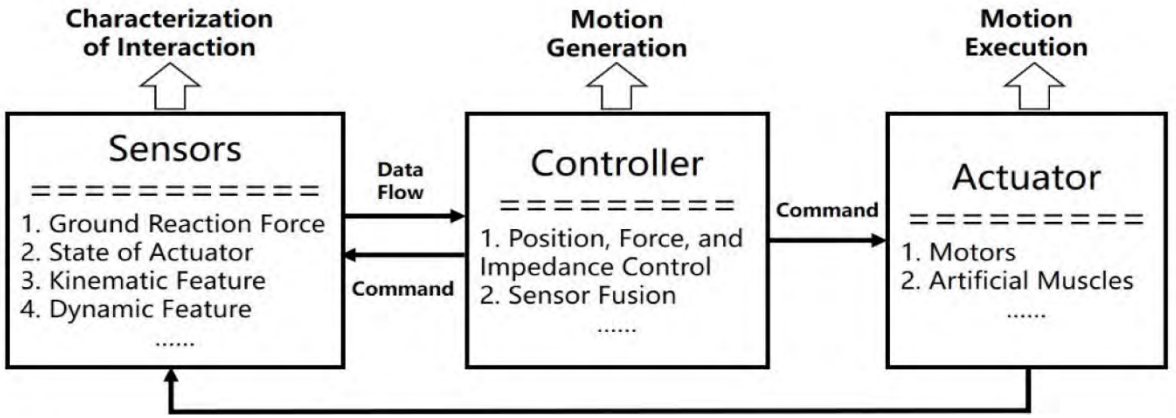
Instrumented Modular Health Monitoring “Pods”



- hospital acute care/ICUs
- infection control
  - higher risk patients
  - surge mobilization in epidemic/disaster settings
- modification for ‘hospital-at-home’

https://www.biopharminternational.com/view/considering-the-promises-of-point-of-care-manufacturing

Robotic Exoskeletons for Injury Rehabilitation and Disability Mitigation

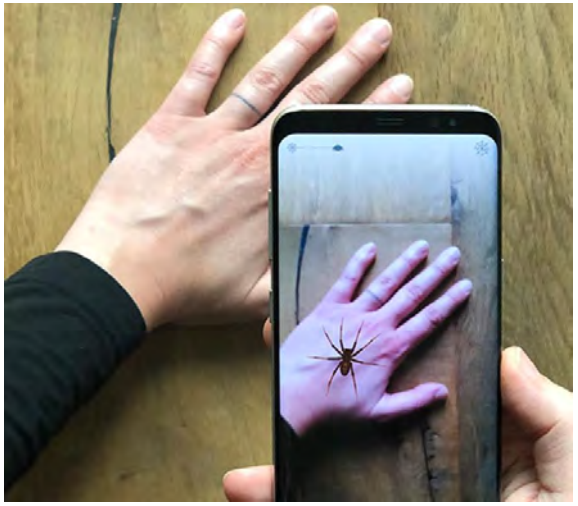


https://www.mdpi.com/2079-9292/11/3/388

Human-Directed Robotics

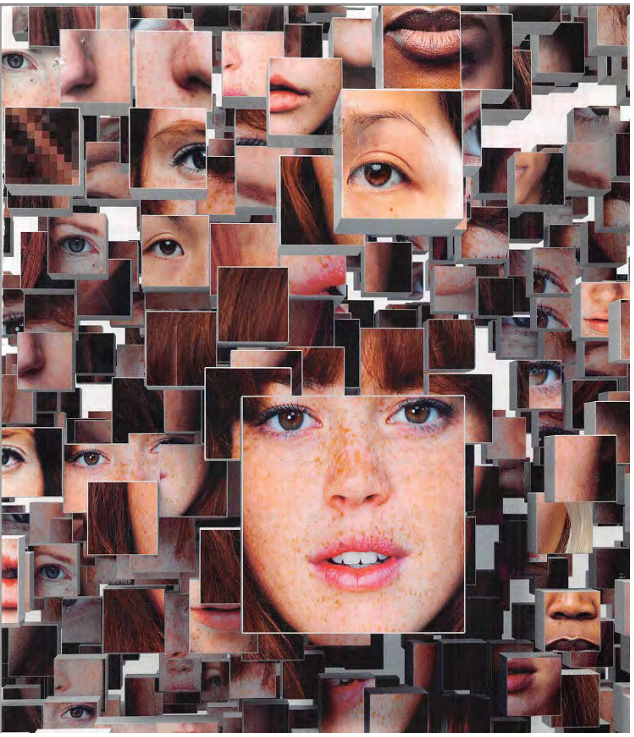
Cyber-Physical-Biological Systems
Immersive Human-Machine Interfaces and Surgery

AR/VR/XR Neuromodulation in Clinical Care

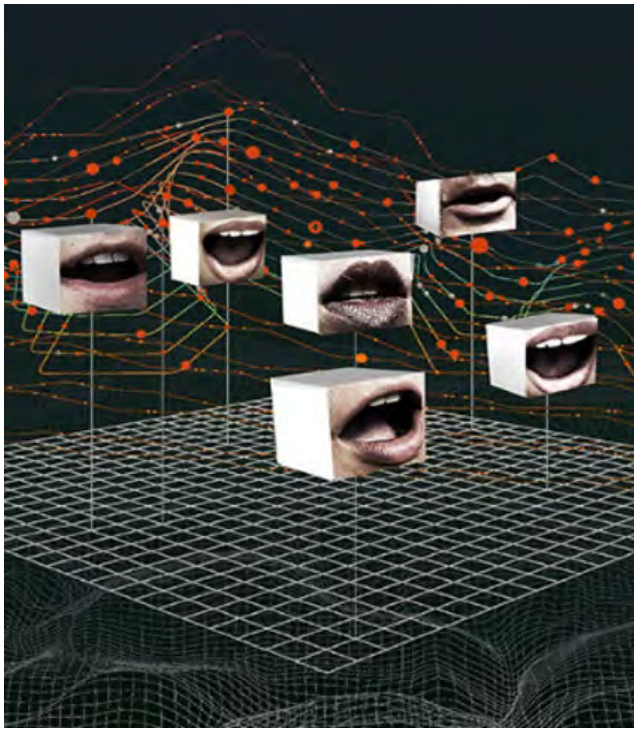


- injury rehabilitation
- reduce apprehension/distraction in painful procedures
- anxiety, depression, PTSD, phobias (digital therapeutics: DTx)

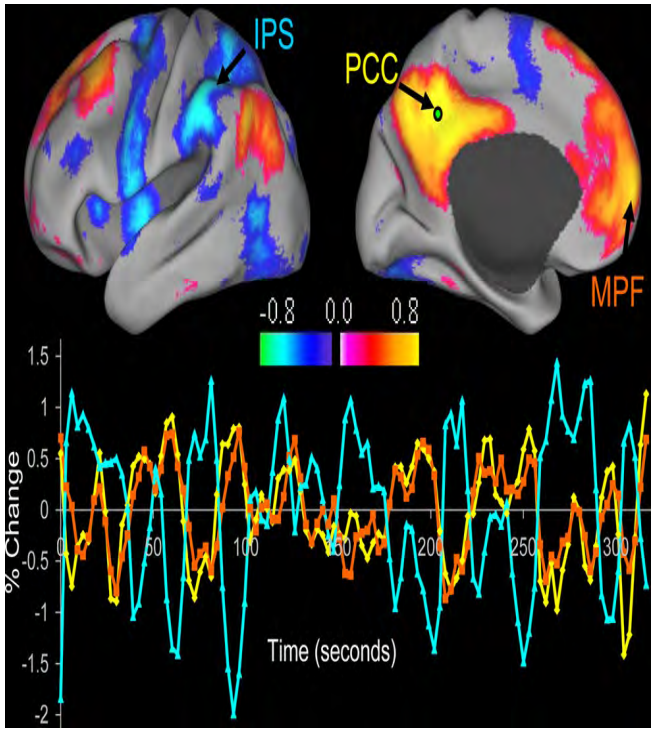
Computer Vision, Facial Recognition and New Digital Psychometrics for Improved Diagnostic Accuracy in Psychiatry



- eye movements
- facial dynamics
- stimulus response reaction and interaction speeds



- speech patterns (rhythm, tone, volume)
- semantic construction



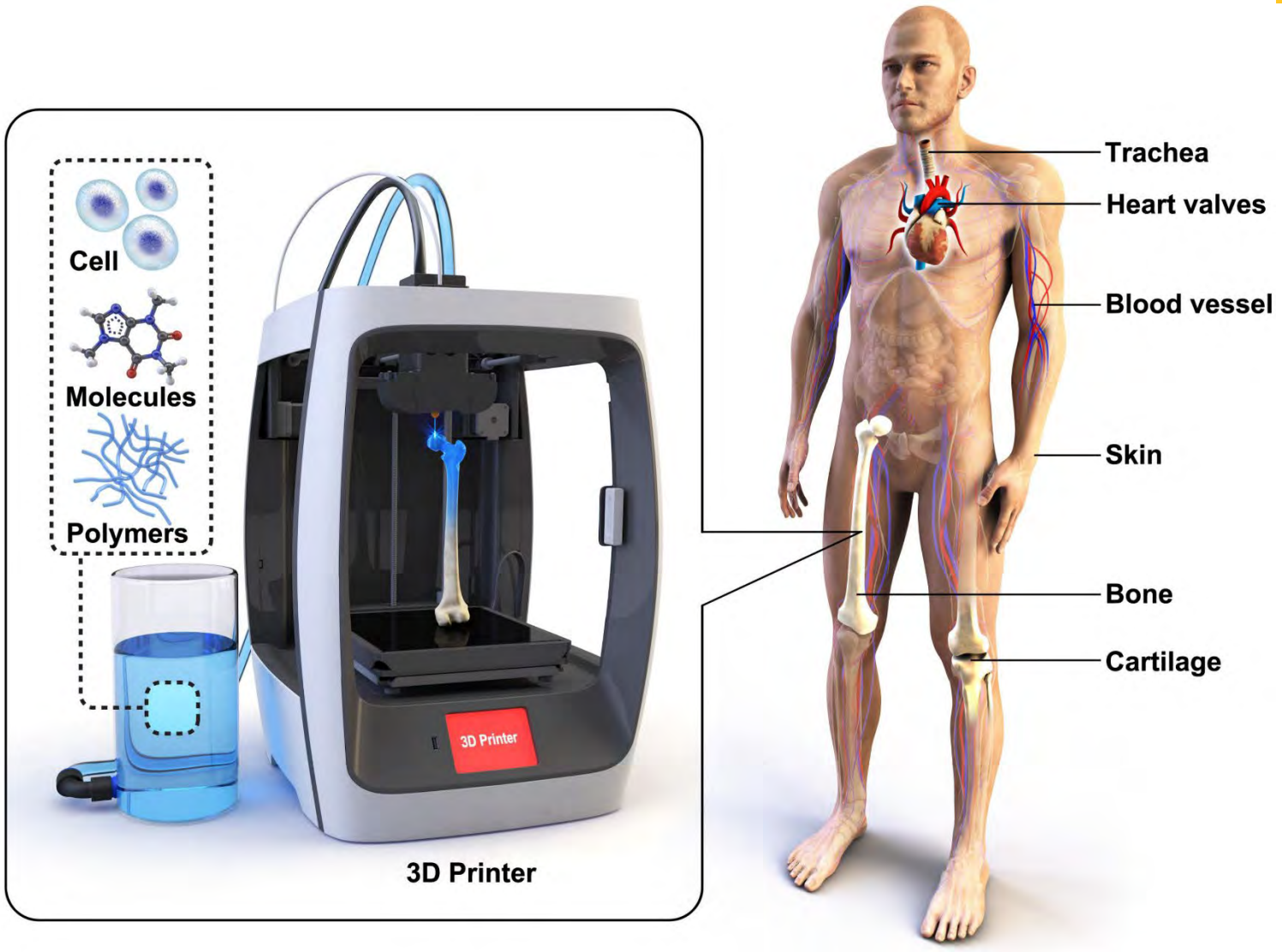
- 256 lead EEG
- brain imaging functional MRI in sensory, motor and cognitive tasks

