Challenges in Healthcare Innovation in An Era of Technology Acceleration, Convergence and New Value-Based Services

Dr. George Poste, DVM, PhD
Chief Scientist, Complex Adaptive Systems Initiative and Regents Professor of Health Innovation
Arizona State University
george.poste@asu.edu
www.casi.asu.edu

EMED 227/127: HEALTH CARE LEADERSHIP
Stanford University School of Medicine
Li Ka Shing room 102
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THE DIGITAL HOSPITAL: 82 COMPANIES REINVENTING THE PRACTICE OF MEDICINE
THE US DIGITAL HEALTH ECOSYSTEM 2019

INCUMBENT PAYERS
- Anthem
- CENTENE Corporation
- Cigna
- aetna
- Humana
- KAISER PERMANENTE

STARTUP PAYERS
- bright health
- Oscar
- zipari
- Devoted Health
- Stride
- bind

INCUMBENT PROVIDERS
- Intermountain Healthcare
- Cleveland Clinic
- Geisinger
- NewYork-Presbyterian
- MGH

STARTUP PROVIDERS
- 98point6
- one medical group
- honor
- iora
- primary care
- OAK STREET HEALTH
- PALADINA HEALTH

RETAIL CLINICS
- Walmart
- RITE AID
- Walgreens
- cvs health
- Kroger

GOVERNMENT PAYERS
- VA
- U.S. Department of Veterans Affairs
- CMS

CONSUMER DEVICES
- amazon
- Cardinal Health
- Medline
- AliveCor
- fitbit
- apple
- amazon alexa

TELEMEDICINE
- CareClix
- on demand
- MDLIVE
- SnapMD
- Teladoc HealthTap
- American Well
- Zipnosis

MEDICAL DEVICES
- Dexcom
- ResMed
- INTUITIVE SURGICAL
- GE Healthcare
- Livongo
- PHILIPS

BUSINESS INSIDER
INTELLIGENCE

The Strategic Environment for Biomedical Research and Healthcare Delivery

- Technology Convergence
- Disruptive Technologies
- Large Scale Data Analytics
- Science & Technology Acceleration
Industry Career Experience
• largest US public university
• fastest growth in research revenues of any US university
A New American University: A Purposeful, Radical Strategic Redesign

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

Ambitious Focus on Cross-Disciplinary/Cross-Sector R&D and Use-Inspired Applications for Major Unmet Needs
### National Science Foundation (NSF) Higher Education Research and Development (HERD) Rankings

**Total Research Expenditures:** 44 of 876 ahead of
- The University of Chicago
- Brown University
- 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
The Strategic Landscape for Healthcare

- Convergence
- Complexity
- Computing
- Cost
- Consumerism
Convergence: Precision Health, Digital Health and Big Data

[Diagram showing the convergence of Precision Health, Digital Health, and Big Data, with various technologies and terms interconnected.]

http://www.onlinejacc.org/content/accj/70/21/2696.full.pdf
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 development of informatics tools to annotate, archive, and analyze the vast volume and diversity of datasets that will be generated will be a key factor in research progress.

Future progress will depend pri-
The Path to Precision Medicine: From Superstitions to Symptoms to (Molecular) Signatures

humors; astrology, shamanism, sin and divine fare

biochemistry and organ-based pathophysiology

molecular biology and multi-omics profiling
Precision Medicine:

- (Epi)Genomics
- MultiOmics Profiling of Molecular Signaling Networks and Disruption in Disease
- Patient-Specific Signatures of Disease or Predisposition to Disease
- Big (Messy) Data

- terabytes per individual
- zettabyte – yottabyte population databases
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

Deep Phenotyping:

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

$3.2$ trillion
• anticipated expansion of molecular data profiles on millions of individuals

• value will reside in defining robust correlations with clinical outcomes and integration into clinical workflows

• transitioning from the current black box of multiOmics signatures of unknown significance to increasingly accurate causal associations and clinically actionable information

• risk mitigation
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 ‘Analyte Space’ for Profiling Health Status and Risk Monitoring

