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
Director, Complex Adaptive Systems Initiative, Arizona State University
george.poste@asu.edu

PUBLPOL/EMED 127/227: Winter 2024
HEALTH CARE LEADERSHIP
Stanford University School of Medicine
24 January 2024
Slides Available @ http://casi.asu.edu/presentations
Disclosures

- Board Member
- Board Member
- Board Member
- Board Member
- Scientific Advisory Board
- Scientific Advisory Board
No GAI Platforms Were Used in Content Selection, Design, Assembly and Formatting This Presentation
IMPROVING POPULATION HEALTH
Preventing and managing prevalent, costly, and chronic diseases

REDUCING COST OF CARE
Reducing resource utilization and readmissions while assuming greater risk

ENHANCING THE PATIENT EXPERIENCE
Motivating and engaging patients to play an active role in their care to improve outcomes and safety

IMPROVING PROVIDER SATISFACTION
Providing access to tools and resources to address provider burden and burnout

QUADRUPLE AIM

https://www.strategiesforqualitycare.com/quadruple-aim
The US Health Ecosystem  
Fragmentation, Fragilities and Looming Disruptions

- isolated silos of expertise and care services
  - poor continuity in care and myriad embedded inefficiencies
- economically unstainable 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%)
  - disease-centric (sick-care) versus health optimization (wellness)
- decoupling of population health initiatives from care delivery to individuals
- myriad fragilities and fault lines revealed and amplified by COVID-19 pandemic
- neglect of social determinants of health and adverse impact on minority/marginalized communities
- systemic vulnerabilities create major opportunities for disruptive innovation
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, big data analytics, AI and social media
• economics of scale with drive increased vertical and horizontal consolidation
• public and political expectations
  – access, availability, affordability and outcomes
  – reduce disparities and inequities
The Evolution of Precision Health: Improved Identification and Mitigation of Health Risks

- increasingly rational public health and clinical interventions to optimized health based on features unique to specific individuals/population cohorts
- improved detection of disease risk predisposition
- earlier detection of overt disease and prognosis/prediction of disease progression patterns
- shift societal disease burden from current predominant focus on treating advanced chronic disease to management of earlier stage disease and disease prevention
- strengthen surveillance and preparedness for rapid, resilient responses to disruptive external biosecurity threats
  - emerging infectious diseases, climate, cyber-risks
Precision Health

- optimize the health of populations and individuals by improved precision in the identification and mitigation of health risks
- the organization, capabilities, incentives and accountabilities of multiple elements of the current health ecosystem are misaligned with this strategic aspiration
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
(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

**Key**
1 - Phase I  
2 - Phase II  
3 - Phase III  
4 - Approved

**Unknown Oncogenic Driver Detected 31%**

**EGFR Sensitizing 17%**
- Gefitinib 4
- Erlotinib 4
- Afatinib 4
- Osimertinib 4
- Necitumumab 4
- Rociletinib 3

**ALK 7%**
- Crizotinib 4
- Alectinib 4
- Ceritinib 4
- Lorlatinib 2
- Brigatinib 2

**MET 3%**
- Crizotinib 2
- Cabozantinib 2

**HER2 2%**
- Trastuzumab emtansine 2
- Afatinib 2
- Dacomitinib 2

**ROS1 2%**
- Crizotinib 4
- Cabozantinib 2
- Ceritinib 2
- Lorlatinib 2
- DS-6051b 1

**BRAF 2%**
- Vemurafenib 2
- Dabrafenib 2

**RET 2%**
- Cabozantinib 2
- Alectinib 2
- Apatinib 2
- Vandetanib 2
- Ponatinib 2
- Lenvatinib 2

**NTRK1 1%**
- Entrectinib 2
- LOXO-101 2
- Cabozantinib 2
- DS-6051b 1

**MEK1**
- Trametinib 2
- Selumetinib 3
- Cobimetinib 1

**PIK3CA**
- LY3023414 2
- PQR 309 1

http://www.iaslc.org/
Understanding the Organization and Dynamics of Molecular Information Networks in Health (Physiology) and Disease (Pathology)