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

Human Computer Interactions for Non-Pharmacological Neuromodulation in Mental Health
Digital Therapeutics Alliance

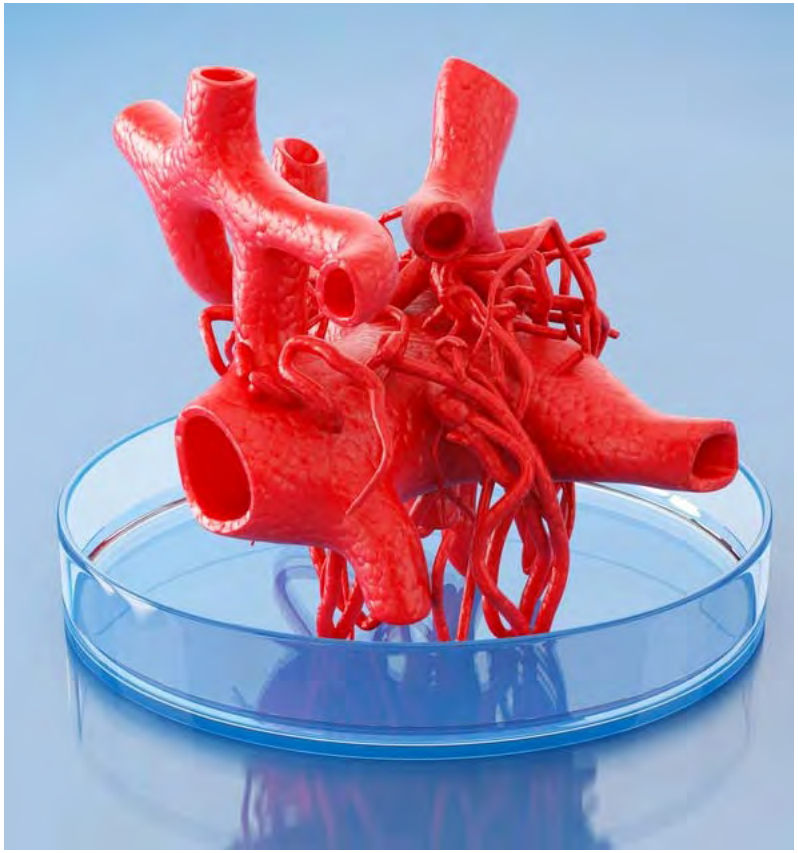
https://www.dtxalliance.org/about-dta/

Biomimetic Scaffolds for Tissue Engineering: 3D Printing Techniques in Regenerative Medicine



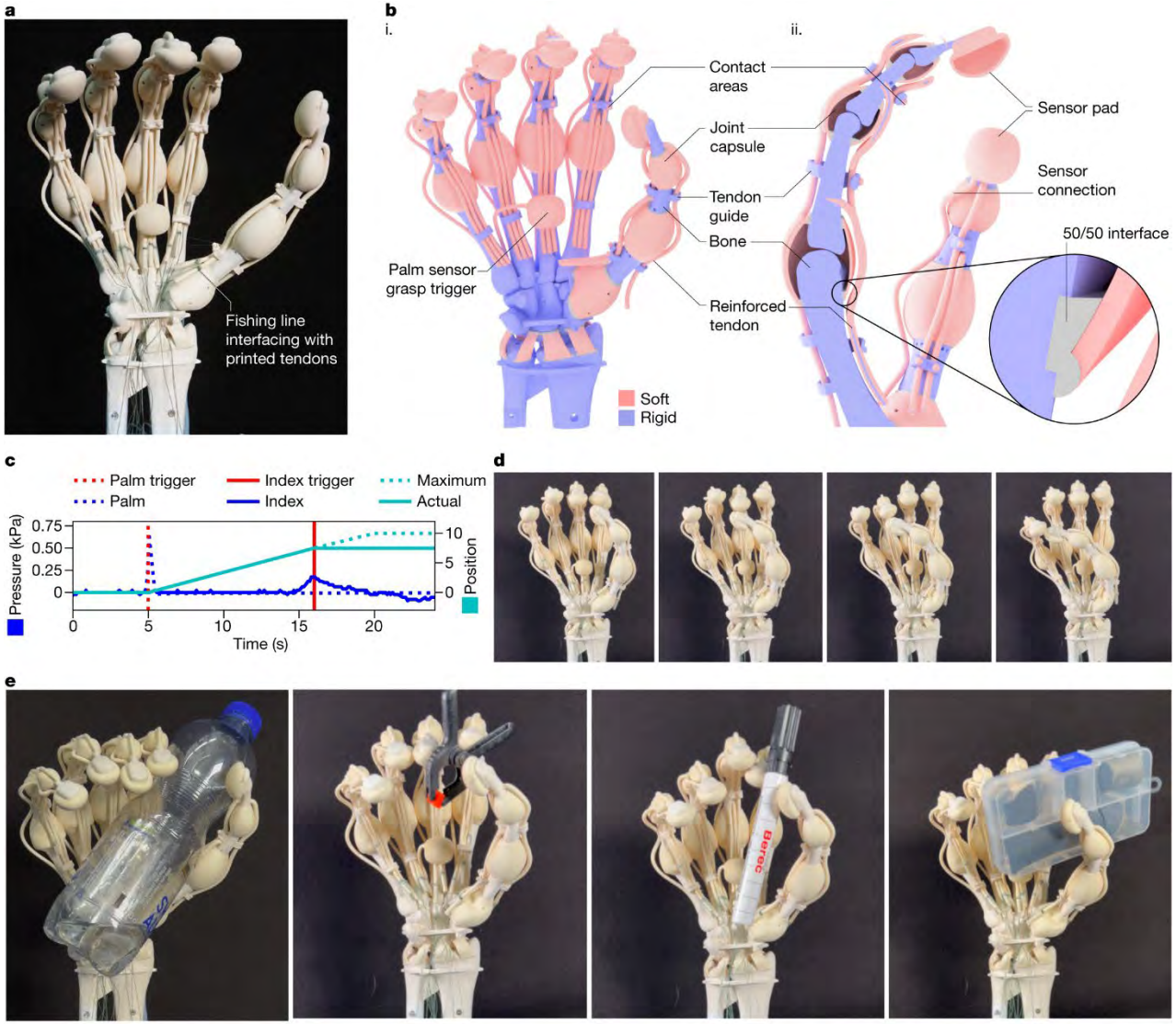
https://www.frontiersin.org/articles/10.3389/fbioe.2020.586406/full

Advances in Materials Science and Bioprinting of New Biological Implants



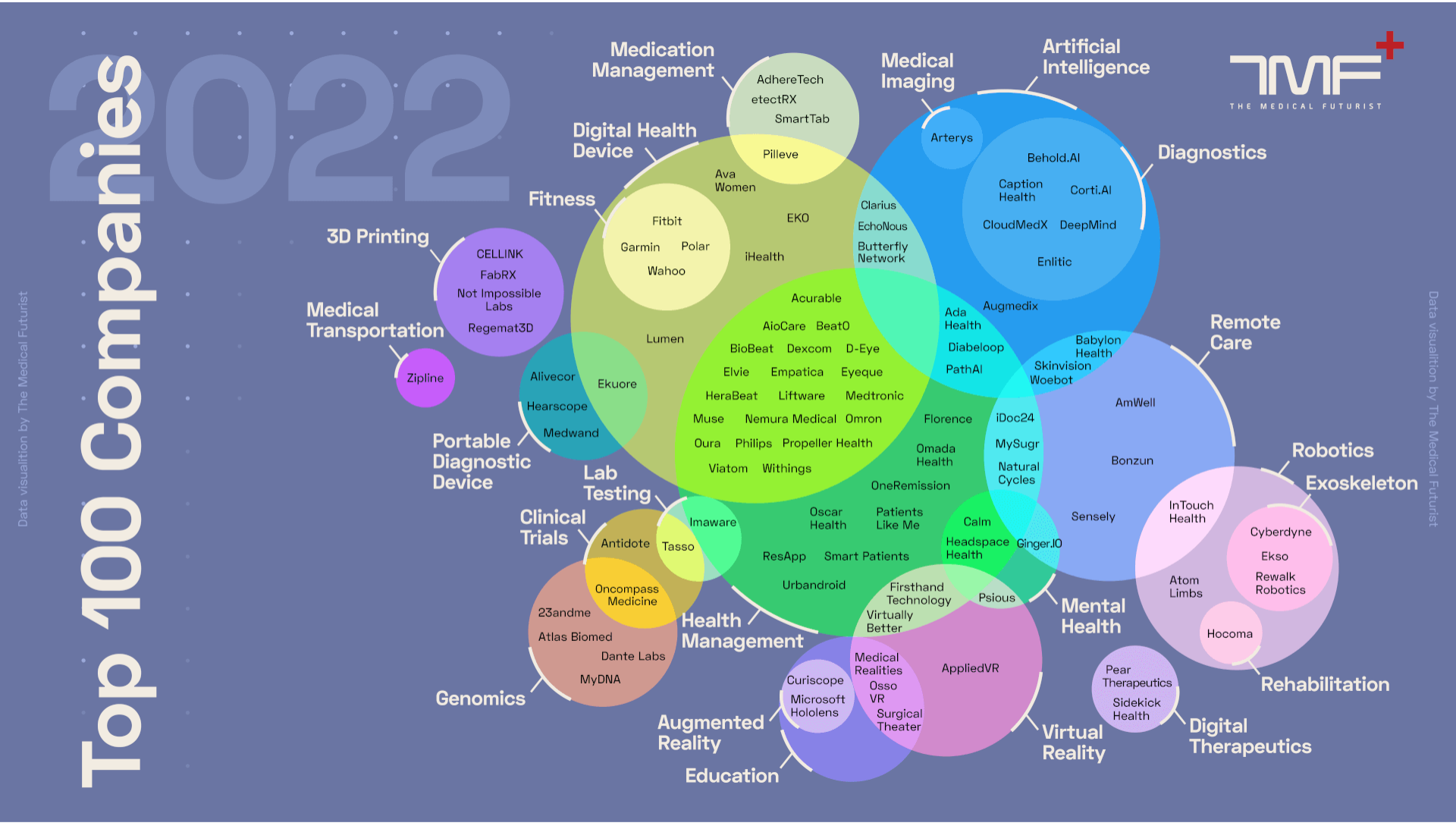
- automated generative design and assembly
- additive manufacturing
  - multi-materials, multi-control elements
  - biotic: abiotic combinations
- integrated sensors for real-time remote data transmission on performance
- automated self-repair and agile reconfiguration in response to altered environments