- multiOmics
- clinical phenotypes
- social determinants of health
- exposome
The “Geno-Enviro-Pheno’ Triad

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

Behavior

Environment
The Growing Burden of Chronic Disease

- economic unsustainability of current care
- 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 unsustainable of current care
- 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
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
“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
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
Leadership and Vision:
Joint University Task Force in Biomedical Innovation
Joint University Biomedical Innovation Task Force: Chair: Dr. G. Poste

- digital platforms to reduce hospital readmission(s)
  - CHF, behavioral health
- design of multiplex sensors and diagnostics for remote health status monitoring
  - RWE-observational protocols to meet new payer and biopharma/device company needs
- robotics and human-machine interactions
- clinical data analytics for proactive risk identification and mitigation in high risk, high complexity participants/settings
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
### Wearables and Health Status Monitoring


<table>
<thead>
<tr>
<th>Sensor Type</th>
<th>Example Data Collection</th>
</tr>
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<tbody>
<tr>
<td>Headbands</td>
<td>Electroencephalogram (EEG)</td>
</tr>
<tr>
<td>Sociometric badges</td>
<td>Digital camera</td>
</tr>
<tr>
<td>Camera clips</td>
<td>Electrocardiogram (ECG)</td>
</tr>
<tr>
<td>Smartwatches</td>
<td>Electromyograph (EMG)</td>
</tr>
<tr>
<td>Sensors embedded in clothing</td>
<td>Electrodermograph (Location GPS)</td>
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<tr>
<td></td>
<td>Microphone</td>
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<tr>
<td></td>
<td>Oximeter</td>
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<tr>
<td></td>
<td>Bluetooth proximity</td>
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<td>Pressure</td>
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<td></td>
<td>Thermometer</td>
</tr>
</tbody>
</table>

- Accelerometer
- Altimeter
- Digital camera
- Electrocardiogram
- Electromyograph
- Electroencephalogram
- Electrodermograph
- Location GPS
- Microphone
- Oximeter
- Bluetooth proximity
- Pressure
- Thermometer
Wellness Apps for Fitness, Diet and Exercise
Building Value in Wellness Apps and Wearables

- clinical value still viewed as marginal by many physicians/payers
- lack of robust RCT data on improved outcomes
- need for third party evaluation and/or regulation
  - accuracy, security and privacy
- vulnerability of many current Apps, devices and text messaging to hacking
- lack of policy transparency for sharing of consumer-patient data with third parties by Apps developers and data aggregators
Current Limitations of Consumer-Based Wearables for Health Status Monitoring

- restricted analyte menu
- limited data integration into EHR and alerts for anomaly events requiring prompt intervention
- inadequate incentives: users, payers and physicians
- rapid abandonment and lack of user ‘stickiness’
Remote Health Monitoring and Reduction in Hospital Readmissions
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%)
Remote Monitoring of Health Status
Trends in Sensors and Devices

- real time data
- miniaturization
- automation
- multiplex analytes
- wireless
- power source
- patient comfort
- interactive
- security
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
The Growth of Telehealth and Telemedicine: Expanding the Care Space

- estimated use by 60% healthcare institutions and 50% hospitals*
- virtual consults in Kaiser Permanente exceeded in-person visits in 2016
- healthcare consumerism and Ux
- 21st Century Cures Act and efficacy evaluation projects for Medicare services
- investment by larger enterprises in centralized telehealth command centers
  - service provision across broad geographies including international
- MD/HCP certification and cross-state licensure

*R.V. Tuckson et al. (2017) NEJM 377, 1585
“The Medical Virtualist” and “Website Manners”: The Next Clinical Specialty?