- mapping information flow (communication) within and between networks
- the progression from health to disease reflects the graded degradation in the fidelity of signal transmission

https://doi.org/10.3892/ijmm.2016.2577
Understanding System State Shifts (Phenomes) and Emergent Perturbations in Molecular Signaling Networks in the Health to Disease Continuum
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 staging, prognosis and predicted progression
  - optimum treatment selection based on specific disease features in individuals and cohorts with similar phenotypes
  - prediction of Rx response, resistance and adverse events
  - faster alert of clinical deterioration and treatment non-adherence
  - tracking social determinants of health and exposure to environmental hazard exposures
  - proactive monitoring to detect pathogens with epi-/pandemic potential
Deep Phenotyping: “Much More Than Omics”

From Womb to Tomb: Systematic Longitudinal Integration of Multi-modal Health Data

SDoH, Lifestyle, Health Disparities, Environmental Hazards (Exposome)
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:
  - Longitudinal tracking
  - Every population cohort/individual becomes their own control (tracking the Delta)
  - Internet-of-Medical Things (IOMT)
Rapid Growth in Wearables, Sensors and Devices for Remote Health Status Monitoring
Wearables and Remote Health Status Monitoring
Smart Devices for Automated Drug Delivery and Improved Therapeutic Adherence

Propeller Health

Gecko (now Teva)

CapMedic

Biocorp Inspair

Help patients get onboard with onbody injections

Aterca Veta EpiPen
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
- 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 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 physician-patient 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
Robot–Human Directed Interactions
Cyber-Physical-Biological Systems
Immersive Human-Machine Interfaces and Surgery

- robotics, automation and AR/VR/XR
- integration of robot controls with advanced 3D imaging
- multiplex sensor arrays and endoscopes/catheters
- precision actuators, sensing and automated controls
- instant presentation of comparable cases into headdress of surgical team members
- address shortages in surgical specialities
  - 331 million US population
  - 4000 cardiothoracic surgeons
  - 3500 neurosurgeons
AR/VR/XR Neuromodulation in Clinical Care

- injury rehabilitation
- reduce apprehension/distraction in painful procedures
- anxiety, depression, PTSD, phobias
The Future of Making: Industry 4.0 Technologies
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
- 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

T.J.K. Buchner et. al. (2023) Nature 623:522–530; doi.org/10.1038/s41586-023-06684-3
The Convergence of Precision Health and Digital Health: The Expanded Care Space and New Classes of Products and Services

- earlier detection of risk and mitigation
- reduce (re)hospitalization
- improved continuity in care
- telemedicine and remote health monitoring
- independent but monitored living for elderly

the expanded care space and continuity in care

new combination product classes, services and new industry alliances/entrants

new cross-sector industry alliances and academic engagement

- Dx-Rx
- Dx-Rx-Ix
- Dx-Rx-Device
- DigRx
- materials science/sensors
- brain-computer interactions
- intelligent agents and robotics
- social data analytics
- big data analytics
The Learning Healthcare System
Welcome to
The World of
Biomedical Research
and
Healthcare Information Systems
Managing Big Data in Biomedicine Will Not Be a Simple Extrapolation from Current Practices

Evolution of New Professional Competencies for Proficient Use of Advanced Computing, AI and Automated Clinical Decision Systems
Precision Health and Deep Phenotyping: Multimodal Data Integration for Longitudinal Management of Health Risks

J.N. Acosta (2022) Nat Med 28, 1784
Precision Health and Digital Health: Building a Learning Health System

- qualitative, descriptive information of variable quality and provenance
- complex ecosystem of largely unconnected data sources
- quantitative data of known provenance and validated quality
- evolving, inter-connected networks of data sources for robust decisions and improved care
Precision Health and Digital Health: Evolving Inter-Dependencies

Individual Data

- Clinical history - EHR/PHR
- Remote health monitoring
- Socio-behavioral data
- Environmental exposures

Population Data

- Integration and analysis of large-scale diverse data
- Exabyte and zettabyte data deluge

Deep Phenotyping:

- multiOmics
- Clinical history - EHR/PHR
- Remote health monitoring
- Socio-behavioral data
- Environmental exposures

- $3.2$ trillion

Deep Phenotyping:

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

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

- Feature Extraction and Classification
- Context Analysis
- Persistent Context
- Knowledge Topologies
- Learning Systems
- Data Fidelity
- Rapid, Robust Decisions
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 Large Language Models (LLMs): Transformation of the Research Process and Clinical Decision-Making

GAI Platforms

Deep Learning and Pattern Analysis in Multi-model Data Integration


The GAI Investment Frenzy 2023

PyTorch, LLaMA (24 Feb.)