3D One Process Manufacture of Sensorized Robotic Hand with Tendon-Driven Grip Capabilities and Haptic Surfaces



T.J.K. Buchner et. al. (2023) Nature 623:522–530; doi.org/10.1038/s41586-023-06684-3

Private Sector and Venture Capital Investments in the Expanded Care Space



CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

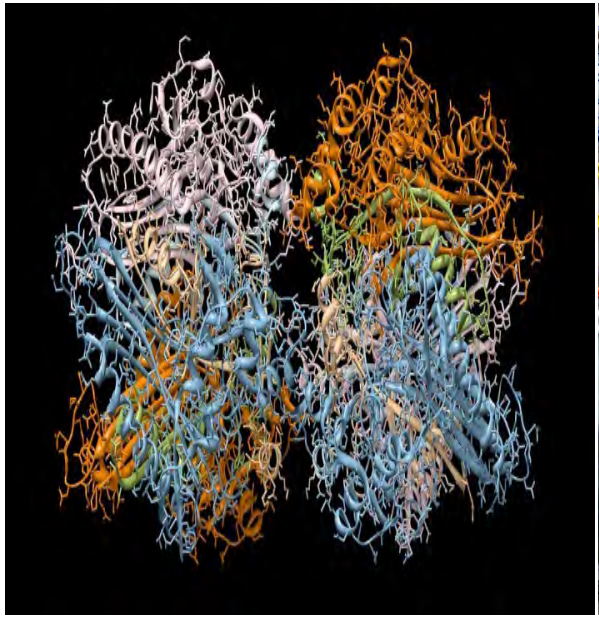
Telehealth, RPM, PRO and the Growth of Decentralized Clinical Trials

Strengthening ASU's Role in Precision Health Clinical Trials

- transition Arizona from fly-over state to vibrant hub for industry–sponsored trials
- increased trial complexity
  - Rx/Dx/Devx/DTx/Ix combinations plus ML/AI analytics
- faster launch/enrollment of eligible patients based on deep phenotyping
- new trial designs and data analysis
  - real-time patient monitoring
  - adaptive/basket, stratified trials, RWE and synthetic data
  - patient reported outcomes (PRO)
- education and training in conduct of clinical trials
- new regulatory legal and ethical issues created by new product classes and AI

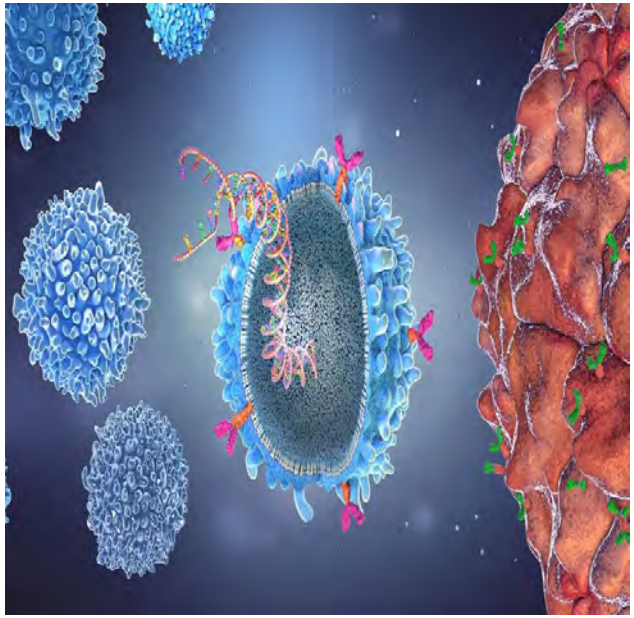
Research Innovation in Molecular Diagnostics and Therapeutics

Protein Structure and Drug Discovery



- high unmet needs for acute diseases
  - AMR, antivirals
  - bacterial sepsis

New Therapeutic Classes and Targeted Delivery Systems



- biomimetic immunotherapeutics
- epitope design for monoclonal antibodies/vaccines
- infection, autoimmunity, cancer

Large-Scale Automation of Biomedical Laboratory Research

Large-Scale Automation of Biomedical Laboratory Research

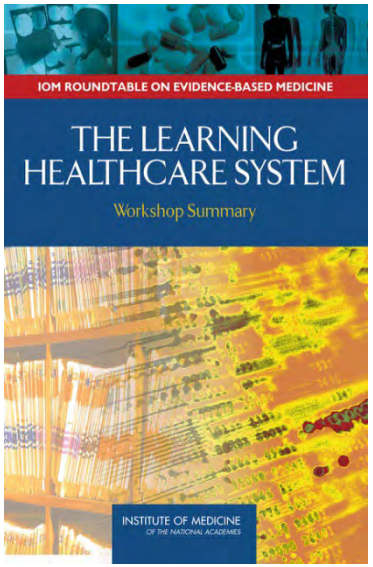
Building an AI Scientist.

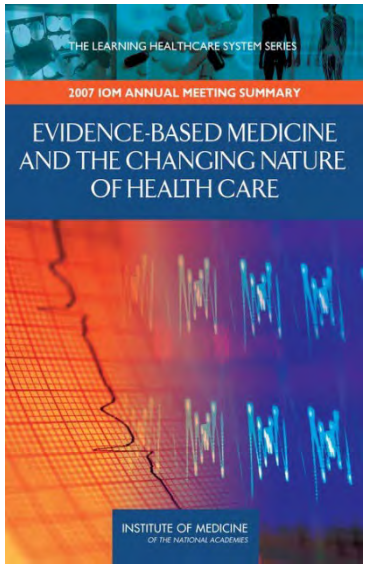
FutureHouse

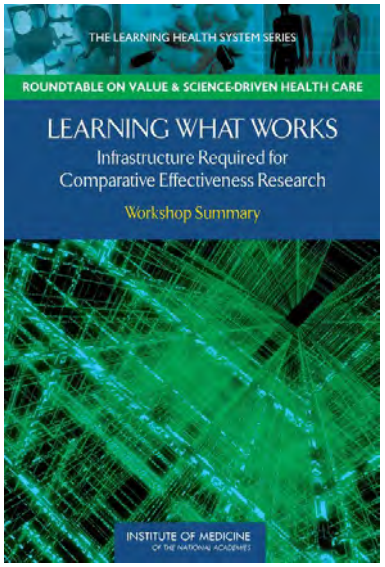
Our 10-year mission is to build semi-autonomous AIs that can scale scientific research, to accelerate the pace of discovery and to provide world-wide access to cutting-edge scientific, medical, and engineering expertise.

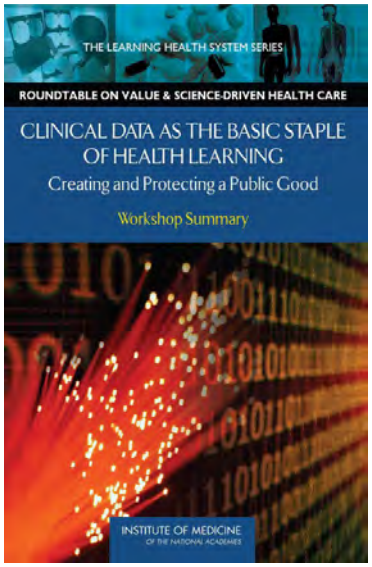
WikiCrow: Automating Synthesis of Human Scientific Knowledge