- M. Nochounite et al. JAMA (2017)e17094

- the rise of virtual consultants
  - tertiary to primary care

- investment by larger enterprises in centralized telehealth command centers
  - service provision across broad geographies including international

- lack of direct training of MD/HCPs in using virtual systems for patient consultations (website manner)
  - multi-specialty, multi-skill teams

- MD/HCP certification and cross-state licensure
Smart Devices for Automated Drug Delivery and Improved Therapeutic Adherence

- Propeller Health
- Gecko (now Teva)
- CapMedic
- Biocorp Inspair
- Aterica Veta
- EpiPen
Chatbots and Support Robots in Healthcare
Vehicles will soon be our most connected device and a hub for our personal data.

Consumers spend an enormous amount of time in the car and will soon be able to use that time more wisely—feeding vital information into a system that can provide encouragement and assistance for living a healthier life.

"Imagine a vehicle that knows whether you’re stressed and nudges you to take a breath before the next scheduled appointment. Because it can read your pulse and see your upcoming schedule. A vehicle that can adjust ambient lighting, sounds, and even scents to soothe the driver and passengers. A vehicle that becomes a key component of an active yet balanced lifestyle, working in unison with smart devices in the home and with wearables to generate a more holistic picture of one’s vital data." — Mercedes Benz
Mobile Apps, Wearables, Sensors and Continuous Health Status Monitoring

- who sets the standards?
- who integrates and interprets the data?
- who pays?
- who consents?
- who owns the data?
Regulatory Issues in Digital Health

- Apps used as accessory to regulated medical device
- Apps which transform mobile platform into a regulated device
- Application of existing FDA risk-based complexity thresholds (510K vs PMA)
- New requirements for software review and constant Vn updates
- Security and privacy
- SEC/State AG enforcement of false claims
Defining Value

- direct acute care savings
  - reduced ER visits, rehospitalization
  - services with easily captured financial metrics
- more complex clinical and econometric evaluation for chronic conditions
  - weight control, HbA1c moderation
  - improved Rx adherence
  - symptom scale improvements in mental health
  - QOL
  - earlier return to workforce/school and duration of benefit
  - ‘spillover’ benefits on co-morbidities
Digital Platforms and Clinical Trials

- faster recruitment by improved screening of potential subjects
- remote health status monitoring, real time data uploads and additional PRO data
- reduced cost and cycle times by fewer site visits
- improved patient compliance with study protocol
- enhanced patient retention by use of virtual visits to reduce time and cost of travel to trial centers
Digital Platforms in Behavioral Health
“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
About Prescription Digital Therapeutics

Prescription Digital Therapeutics, or PDTs, are a new therapeutic class.

Similar to traditional biologics or drugs, PDTs:

- Directly treat serious diseases
- Are built under current Good Manufacturing Practices
- Demonstrate safety and efficacy in randomized clinical trials
- Receive labeled claims from the FDA
- Are used by physician prescription
- Are reimbursed as products, via Pharmacy and Medical benefits
- Have barriers to entry that span regulatory exclusivity and intellectual property

https://peartherapeutics.com/
Behavioral Health Resources: Disturbing Trends

- more than 60% of practicing psychiatrists are 55 or older
  - one of the highest proportions among all clinical specialties
- number of public inpatient psychiatric beds has decreased by 17% since 2010
- 42 states have less than half of the minimum recommended public hospital psychiatric beds
  - 50 beds/100,000 people
- HHS analysis (Nov. 2016)
  - projected need for up to 10,000 providers to the seven behavioral health professions by 2025 to meet demand
Digital Psychometrics and Mental Illness

- high variation in assessment of same patients by different psychiatrists
- objective measurements of nuanced behavior and visit deltas
  - (micro) saccades, facial dynamics,
  - motor functions, gait
  - speech prosody (rhythm, tone, volume)
  - stimulus response reactions and interaction speed
Digital Psychometrics and Mental Illness

- interaction with digital assistants/chatbots
- machine learning and AI analytics of large video banks
  - bipolar disorder, schizophrenia, depression
  - suicidal ideation
  - PTSD
- signal alerts to care teams when immediate intervention indicated
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

