Precision Health and Digital Health: The Inter-Dependent Strategic Drivers of Innovation in Healthcare Delivery

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Precision Health and Digital Health: The Strategic Drivers of Biomedical Research and Healthcare Delivery

- Technology Convergence
- Science & Technology Acceleration
- Disruptive Technologies
- Large Scale Data Analytics
The Strategic Environment for Biomedical Research and Healthcare Delivery

- ageing populations
- chronic disease
- SDoH
- new patterns of care delivery

- reduce cost of care
- improve clinical outcomes
- learning healthcare systems

- Technology Convergence
- Science & Technology Acceleration
- Large Scale Data Analytics
- Disruptive Technologies

a complex multi-dimensional, multi-stakeholder ecosystem
The Growing Burden of Chronic Disease

- economic unsustainability of current care systems
- insufficient clinical infrastructure
- disparities in access to care and patterns of care
- inadequate health information systems and poor coordination and continuity of care
- cost of innovation (Rx price as political target)
- rise of consumerism in healthcare and entry of new corporate players
The Growing Burden of Chronic Disease

- cancer
- neurodegeneration
- cardiovascular/metabolic disease
- mental illness

- economic unsustainability of current care systems
- insufficient clinical infrastructure
- disparities in access to care and patterns of care
- inadequate health information systems and poor coordination and continuity of care
- cost of innovation (Rx price as political target)
- rise of consumerism in healthcare and entry of new corporate players
Healthcare: A Complex, Multidimensional, Multi-stakeholder Ecosystem

innovation ecosystem

care delivery ecosystem

political will

insurance ecosystem

media/public perception

regulation and public policy

patient advocacy

access and affordability

outcomes

clinical decisions

Value and Sustainability
The Path to Precision Medicine: 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

Precision Medicine:

• terabytes per individual
• zettabyte – yottabyte population databases

MultiOmics Profiling of Disrupted Molecular Signaling Networks in Disease:
The New Taxonomy of Disease Subtypes

Patient-Specific Signatures of Disease and Optimized Treatment Selection for Disease Subtypes

Big (Messy) Data

(Epi)Genomics
Genetic Overlap Between Stroke and Related Vascular Traits at 32 Genome Loci for Stroke Profiled in 520,000 Subjects

Molecular medicine and information-based targeted healthcare

The convergence of genomics and informatics heralds a new era of biomedical research, offering unbridled opportunities for bioentrepreneurs.

George Poste

The accelerating momentum of technological innovation in the life sciences has been accompanied by equally profound changes in the competitive landscape for industrial R&D. New entrepreneurial companies have emerged on an unprecedented scale to exploit advances in molecular biology, genomics, combinatorial chemistry, robotics, microelectronics, and informatics to generate new products and services for medicine, agriculture, and the prevention and treatment of disease.
Still Two Largely Separate Worlds

Precision medicine

Routine healthcare delivery and SOC

- One-size-fits-all protocols
- Wide variation in clinical practice and outcomes
- Fragmented continuity of care
- Inefficient use of available data

Slow incremental adoption of technological advances

Research and early clinical adopters (largely oncology)

$100-125* billion (estimated)

$3.6 trillion (19% GDP)

*Includes investment in investigational Rx candidates
If It Sounds Too Good To Be True….?
Popular Delusions and The Madness of Crowds: Charles Mackay 1841

Theranos’ Nanotainer holds just a drop of blood. As many as 30 lab tests can be done from this one tiny sample.

Bloomberg Businessweek

BAD BLOOD
Secrets and Lies in a Silicon Valley Startup
John Carreyrou
Over 100 Companies Pursuing “Liquid Biopsy” for Blood-Based Molecular Biomarkers Precision Medicine

Early Detection / Screening*

- AcuamarkDx
- epiigenomics
- freenome
- GUARDANT HEALTH
- MDx Health
- OncoCyte
- exact sciences
- MDNA Life Sciences
- Volition

Diagnosis

- OncoCyte
- Indi
- epiigenomics

Treatment Selection

- AccuraGen
- admera
- AnchorDX
- BOREAL
- GRAIL
- Invitae
- Biocartis
- trovagene
- PGD
- Guardant Health
- Neo Genomics
- ArchGen
- BioFluidica
- SINGLERA GENOMICS
- OncoCyte
- sysmex
- TEMPUS