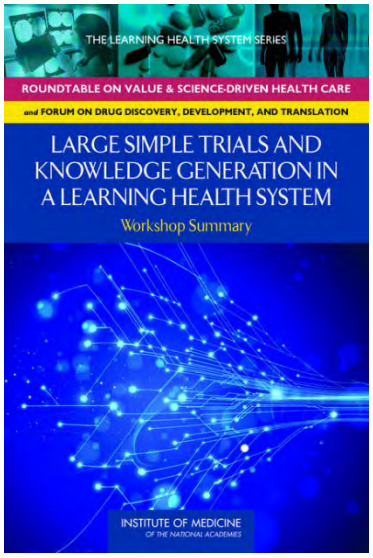
The Learning Healthcare System

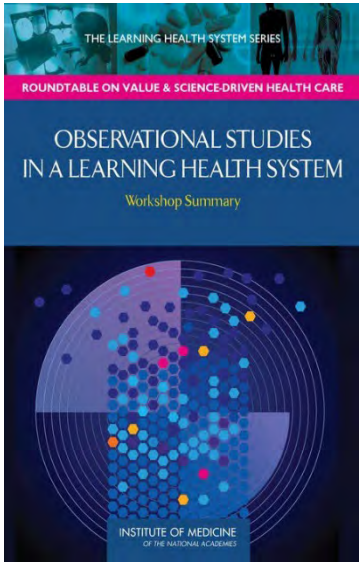


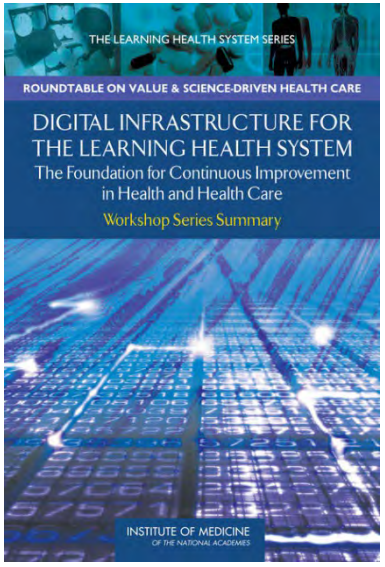


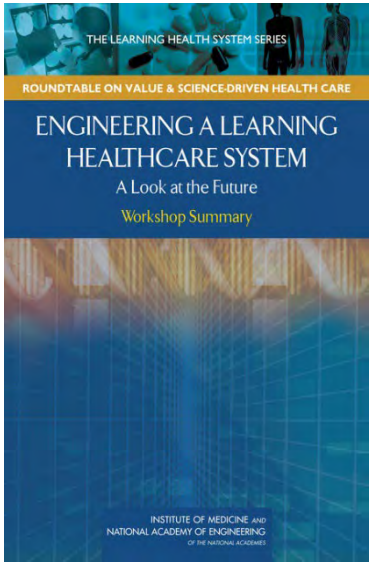












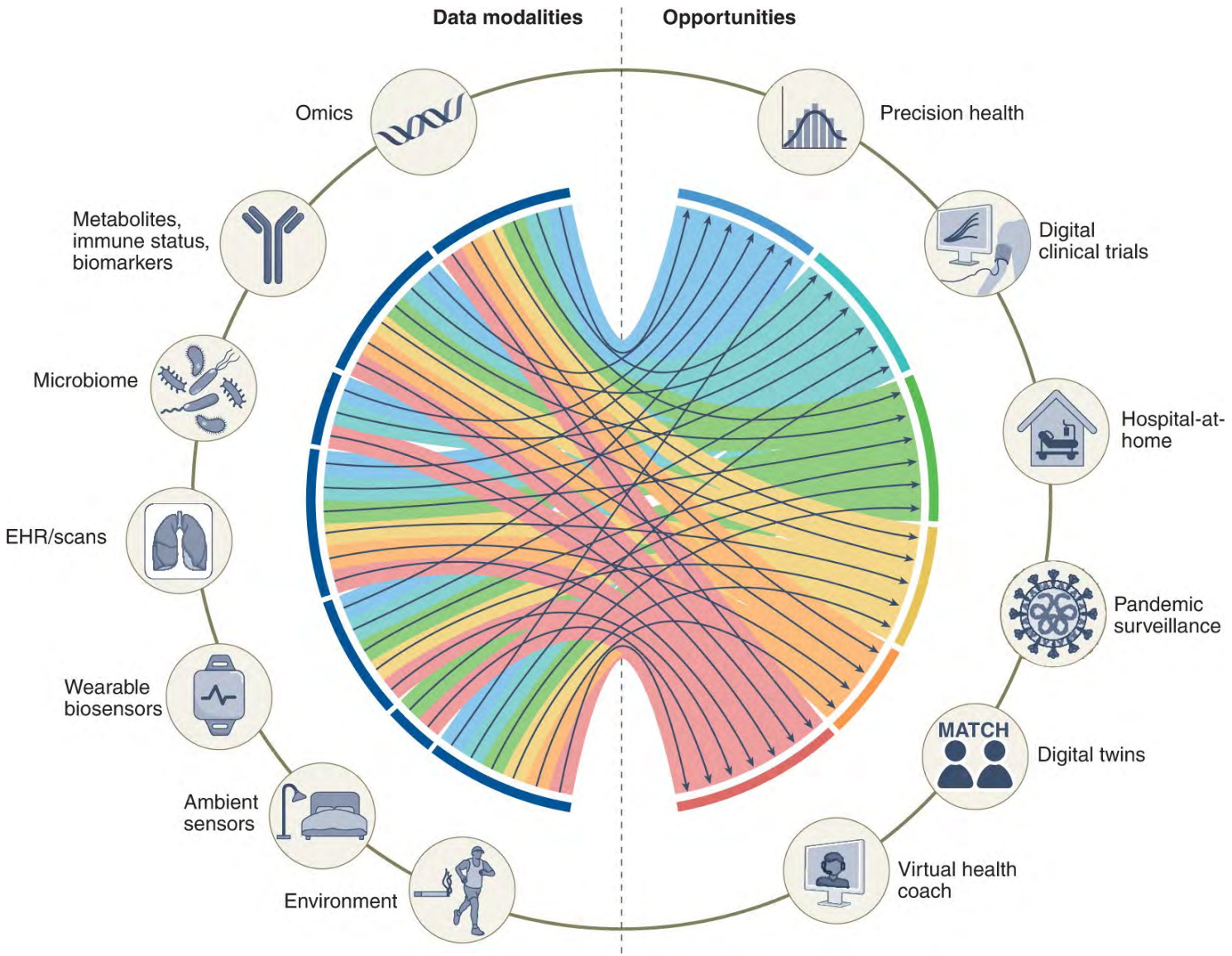
The Health Ecosystem
Data Rich: Application Poor

- biomedical research and healthcare are among the largest producers of data but among the least proficient in translation to optimize health outcomes

- projected zettabyte data deluge by 2030 (10^{21} or one sextillion bytes)

- making precision health a reality will require adoption of holistic, systems-based integration of diverse (multimodal) data categories on an unprecedented scale

Deep Phenotyping:
Multimodal Data Integration for Management of Health Risk



J.N. Acosta (2022) Nature Med 28, 1784

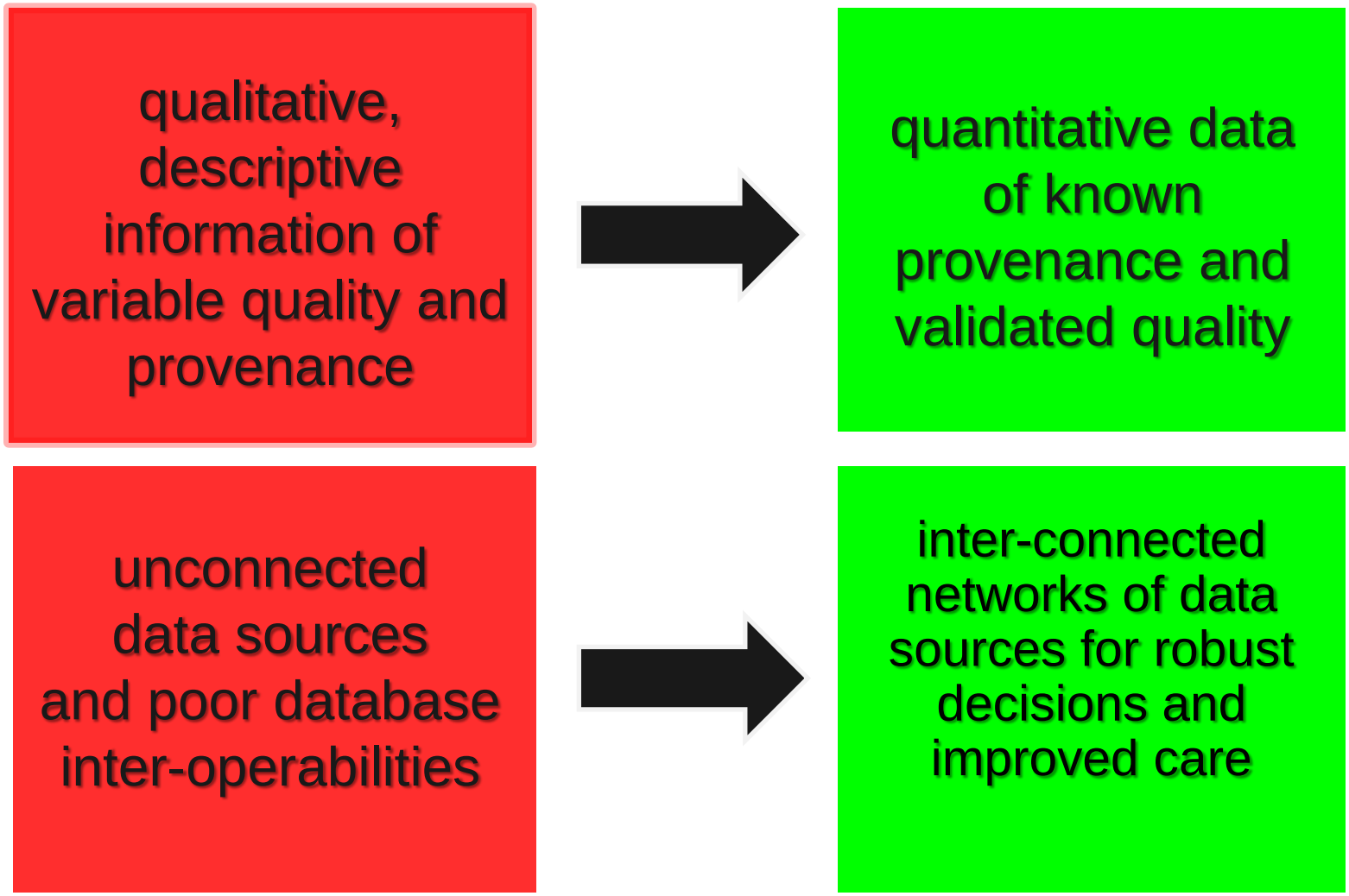
Building Personalized ‘Digital Twins’: Matching Individual Deep Phenotypes to ‘Best Fit’ Cohorts

Individual Data

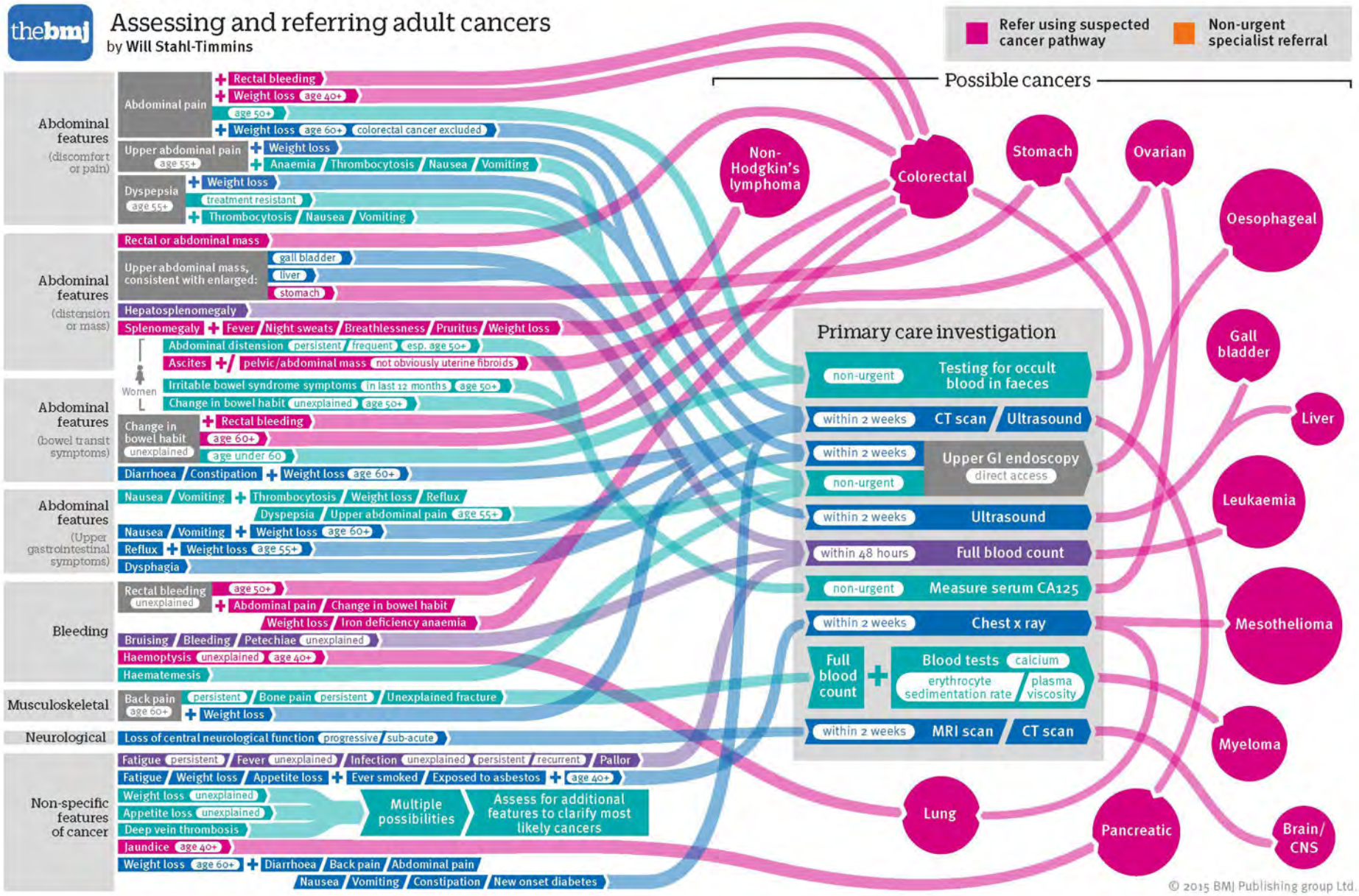
Population Databanks

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

Building a Learning Health Ecosystem
The Co-evolution of Precision Health and Digital Health:



Keeping Current in an Era of Rapid Innovation



https://www.bmj.com/content/bmj/suppl/2015/07/17/bmj.h3044.DC1/adult_cancer_NICE_graphic_v3.1.pdf

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

Data Deluge

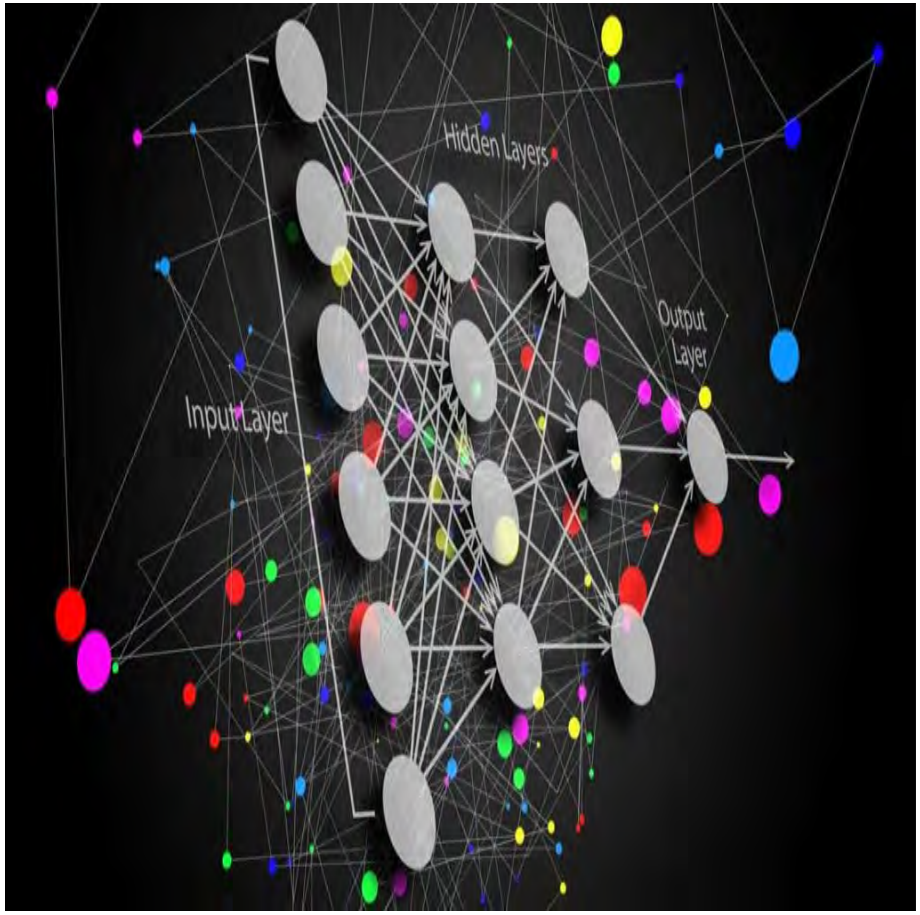
Cognitive Bandwidth Limits

Automated Analytics and Decision Support

Facile Formats for Actionable Decisions

AI and Large Language Models (LLMs): Transformation of Many Elements of the Health Ecosystem

GAI Platforms

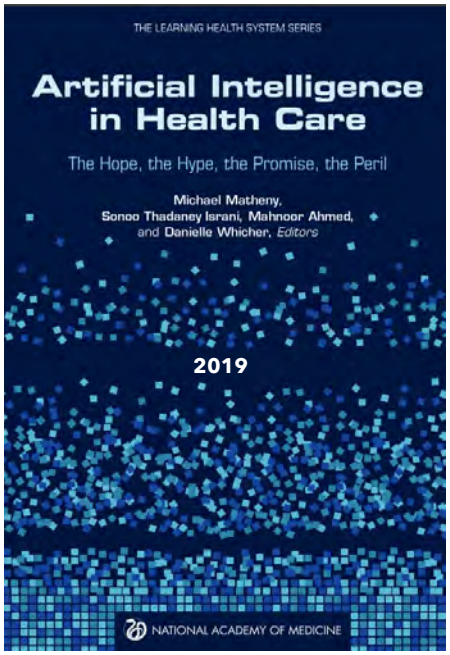


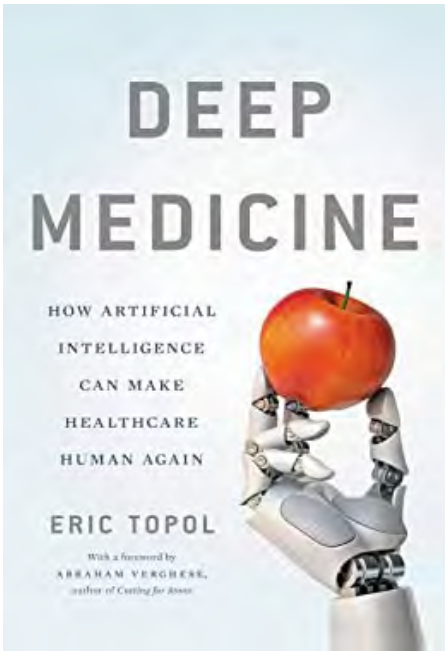
https://insidebigdata.com/2023/10/01/video-highlights-vicuna-gorilla-chatbot-arena-and-socially-beneficial-llms-with-prof-joey-gonzalez/

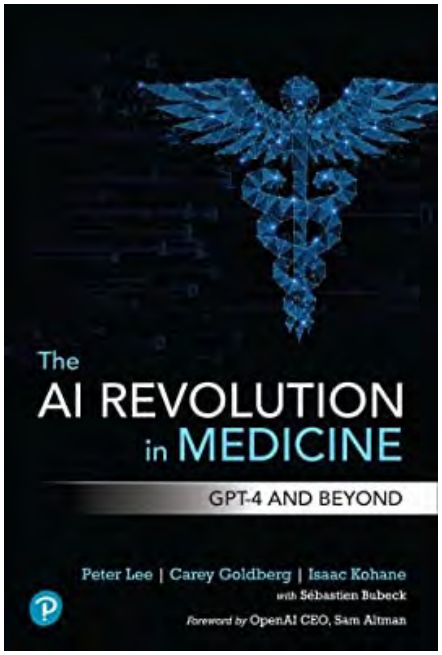
Deep Learning and Pattern Analysis of Integrated Multi-model Data

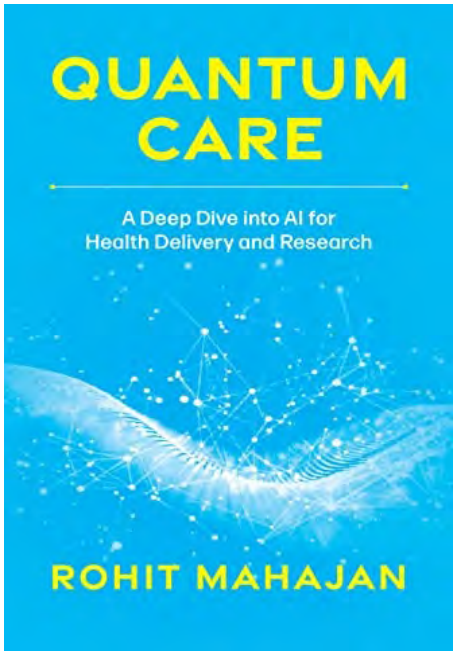
https://techxplore.com/news/2023-07-chatgpt-people-surprisehere-technologies-difference.html