Robot–Human Directed Interactions
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
“Do you solemnly swear to have no involvement in your own care?”
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
Major Investments in Digital Health by Major Corporations From Within and Outside of Traditional Healthcare Services
Amazon and Healthcare
Strategic Acquisitions and Alliances and Entry into Diverse Healthcare Services

- leverage distribution logistics and supply chain scale
- AWS, cloud storage and large scale data analytics
- 310M active customers, 100M Amazon Prime members
- Alexa-AI
  - in-home health concierge and support services?
  - real time HCP resource?
- disintermediation of PBMs and pharmacy wholesalers (PillPack)?
- claims administration and processing (AWS) and new insurance offerings (AMZ-JPM-BH)?
- Whole Foods and creation of new primary care sites?
Making Alexa HIPPA Compliant

HIPAA Compliance Lead
Job ID: 602824 | Amazon.com Services, Inc.

DESCRIPTION

The HIPAA Compliance Lead is an experienced HIPAA professional who will own and operate the security and compliance elements of a new initiative. You will work alongside product managers, software developers, bizdev, and legal teams to ensure that our services are in compliance with HIPAA security and privacy requirements. Core responsibilities include:

- Creating a HIPAA security and compliance program to ensure that technology and business processes meet our HIPAA Business Associate Agreement (BAA) requirements, as well as all applicable federal and state laws, regulations and standards.
- Managing all aspects of the program, including employee education and training, monitoring and auditing, conducting and documenting investigations, addressing violations, and monitoring corrective actions.
- Tracking & reporting against the program's operational readiness goals, to ensure all milestones are met, and that blocking issues are escalated and resolved effectively.
- Delivering data analysis, metrics and executive dashboards for the program.
- Owning and managing stakeholder communications, providing status as needed and be the point of contact for questions and concerns.
- Maintaining the program’s audit- and inspection-readiness posture.
- Monitoring relevant federal and state regulations, and modifying the compliance program to accommodate any changes.
- Acting as a consultative resource for health care regulatory matters.

Amazon Echo and Home Care

Development of Third-Party Alexa Apps

- **Libertana**
  - 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 burn"

- **Ask My Buddy**
  - "Alexa, ask My Buddy to alert everyone."

Rockpointe and AudioEducate Launch First Ever Accredited CME Program on Amazon’s Alexa

By Thomas Sullivan — Last Updated Jul 9, 2018

Rockpointe & AudioEducate Launch First Ever Accredited CME Program on Amazon’s Alexa
The Next Competitor for Amazon?
# Big Tech in Healthcare

How the Big Four tech companies are transforming healthcare in the US

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Alphabet</th>
<th>Amazon</th>
<th>Apple</th>
<th>Microsoft</th>
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</thead>
<tbody>
<tr>
<td>- Google Cloud Platform</td>
<td>- AWS</td>
<td>- iPhone consumer base</td>
<td>- Azure</td>
<td></td>
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<tr>
<td>- AI</td>
<td>- Alexa</td>
<td>- Apple Watch</td>
<td>- Healthcare NExT</td>
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<tr>
<td>- Cloud infrastructure</td>
<td>- Supply delivery</td>
<td>- App Store frameworks</td>
<td>- Microsoft Genomics</td>
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<td>- Verily Life Sciences</td>
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<table>
<thead>
<tr>
<th>Weaknesses</th>
<th>Alphabet</th>
<th>Amazon</th>
<th>Apple</th>
<th>Microsoft</th>
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<tbody>
<tr>
<td>- Fragmentation</td>
<td>- Limited clinical evidence of platform effectiveness</td>
<td>- Audience limited to iOS</td>
<td>- Muted customer awareness</td>
<td></td>
</tr>
<tr>
<td>- Limited clinical evidence of platform effectiveness</td>
<td>- Health system relationships</td>
<td>- Limited clinical evidence of device effectiveness</td>
<td>- Small developer community</td>
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<tr>
<th>Opportunities</th>
<th>Alphabet</th>
<th>Amazon</th>
<th>Apple</th>
<th>Microsoft</th>
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</thead>
<tbody>
<tr>
<td>- Population health</td>
<td>- Medical supply services</td>
<td>- Personalized health insurance</td>
<td>- Population health</td>
<td></td>
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<tr>
<td>- Precision medicine</td>
<td>- Personalized health benefits</td>
<td>- Remote patient monitoring</td>
<td>- Precision medicine</td>
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<tr>
<td>- Clinical decision support</td>
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<th>Apple</th>
<th>Microsoft</th>
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<tbody>
<tr>
<td>- AWS' and Microsoft's IaaS</td>
<td>- Google's and Microsoft's IaaS</td>
<td>- Competing device manufacturers</td>
<td>- AWS' and Google's IaaS</td>
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<tr>
<td>- Data security</td>
<td>- Incumbent M&amp;A activity</td>
<td>- Non-iOS ecosystem growth</td>
<td>- Data security</td>
<td></td>
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<tr>
<td>- Consumer trust</td>
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Digital Therapeutics Formularies