Monitoring

- OncoDNA
- admera
- NEO
- BGI
- BGI
- BIOTECH
- Trovagene
- neo
- Neogene
- AmoyDx
- Natera
- NanHealth
- NanHealth
- NantHealth
- NeoGenomics
- Resolution Bio
- Resolution Bio
- OncoCyte
- OncoCyte
- Agena
- cynvenio
- BioFluidica
- SINGLERA GENOMICS
- OncoCyte
- sysmex
- TEMPUS

Legend:
- ccfDNA
- CTCs
- Other (e.g., exosomes)

Note: *Includes risk stratification (e.g., to determine whether a tissue biopsy is needed) as part of pre-diagnosis process
Source: DeciBio Liquid Biopsy White Paper, Cl Tool
Precision Medicine and Digital Medicine: Evolving Inter-Dependencies

Individual Data

- “digital siblings and imputed phenotypes”
- matching individual profiles to ‘best fit’ data cohorts
- to identify risk and selection of optimum treatment regimens

Population Databanks

integration and analysis of large scale, diverse data categories
The “Geno-Enviro-Pheno’ Triad

Systematic Integration of Diverse Data for Population Health Analytics
Continuity of Care Record: From Womb to Tomb

Behavior

Environment
Social Determinants of Health (SDoH):
Precision Medicine and Digital Medicine: Evolving Inter-Dependencies

**Individual Data**
- Matching individual profiles to "best matched" cohorts for clinical decisions

**Population Databanks**
- Integration and analysis of large scale, diverse data categories

**Deep Phenotyping:**
- Integration of (epi)genomic and multiOmic profiles,
  clinical, environmental and socio-behavioral data

$3.2$ trillion
Precision Health and Digital Health

Expanding ‘The Analyte Space’ in Health and Disease

Monitoring Health Beyond the Clinic
• the majority of events that influence wellness/disease risk and treatment adherence occur largely 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
Social Spaces Become Quantifiable

- who knows why people do what they do?
  - the fact is that they do!
- these actions can now be traced and measured with unprecedented precision
- with sufficient data, the numbers reveal increasingly predictable behavior and individual risk patterns
- the confessional of social media
- the blurring of private and public spaces
- complex ethical and legal issues
  - consent, privacy, security, surveillance
“People Analytics” and Large-Scale Databanks: Blurring the Boundaries Between Medical Research, Clinical Care and Daily Life

• every monitored event (clinical and non-clinical) is a potential data point
• every individual is a data node
• every individual is a research asset
• every individual is their own control
Healthcare Beyond the Clinic
Changing The Touch Points in Healthcare Delivery

Remote Health Status Monitoring

Smartphones, Wearables, Devices and Telemedicine Services

AORTA: Always On, Real Time Access

M4: Making Medicine More Mobile
Wellness Apps for Fitness, Diet and Exercise
Remote Monitoring of Health Status
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
Grey Technologies and Ageing in Place: Independent But Monitored Living for Ageing Populations

- Rx adherence
- Cognitive stimulation
- In-home support and reduced readmissions
- Reduced office visits
Remote Health Monitoring and Reduction in Hospital Readmissions
Hospital Readmission Rates

# 1  CHF (22 - 30%)
# 2  behavioral health and substance abuse (20 - 26%)
# 3  respiratory (158 - 26%)
# 4  diabetes mellitus (15 - 22%)
# 5  acute renal failure (15 - 22%)
Reducing Hospital Readmissions

• identification and focus on higher-risk, higher-complexity patient
• patient coaching/education on discharge instructions and self-management
• engage family members
• use of transitional care nurses and other care coordination professionals
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

Onbody Trainers
- Device Regulation
- Activation Sensation
- Spillage Sensation
- Replaceable Device Adhesion
- Injection Site Sensation

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

Aterica Veta EpiPen
Chatbots and Support Robots in Healthcare
Amazon and Home Care

Development of Third-Party Alexa Apps

Allows seniors to verbally report medical data, get exercise and adherence reminders, call a caregiver, and coordinate transport.