Generalized Artificial Intelligence (GAI) and Healthcare





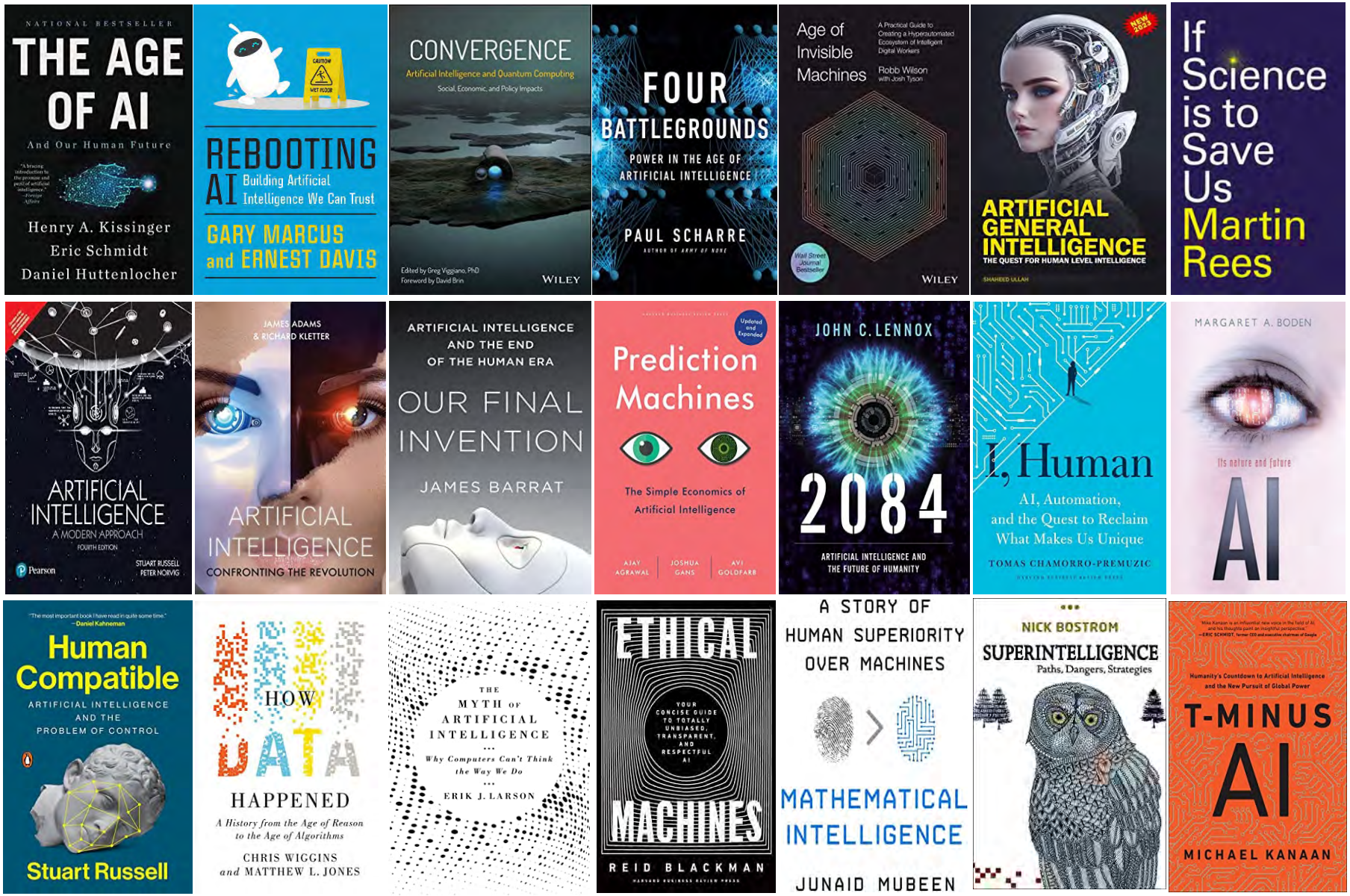




GAI and Healthcare

- pass US medical licensure and board certification requirements
- impressive examples of generation of rapid and accurate responses to questions from HCPs and patients
- frequency of inaccurate and/or nonsensical responses (“hallucinations”) remains problematic
- intrinsic learning properties of LLMs plus access to more data, better hallucination detection filters and refined ‘prompt semantics’ anticipated to rapidly overcome these limitations
- current platforms not HIPAA-compliant

No Shortage of Commentaries on the Potential of AI for Limitless Benefits or the Road to Dystopian Futures and Machine Control



OCTOBER 30, 2023

FACT SHEET: President Biden Issues Executive Order on Safe, Secure, and Trustworthy Artificial Intelligence

European Parliament

9/5/2023

KMB/DA/AS Committee on the Internal Market and Consumer Protection
Committee on Civil Liberties, Justice and Home Affairs

Version: 1.0

DRAFT Compromise Amendments

on the Draft Report

Proposal for a regulation of the European Parliament and of the Council on harmonised rules on Artificial Intelligence (Artificial Intelligence Act) and amending certain Union Legislative Acts

(COM(2021)0206 – C9 0146/2021 – 2021/0106(COD))

OpenAI

December 18, 2023

Preparedness Framework (Beta)

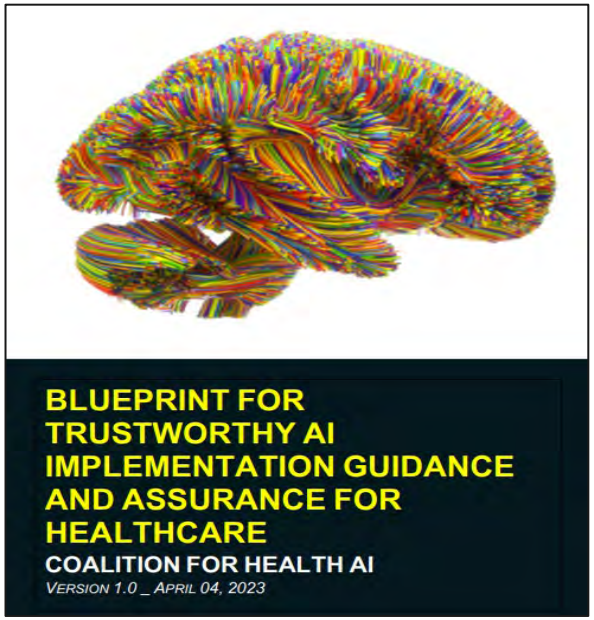
We believe the scientific study of catastrophic risks from AI has fallen far short of where we need to be.

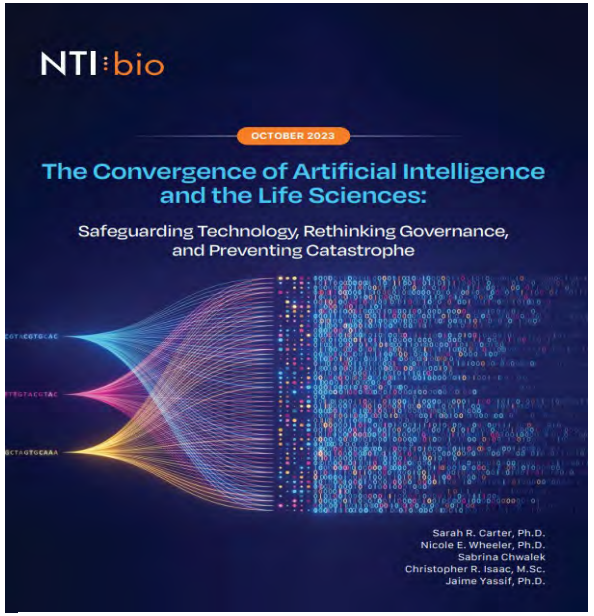
To help address this gap, we are introducing our Preparedness Framework, a living document describing OpenAI's processes to track, evaluate, forecast, and protect against catastrophic risks posed by increasingly powerful models.

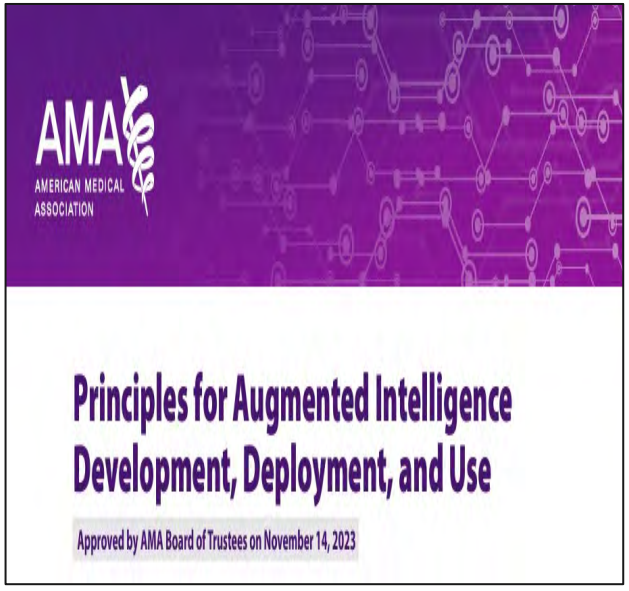
U.S. DEPARTMENT OF DEFENSE RESPONSIBLE ARTIFICIAL INTELLIGENCE STRATEGY AND IMPLEMENTATION PATHWAY

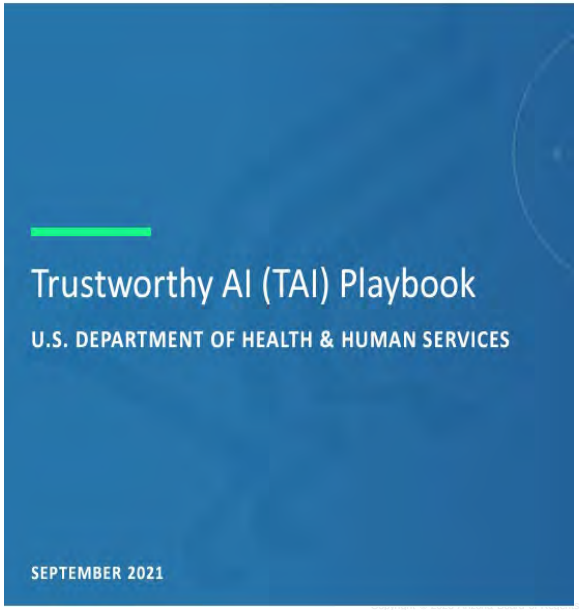
Prepared by the DoD Responsible AI Working Council in accordance with the memorandum issued by Deputy Secretary of Defense Kathleen Hicks on May 26, 2021, Implementing Responsible Artificial Intelligence in the Department of Defense.
June 2022

Oversight and Regulation of AI in Healthcare

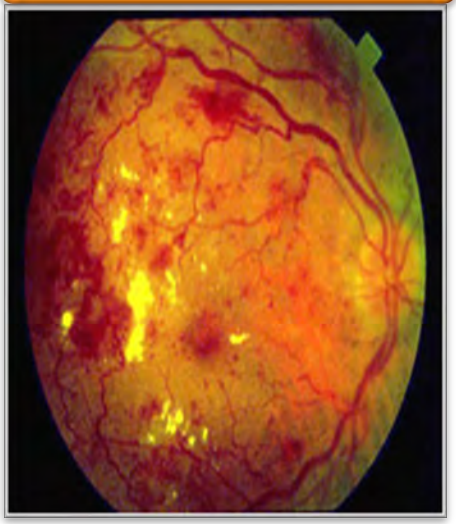








ML/AI and Image Analysis in Clinical Medicine

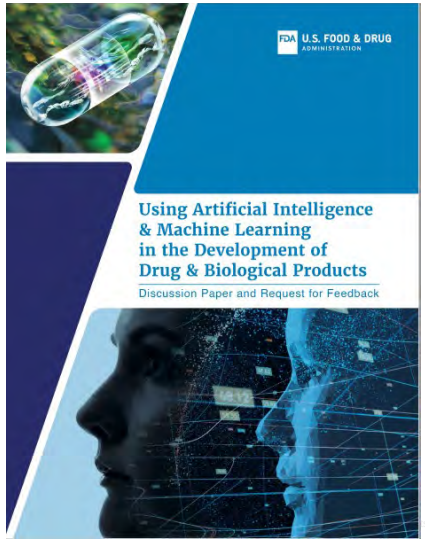
pathology	radiology	dermatology	ophthalmology
			

- large scale training sets and classification parameters
- standardized, reproducible and scalable
- 260 million images/day for $1000 GPU

US Regulation of AI Platforms in Healthcare

“FDA needs to be nimble in
the use and regulation of large language models
to avoid being swept up quickly
by something we hardly understand.”

