The Strategic Landscape for the Evolution of Precision Health:

Disruptive Changes in Biomedical Research, Public Health and Care Delivery

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Slides Available @ http://casi.asu.edu/presentations
The Quadruple Aim

**IMPROVING POPULATION HEALTH**

Preventing and managing prevalent, costly, and chronic diseases\(^2,^4\)

**REDUCING COST OF CARE**

Reducing resource utilization and readmissions while assuming greater risk\(^2\)

**ENHANCING THE PATIENT EXPERIENCE**

Motivating and engaging patients to play an active role in their care to improve outcomes and safety\(^4\)

**IMPROVING PROVIDER SATISFACTION**

Providing access to tools and resources to address provider burden and burnout\(^3\)

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

The Challenge of Big (Messy) Data

- terabytes per individual
- zettabyte – yottabyte population databases

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

(Epi)Genomics and MultiOmics Profiling
Molecular Classification of Non-Small Cell Lung Cancer

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

**EGFR Sensitizing**
- Gefitinib  
- Erlotinib  
- Afatinib  
- Osimertinib  
- Necitumumab  
- Rociletinib

**ALK**
- Crizotinib  
- Alectinib  
- Ceritinib  
- Lorlatinib  
- Brigatinib

**MET**
- Crizotinib  
- Cabozantinib

**HER2**
- Trastuzumab emtansine  
- Afatinib  
- Dacomitinib

**ROS1**
- Crizotinib  
- Cabozantinib  
- Ceritinib  
- Lorlatinib  
- DS-6051b

**BRAF**
- Vemurafenib  
- Dabrafenib

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

**NTRK1**
- Entrectinib  
- LOXO-101  
- Cabozantinib  
- DS-6051b

**PIK3CA**
- LY3023414  
- PQR 309

**MEK1**
- Trametinib  
- Selumetinib  
- Cobimetinib

**Unsure**
- Unknown Oncogenic Driver Detected 31%

**Other**
- Other 4%

- > 1 Mutation 3%
- HER2 2%
- ROS1 2%
- BRAF 2%
- RET 2%
- NTRK1 1%
- MEK1 <1%
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 rehospitalization
  - 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

- $T_{1(n)}$: baseline health demographics
- $T_{2(n)}$: identification of risk foci: SDoH, disparities, EIDs
- $T_{3(n)}$: 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

Smart Devices for Automated Drug Delivery and Improved Therapeutic Adherence

Help patients get onboard with onbody injections

Onbody Trainers
- Robust 3D Replication
- Actuator Sensation
- Speaker Feedback
- Replaceable Device Adherence
- Targeted Needle Simulation

Find out how a Noble onbody trainer can improve patient onboarding and boost your platform's competitive edge.

Contact us today: 888.933.5646 or GoNoble.com/Onbody

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Implantable Devices and Wireless Monitoring (and Modulation)

next-generation miniaturized power sources

security and hacker protections
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
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

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

- ‘one stop’ shopping and telemedicine
  - disease prevention/screening
  - primary care
  - pharmacy
  - discounted pricing
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’
Robotic Exoskeletons for Injury Rehabilitation and Disability Mitigation

Characterization of Interaction

Sensors
1. Ground Reaction Force
2. State of Actuator
3. Kinematic Feature
4. Dynamic Feature

Motion Generation

Controller
1. Position, Force, and Impedance Control
2. Sensor Fusion

Motion Execution

Actuator
1. Motors
2. Artificial Muscles

Data Flow

Command

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

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
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
Building an AI Scientist.

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
Welcome to The World of Biomedical Research and Healthcare Information Systems
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

Data modalities
- Omics
- Metabolites, immune status, biomarkers
- Microbiome
- EHR/scans
- Wearable biosensors
- Ambient sensors
- Environment

Opportunities
- Precision health
- Digital clinical trials
- Hospital-at-home
- Pandemic surveillance
- Digital twins
- Virtual health coach

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

- ‘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:

- Qualitative, descriptive information of variable quality and provenance
- Unconnected data sources and poor database inter-operabilities
- Quantitative data of known provenance and validated quality
- Inter-connected networks of data sources for robust decisions and improved care
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

Deep Learning and Pattern Analysis of Integrated Multi-model Data


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

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

- Ethics and Governance of Artificial Intelligence for Health
- Blueprint for Trustworthy AI: Implementation Guidance and Assurance for Healthcare
- AMA: American Medical Association
- Health Care Artificial Intelligence Code of Conduct
- Trustworthy AI (TAI) Playbook
- Principles for Augmented Intelligence Development, Deployment, and Use

Approved by AMA Board of Trustees on November 14, 2023

NTI:bio
The Convergence of Artificial Intelligence and the Life Sciences: Safeguarding Technology, Rethinking Governance, and Preventing Catastrophe

Gail R. Gutin, Ph.D.
Nicole B. Wheeler, Ph.D.
Garth Gardner
Christopher R. Nye, M.D.
Jaime Yassar, Ph.D.
ML/AI and Image Analysis in Clinical Medicine

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

- 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
“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
Major Transitions in Medical Education

1910

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 S. Pritchett PRESIDENT OF THE FOUNDATION

847 MADISON AVENUE
NEW YORK CITY 10028

2000

THE LEARNING HEALTHCARE SYSTEM
Workshop Summary

2023

Artificial Intelligence in Health Professions Education

Proceedings of a Workshop

Issue Brief

AL Faculty Shortages
Are U.S. Universities Meeting the Growing Demand for AI Skills?

Authors
Ronco Zwiethoof Jack Carriem

CSET CENTER FOR SECURITY AND TECHNOLOGY
July 2022
January 2024
ASU first University to partner with OpenAI for education and research
“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

- **Precision Health**
  - multiOomics
  - deep phenotyping

- **IoMT**
  - remote health monitoring

- **Big Data Analytics**
  - multi-modal data
  - ML/AI

- **Accelerating Technology Convergence**
  - innovation in education, research and care

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Improved Identification and Mitigation of Health Risk

New Knowledge Networks

New Participants

New Organizational Models
Improved Identification and Mitigation of Health Risk

New Knowledge Networks

New Participants

New Organizational Models

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