Mayo Clinic First Aid

“Tell me about spider bites”
“Help for a bum”

Ask My Buddy

“Alexa, ask My Buddy to alert everyone.”

Digital Platforms in Behavioral Health
Growing Demand: Increased ED Presentations of Behavioral Health Emergencies

- reported range of 8-25% of ED volume (outliers higher)
- 70% of behavioral health patients also have one or more co-morbidities
- opioid-related visits tripled between 2005-16
- approx. 1 in 4 individuals with serious mental illness also have SUD
- 60% of adolescents in community-based SUD treatment programs also meet diagnostic criteria for mental illness

*mental illness and substance use disorder (SUD)*
Digital Psychiatry: Digital Psychometrics and Evaluation of Mental Illness

- (micro)saccades
- facial dynamics

- speech prosody (rhythm, tone, volume)
- semantic construction
- stimulus response and interaction speed
“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
Robotics and Human-Machine Interactions

Brain-Machine Interface Technologies and Augmented Sensory, Motor and Cognitive Functions
Robot–Human Directed Interactions
Robotic Assist Systems and Exoskeletons for Rehabilitation
Co-evolution of Human-Machine Interactions, Robotics and Augmented Cognition

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

- promote behavior change via altered sensory inputs and feedback
- mental illness: PTSD, physical rehabilitation, substance abuse and pain control
Next-Generation Non-Surgical Neurotechnology (N³) Program

- brain-machine (computer) interface technologies
- non-invasive interfaces
- “minimally invasive” technologies
  - ingest chemical compounds that enable external sensors to read brain’s activity
- bidirectional information links

“Do you solemnly swear to have no involvement in your own care?”

The New Yorker. Artist: Andrew Toos
Empowered Patients: Social Networking Sites (SNS) 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
The Principal Forces Shaping Biomedical R&D and Healthcare Delivery

- engineering and device-based medicine
  - sensors
  - smart implants
- remote health monitoring
  - telemedicine
  - robotics
- molecular (precision) medicine
  - panOmics profiling
  - analysis of disruption in biological networks
- information-based healthcare
  - m.health/e.health
  - data- and evidence-based decisions and Rx selection

BIG DATA
- outcomes-based healthcare and sustainable health
- new value propositions, new business models and services
• radical disruption always occurs at the margins of existing fields or at points of convergence between previously separate fields

• history shows that the competitive threat posed by disruptive vectors of innovation are typically denied by the then current leading institutions/companies/public sector plans
HIPPA-Complaint Intelligent Agents
The Next Competitor for Amazon?

Walgreens

Microsoft
Economies of Scale and Convenience Come to Primary Care
Turning Data Into Decisions

“Data!, Data!, Data!”
Holmes cried impatiently
“I can’t make bricks without clay.”

The Adventure of the Copper Beeches
Sir Arthur Conan Doyle
Strand magazine June 1892
Now Comes the Hard Part!

Driving Precision Medicine and Data-Driven Healthcare Into Routine Clinical Practice
Welcome to The World of Biomedical Research and Healthcare Information Systems
The Health Information Supply Chain

• fragmented, disconnected, incomplete and inaccurate data

• incompatible data formats as barrier to data integration and sharing

• obstacles to EHR integration of new data classes (multi-Omics; wearables; IoMT)

• legislative barriers to data transfer based on well intentioned privacy protections (HIPAA)

• organizational, economic and cultural barriers to open data sharing

• static episodic snap shots of complex dynamic systems (patients and delivery channels)
Precision Medicine and Digital Health: Building a Learning Healthcare 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
The Increased Importance of Real World Data (RWD) and Evidence (RWE)

- expanded payer requirements to demonstrate efficacy/utility/value in intended-use population(s) with different characteristics to trial population(s) studied in investigational clinical trials
  - age, co-morbidities, polypharmacy
  - clinical setting (AMCs, community hospitals, primary care)
- analyze treatment outcomes in sub-populations
- quantify treatment outcomes for value-based contracting
Alexa, What’s Privacy?