Dr. R. Califf
FDA Commissioner, 9 May 2023
2023 Science for Patient Engagement Symposium



AI and Potential Disruptive Challenges Across the Health Ecosystem

- new regulatory, legal, policy and ethical issues posed by algorithm-driven methods/decisions
  - algorithm validation, transparency, explainability
  - privacy protections
  - trust
  - liabilities and malpractice
- amplification of threat from dissemination of health misinformation/disinformation and fake images/videos

Regulatory Oversight and Validation of AI Large Language Models in Clinical Decisions

- transparency and patient informed consent when AI tools used in their care
- malpractice liabilities
  - harm from premature use and poorly validated algorithms (liability of platform developers, HCPs, or the health systems which approved adoption?)
  - harm from failure to use validated platforms incorporated into future SOC, professional guidelines or regulatory labeling

Stanford MEDICINE | HAI Stanford University Human-Centered Artificial Intelligence

RAISE-Health

Responsible AI for Safe and Equitable Health

Lloyd Minor, MD

Carl and Elizabeth Naumann Dean,
Stanford University School of Medicine

Fei-Fei Li, PhD

Co-Director, Stanford Institute for Human-Centered Artificial Intelligence (HAI)

LLMs and AI in Healthcare*

- **medical profession did not play an active role in the design of most current IT platforms in healthcare**
  - **user frustration at burdensome formats of EHRs, poor database designs and inter-operabilities**

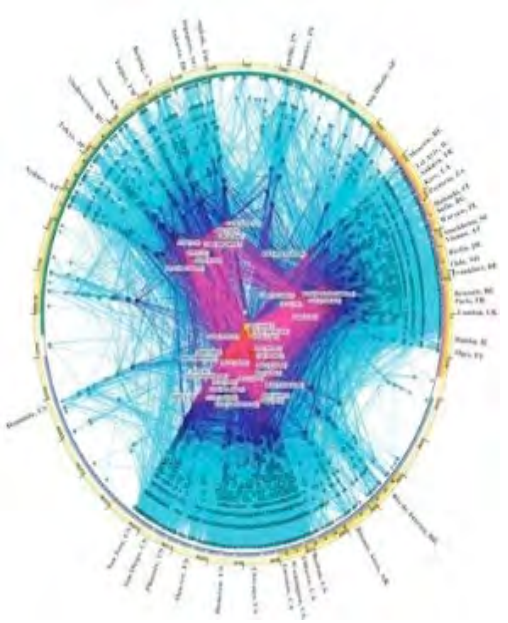
- **importance of avoiding the same mistakes in the rapid deployment of LLMs/AI without input on user requirements**

***N.H. Shah et al. (2023) JAMA 330, 866**

Big Data Changes the Questions That Can Be Asked

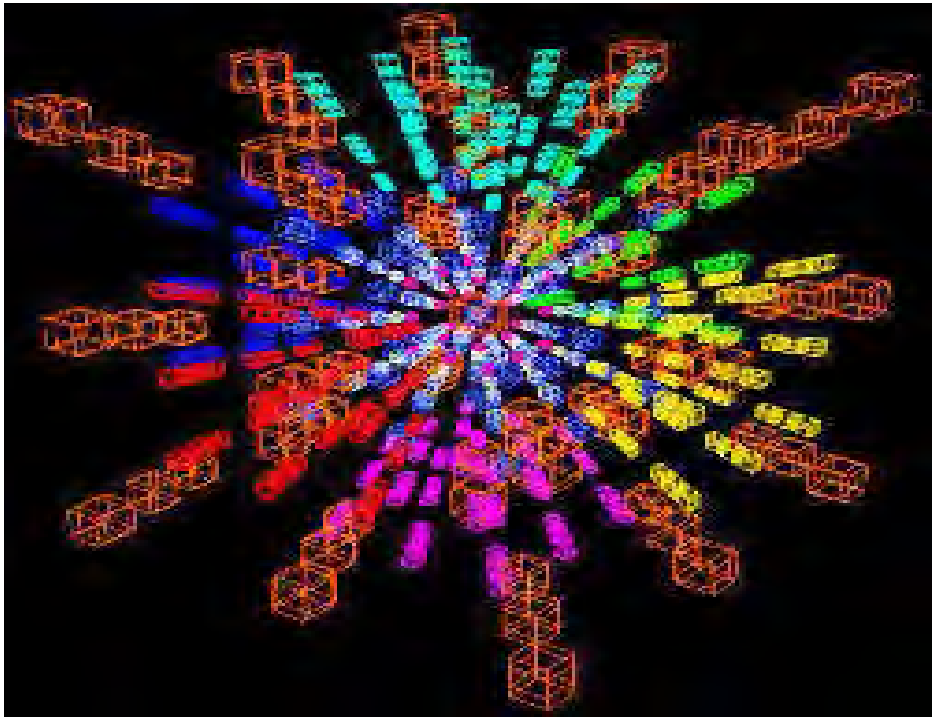
Isolated Data

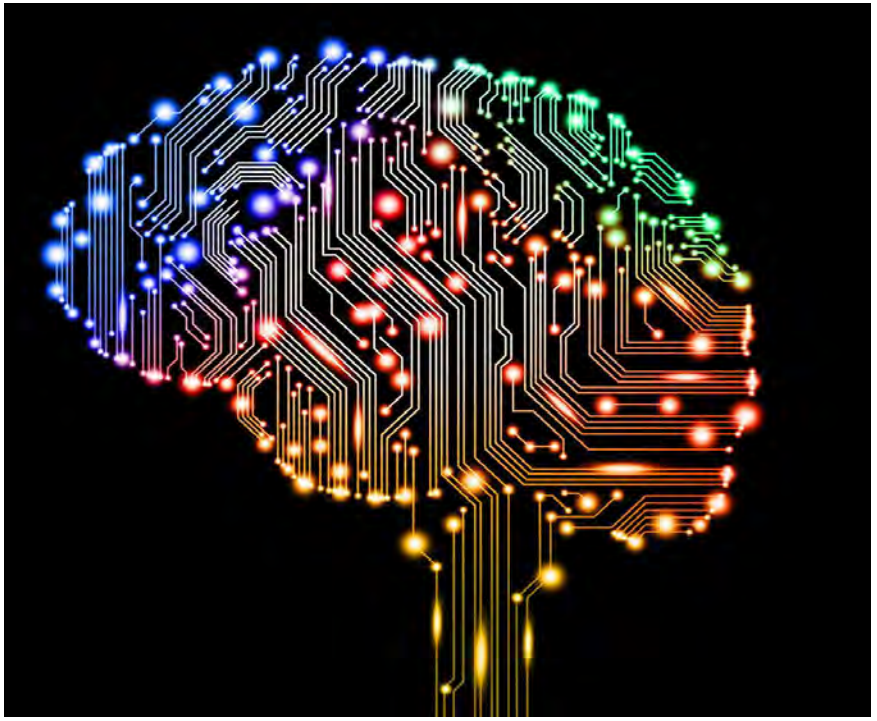
Complex Networked Data



Complex Computational Data

Automated Context: Data Finding Data
"Intelligence at Ingestion" and Collapse Time to Decision





- Data Fidelity
- Feature Extraction

→

Context Analysis

↕

Persistent Context

→

- Knowledge Topologies
- Learning Systems

→

- Rapid, Robust Decisions

“Public sector investment in AI is absurd.
Not a single university today
can train a chatGPT model.
Academia cannot develop its own versions
so that it can be used
for more open scientific research.”

Fei-Fei Li
Institute for Human-Centered Artificial Intelligence
Stanford University
Financial Times 15 Dec. 2023

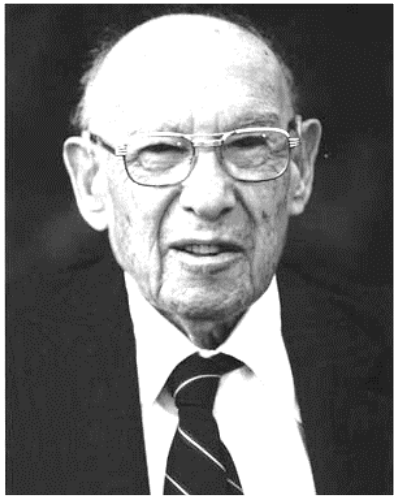
AI and Evolution of a Learning Health Ecosystem

BIG TECH COMPANIES INVEST BILLIONS IN HEALTH RESEARCH

- private sector dominance?
  - compute scale
  - proprietary datasets
  - talent
- expanded academic-industry collaborations
  - design of problem-specific platforms
  - generation of novel (orthogonal) hypotheses from deconvolution of complex networks
  - funding education and training to sustain the talent pipeline

P. Webster (2023) Nat. Med. 29:1034-1037;
doi.org/10.1038/s41591-023-02290-y

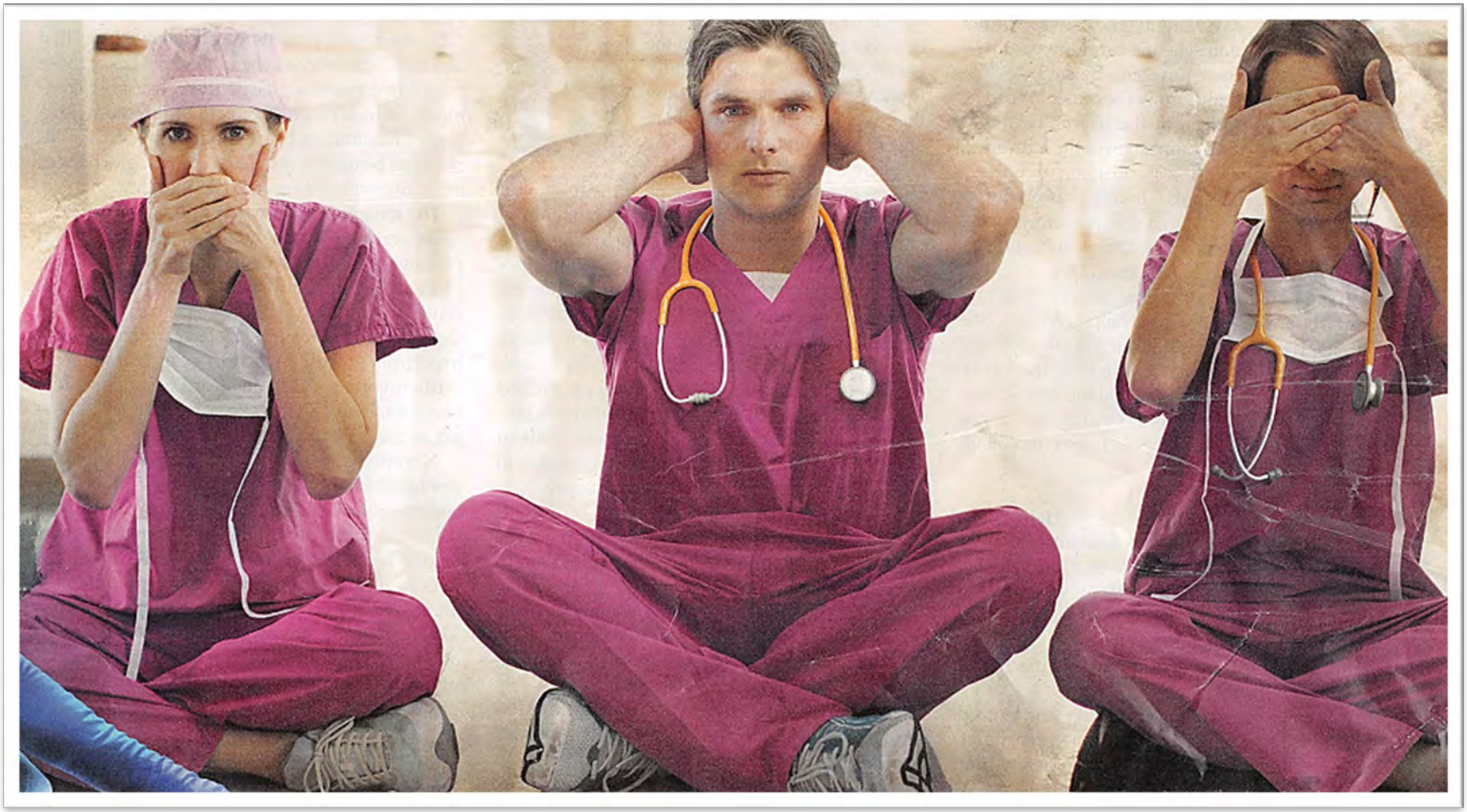
Navigating Disruptive Change: New Thinking and New Capabilities



“The greatest danger in times of turbulence,
is not the turbulence,
it is to act with yesterday’s logic.”