Palm (10 March) BARD

GPT4 (14 March) Microsoft Bing (7 March)

ERNIE (15 March)

Copilot X (22 March)

ChatGPT app added its Slack and Einstein platforms
Generalized Artificial Intelligence and Healthcare
AI and Healthcare

- impressive examples of generation of rapid and accurate responses to questions from HCPs and patients
- but frequency of inaccurate and/or nonsensical responses ("hallucinations") remains problematic
- intrinsic learning property of LLMs with access to more data, new hallucination detection filters and refined ‘prompt semantics’ is anticipated to rapidly overcome this vulnerability
No Shortage of Commentaries on the Potential of AI for Limitless Benefits or the Road to Dystopian Futures and Machine Control
FACT SHEET: President Biden Issues Executive Order on Safe, Secure, and Trustworthy Artificial Intelligence

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.
Oversight and Regulation of AI in Healthcare
The Rush to Regulate AI: We’ve Been There Before

Wall Street Journal, 2 January 2024

- each new technology with broad multi-domain applications evokes calls for one-size-fits-all governance policies and regulation
- 1980s: biotechnology
- 1990s: www and internet
- 2023: generative artificial intelligence

Cyberspace and the Law of the Horse:
1996 Opinion by Judge Frank Easterbrook 7th US Grand Court of Appeals

- calls for a single regulator/regulation for governance of the web and the emerging internet would be as futile as an effort to create a single pathway to regulate the multiple uses of horses in the 19th century economy
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
Regulatory Oversight and Validation of Large Language Model (LLM) AI Platforms in Clinical Decisions

• transparency and patient informed consent when AI tools used in their care

• malpractice liabilities
  – harm from use (platform developers, HCPs, or the health systems which approved adoption)
  – harm from failure to use or ignored recommendations when AI-decision support systems are integrated into SOC, professional guidelines or regulatory labeling
Navigating Disruptive Change

“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
New Thinking and New Capabilities
RAISE-Health
Responsible AI for Safe and Equitable Health
Navigation of Escalating Scientific and Clinical Complexities
Major Transitions in Medical Education and Healthcare

1910 - present

MEDICAL EDUCATION IN THE UNITED STATES AND CANADA
A REPORT TO THE CARNEGIE FOUNDATION FOR THE ADVANCEMENT OF TEACHING
BY ABRAHAM FLEXNER
WITH AN INTRODUCTION BY HENRY E. PRITCHETT PRESIDENT OF THE FOUNDATION

2000 - present

THE LEARNING HEALTHCARE SYSTEM
Workshop Summary

2015 - ?

PROCEEDINGS OF A WORKSHOP
Graduate Medical Education Outcomes and Metrics

Complexity
Ethics
Innovation
Interprofessionalism

Health Economics & Policy
Health Care Management
Informatics
Systems Engineering
Population Health
Leadership
“Digital Darwinism”: A Looming Digital Divide

- understanding data structure and its productive application/customization for acceleration of research and clinical care 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
The Co-Evolution of Precision Health, Digital Health and AI

- multi-technology integration
- AI and navigating the zettabyte world
- integration of multi-modal health data

- multiOmics
- remote health monitoring
- robotics, computing and automation

- molecular clinical
- consumer/patient engagement

- SDoH
- lifestyle
- environmental

- population databases
- individual EHRs
- claims data
- risk signatures
- synthetic data
- digital twins

- mapping the complexity of genophenotypic relationships and individual disease risk(s)
- diagnostic accuracy, optimum Rx selection, improved outcomes, and QOL (clinical and economic value)
- longitudinal monitoring of individual health status
The Evolution of Data-Intensive Precision Health

- Technology Convergence and Acceleration
- Mapping Geno-Phenotype Complexity
- Topology of Biological Information Networks
- Multi-modal Data Integration
- Data Security and Privacy
- Robotics and Human Machine Interactions
- Artificial Intelligence and Decision Support
- Public Policy: Ethics, Risk and Regulation
The Evolution of Data-Intensive Precision Health

Technology Convergence and Acceleration

Mapping Geno-Phenotype Complexity

Topology of Biological Information Networks

Multi-modal Data Integration

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

Data Security and Privacy

Robotics and Human Machine Interactions

Artificial Intelligence and Decision Support

Public Policy: Ethics, Risk and Regulation