“Smart” devices are listening—and so are humans.
Protection and Privacy Provisions for Personal Healthcare Data

- Informed consent
- Legal provisions/penalties for breach

Identifiable individual data

Aggregated de-identified databanks and metadata

- Variable levels of consent
- Probabilistic, multi-parameter individual ‘match’
Google Ascension Partnership Fuels HIPAA Privacy Debate (1/2020)

Data Brokers and ‘Selling-On”

23andMe, moving beyond consumer DNA tests, is building a clinical trial recruitment business

By REBECCA ROBBINS @rebeccadrobbins / SEPTEMBER 26, 2019
MEMORANDUM FOR: SEE DISTRIBUTION

DEC 20 2019

SUBJECT: Direct-to-Consumer Genetic Testing Advisory for Military Members

It has come to the attention of the DoD that some direct-to-consumer (DTC) genetic testing companies are encouraging DoD personnel to purchase genetic ancestry and health information through the offering of military discounts or other incentives. These DTC genetic tests are largely unregulated and could expose personal and genetic information, and potentially create unintended security consequences and increased risk to the joint force and mission.

Exposing sensitive genetic information to outside parties poses personal and operational risks to Service members. DTC genetic tests that provide health information have varying levels of validity, and many are not reviewed by the Food and Drug Administration before they are offered, meaning they may be sold without independent analysis to verify the claims of the seller. Possible inaccuracies pose more risk to DoD military personnel than the public due to Service member requirements to disclose medical information that affects readiness (see DoD Instruction 6025.19, "Individual Medical Readiness"). Testing outside the Military Health System is unlikely to include a clear description of this risk.

Moreover, there is increased concern in the scientific community that outside parties are exploiting the use of genetic data for questionable purposes, including mass surveillance and the ability to track individuals without their authorization or awareness.

Until notified otherwise, DoD military personnel are advised to refrain from the purchase and/or use of DTC genetic services.

Joseph D. Kernan
Under Secretary of Defense for Intelligence

James N. Stewart
Assistant Secretary of Defense for Manpower and Reserve Affairs, Performing the Duties of the Under Secretary of Defense for Personnel and Readiness
Reinforcement learning in artificial and biological systems

Emre O. Nefci and Bruno B. Averbeck

High-performance medicine: the convergence of human and artificial intelligence

Eric J. Topol

Deep learning sequence-based ab initio prediction of variant effects on expression and disease risk

Jian Zhou, Chandra L. Theesfeld, Kevin Yao, Kathleen M. Chen, Aaron K. Wong and Olga G. Troyanskaya

Predicting the clinical impact of human mutation with deep neural networks

Lakshman Sundaram, Hong Gao, Samskruhti Reddy Padigepati, Jeremy F. McRae, Yanjun Li, Jack A. Kosmicki, Nondas Fritzas, Jörg Hakenberg, Anindita Dutta, John Shon, Jinbo Xu, Serafin Batzoglou, Xiaolin Li and Kyle Kai-How Farh
AAIH Founding Members: Unified Vision for Healthcare
90+ Startup AI Companies in Healthcare
Machine Learning and Image Analysis in Clinical Medicine

- large scale training sets and classification parameters
- standardized, reproducible and scalable
- 260 million images/day for $1000 GPU
Machine Intelligence and Algorithms for Clinical Diagnosis and Treatment Decisions

Just What the Data Ordered

Black Box Medicine?
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
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
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
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
Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

Discussion Paper and Request for Feedback
Machine Learning (ML), Artificial Intelligence (AI) and Healthcare

- which clinical specialties/processes will be at risk of replacement by ML-AI 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
- what new malpractice liabilities will emerge by failure to use/interpret ML-AI platforms
The Future of Work and The Future Workforce
“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
Welcome to the Age of One-Shot Miracle Cures That Can Cost Millions
Healthcare and the Washington Asylum

- aging demographics and the chronic disease burden
- Affordable Care Act
- “Medicare-for-All”
- drug prices and importation
- opioids, fentanyl(s), SUD, PTSD and suicide
- cybersecurity and data protection
- neglect of global public health as a national security risk
- ethical and legal issues for dual-use technologies
ON THE ROAD TO SUCCESS, THERE ARE NO SHORTCUTS.
The Evolution of Data-Intensive Precision Medicine