- Peter Drucker

DNR: Cultural Barriers to Adoption of Innovation



Denial

Negativity

Resistance

MITRE

FDA

AHRQ Agency for Healthcare Research and Quality

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

NIH

MAYO CLINIC

OPTUM

The Office of the National Coordinator for Health Information Technology

sas

Microsoft

Google

Stanford University

Drake UNIVERSITY

UCSF University of California San Francisco

Berkeley UNIVERSITY OF CALIFORNIA

VANDERBILT UNIVERSITY

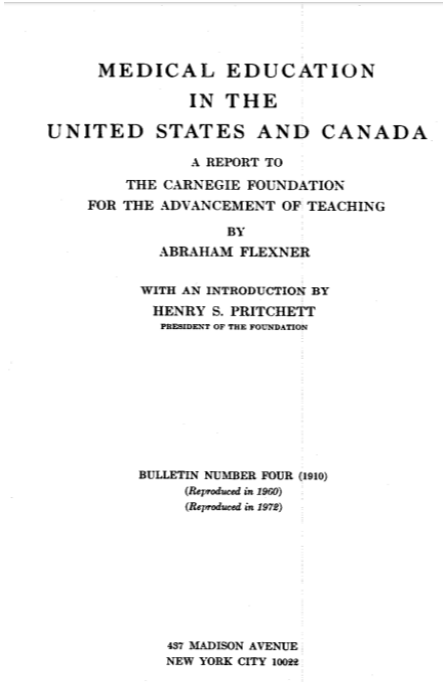
JOHNS HOPKINS UNIVERSITY

PARTNERSHIP ON AI

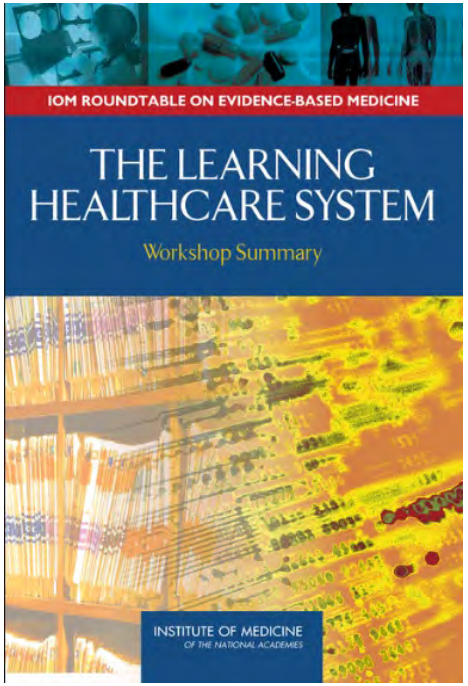
GORDON AND BETTY MOORE FOUNDATION

Major Transitions in Medical Education

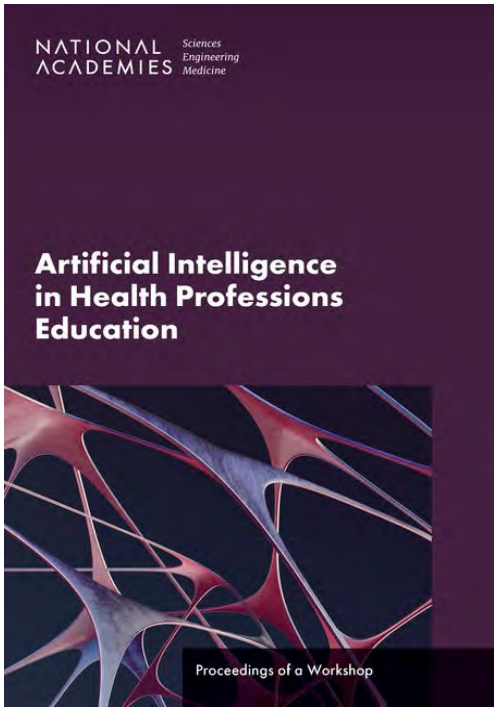
1910

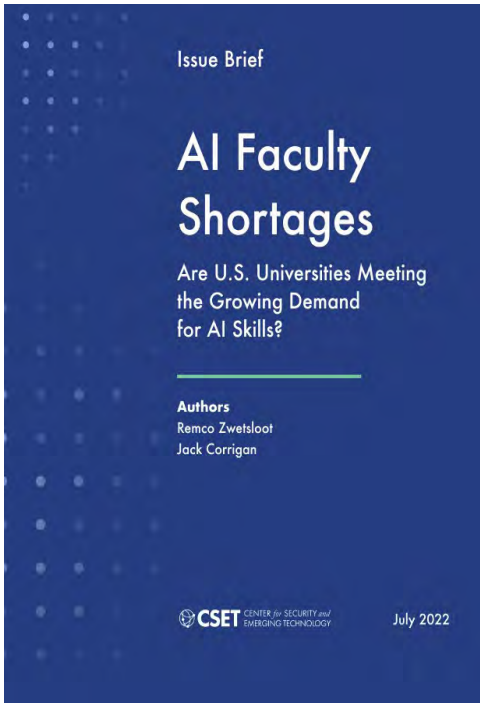


2000



2023





January 2024
ASU first University to partner with OpenAI for education and research

Learning in the Age of Generative Artificial Intelligence (GAI)

“Opportunity to transform lives and communities through learning at a scale that probably hasn’t been since the invention of the printing press.”

“Transform learning and unlock the nascent interest and abilities of our students.”

“ChatGPT is fine tuning my brain to be a better instructor.”

Andrew Maynard
Arizona State University
Slate, July 2023

“Digital Darwinism”: A Looming Digital Divide

- technology convergence between biomedicine, engineering and computing and escalation of scientific and clinical complexity
- new opportunities for different organizational models and capabilities to improve integration and process efficiency across multiple areas of the health ecosystem

“Digital Darwinism”: A Looming Digital Divide

- **leadership in technology convergence and assimilation of advances in data science and AI will be a critical determinant in institutional differentiation and competitiveness**
- **institutions that lack critical mass of data science/AI expertise and computational infrastructure for large scale multi-modal health data analytics will suffer ‘cognitive starvation’ and relegation to competitive irrelevance**

Not Just Another Medical School

- “future, future, future!”
- graduates who are better trained, more capable and more innovative
- new competencies to navigate the escalating complexity of a learning health ecosystem
- forge new career pathways that reflect recalibration of the roles of MDS/HCPs in optimizing health for individuals and populations
- our graduates choose to stay in Arizona

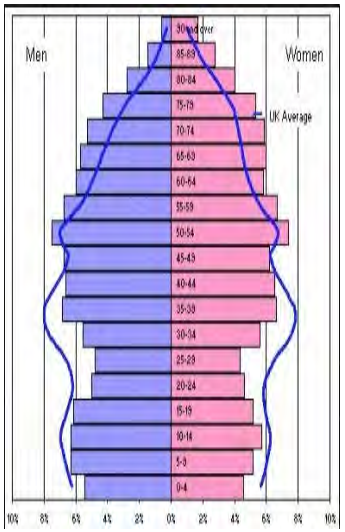
ASU Health

- building a learning health ecosystem
- innovation in education, research, translational science and precision health
- new organizational linkages across ASU and external partners
- increased collaboration with the private sector

Strategic ‘Design Spaces’ for the Evolution of Integrated Health Systems Science and a Learning Health Ecosystem

The Health Observatory

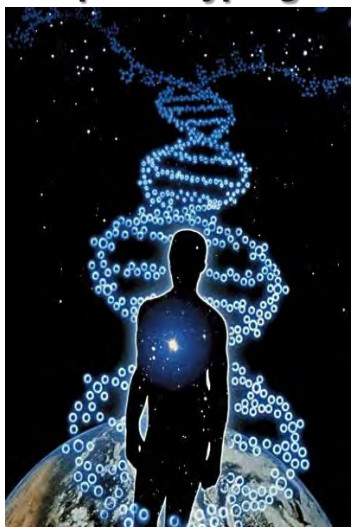
- population health dynamics



“Unmet Need Space”

Precision Health

- multiOmics
- deep phenotyping



“Bio-Space”

IoMT

- remote health monitoring

“Connected Space”

Big Data Analytics

- multi-modal data
- ML/AI

“Decision Space”

Accelerating Technology Convergence

- innovation in education, research and care

“Opportunity Space”

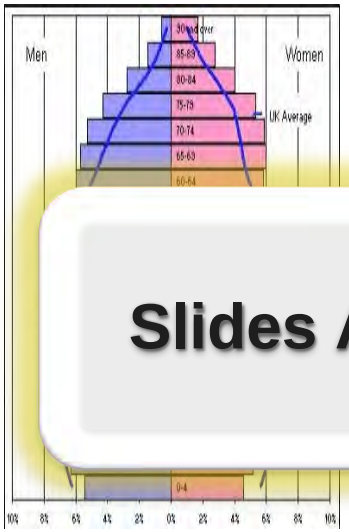
Improved Identification and Mitigation of Health Risk

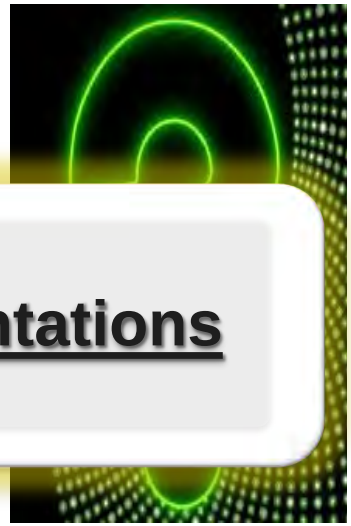
New Knowledge Networks

New Participants

New Organizational Models

The Health Observatory	Precision Health	IoMT	Big Data Analytics	Accelerating Technology Convergence
• population health dynamics	• multiOmics • deep phenotyping	• remote health monitoring	• multi-modal data • ML/AI	• innovation in education, research and care





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

"Unmet Need Space"	"Bio-Space"	"Connected Space"	"Decision Space"	"Opportunity Space"