- Technology Convergence and Acceleration
- Mapping Geno-Phenotype Complexity
- Topology of Biological Information Networks
- V7 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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- Robotics and Human Machine Interactions
- Artificial Intelligence and Decision Support
- Public Policy: Ethics, Risk and Regulation
Engagement in National Policy Development in Science and Technology

Defense Science Board
Global Forum on Microbial Threats
Biosecurity

National Academy of Medicine
NASA & Future of the ISS
National Biomarker Development Alliance
• largest US public university
• fastest growth in research revenues of any US university
ASU Charter

ASU is a comprehensive public research university, measured not by whom it excludes, but by whom it includes and how they succeed; advancing research and discovery of public value; and assuming fundamental responsibility for the economic, social, cultural and overall health of the communities it serves.

Building Unique Value Propositions in Higher Education and Use-Inspired Research
A New American University: Use-Inspired Research on Complex Global Challenges

- Pragmatic Engagement with “Real World Problems”
- Leverage Technology Convergence and Scale
- Cultural and Organizational Challenges

“Urgency”, Competitiveness, Focus, Resolve Metrics and Accountability
A New American University:
A Purposeful, Radical Strategic Redesign

- Party School
- Strategic Premise That Many Features of Contemporary Academia Lack the Agility to Address the Forces Reshaping Research and Education

- Silos Subvert Solutions
- Ambitious Focus on Cross-Disciplinary/Cross-Sector R&D and Use-Inspired Applications for Major Unmet Needs
Design of A New American University

- 15-year transition from a second-tier public university with reputation as a ‘party school‘ to highly competitive rankings in both education and research

- radical nature of the changes in organization and internal culture would have been far difficult to implement in institutions with long established entrenched cultures and complacency
Higher Education Research and Development (HERD) Rankings

ASU Rank versus Total Institutions in the NSF Analysis

Total Research Expenditures: 44 of 903

Total Research Expenditures among Institutions without a Medical School: 8 of 747

HHS (including NIH) Funded Expenditures among Institutions without a Medical School: 8 of 417

NSF Funded Expenditures: 22 of 594

Transdisciplinary 3 of 253
Higher Education Research and Development (HERD) Rankings

DOE Funded Expenditures: 28 of 345

NASA Funded Expenditures: 8 of 430

Engineering Expenditures: 18 of 395

Electrical, Electronic, and Communications Engineering: 9 of 283

Geological and Earth Sciences: 2 of 360
A Transformative Decade

**National Science Foundation (NSF)**
**Higher Education Research and Development (HERD) Rankings**

**Total Research Expenditures:** 44 of 876 ahead of

- THE UNIVERSITY OF CHICAGO
- BROWN
- PRINCETON UNIVERSITY
- Caltech
- University of Colorado Boulder
- CASE WESTERN RESERVE UNIVERSITY

**Total Research Expenditures among Institutions without a Medical School:** 9 of 718 ahead of

- Caltech
- PRINCETON UNIVERSITY
- Carnegie Mellon University
- THE ROCKEFELLER UNIVERSITY
- The Scripps Research Institute
- University of Notre Dame

**Non-Medical School Expenditures:** 22 of 876 ahead of

- Stanford University
- COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK
- Rutgers University
- THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
- THE UNIVERSITY OF ARIZONA
- The Ohio State University
#1 in the U.S. for innovation

ASU ahead of Stanford and MIT

– U.S. News & World Report 5 years, 2016–2020

Top 10 in the world for patents

among universities granted U.S. patents

U.S. National Academy of Inventors and the Intellectual Property Owners Association
• over 100 new spin-out companies launched from ASU research since 2010
• dedicated facility (SkySong) as incubator for translational R&D
• 40 start-up companies currently reside in the facility
Top producer of Fulbright students
—Chronicle of Higher Education, 2019
Graduate, Education

#2 online undergraduate degree program in the nation
—U.S. News & World Report, 2019
Education, U.S. News & World Report

A best-in-U.S.: health and well-being programs for students
—Active Minds, 2018

Top 5 campus for sustainability
—Sierra Club, 2018
The Improbable Burger

"Is it meat? We doubt it."