Digital Platforms Formularies
Digital Platform Formularies

- Analogy with current Pharmacy and Therapeutics (“P&T”) Committees
- Well developed P&T ecosystem for therapeutics
  - FDA approval
  - SOC guidelines
  - Data available for comparative evaluation
  - Facile integration into workflow and EHR
  - Coding schemes for reimbursement
- Comparable and robust ecosystem not yet available for digital platforms
The Principal Forces Shaping Biomedical R&D and Healthcare Delivery

- **Engineering and device-based medicine**
  - sensors
  - smart implants
- **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**
Now Comes the Hard Part!

Driving Precision Medicine and Data-Driven Healthcare Into Routine Clinical Practice
The Problem with Real World Data is the Real World

Now Comes the REALLY Hard Part!
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
Precision Medicine and Computational Medicine: Evolving Inter-dependencies

molecular classification of disease and elucidation of disease mechanisms

large scale data aggregation, curation and analysis

RWE and learning healthcare systems

The Big Data Challenge

V7: volume, variety, velocity, veracity, visualization, virtualization, value

D3: distributed, dynamic, decision support

I3: infrastructure, investment, intelligent systems
Integration of Molecular Profiling, Clinical and Social Data for Computable Disease Phenotypes

- need for generalizable computational infrastructure for diverse deep phenotyping data classes
  - HL7 Fast Healthcare Interoperability Resources (FHIR)
- 21st Century Cures Act requirements for EHR interoperability
- increased payer focus on RWE and value-based contracts
  - new RWE observational trial designs and patient registries
From Bedside to Bench

- reverse engineering of disease mechanisms from multi-dimensional profiling of disease sub(cohorts)
- increased focus on capture of high quality RWE via observational trials and patient registries
- end-to-end integration of diverse data classes – clinical, socio-behavioral, familial pedigrees – multiOmmics
- dynamics longitudinal mapping of disease risk, progression and outcome patterns
- premium on more systematic and standardized clinical phenotyping
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 investigational trial population(s)
  - age, co-morbidities, polypharmacy
  - clinical setting (AMCs, community hospitals, primary care)
- analyze treatment outcomes in sub-populations
- quantify treatment outcomes for value-based contracting
Use of RWE in Regulatory Decisions Regarding Rx Efficacy

- FDA and payer receptivity to use of external (virtual) control arms generated from EHRs
- Rx approval from single arm trials and RWE-generated historical trials
  - Blincyto for ALL (blinatumomab: Amgen)
  - Bavencio for Merkel cell carcinoma (avelumab: Pfizer-Merck KGAA)
  - Tecentriq (atezolizumab) for 2L NSCLC (Roche-Genentech-Flatiron)*
  - Alecensa (alectinib) for NLSC (Roche-Flatiron)*
  - Opdivo (nivolumab) for esophageal cancer (BMS-Flatiron)*

*use for reimbursement pricing (US) and UK (NICE)
Genetic Overlap Between Stroke and Related Vascular Traits at 32 Genome Loci for Stroke Profiled in 520,000 Subjects

The UK Biobank resource with deep phenotyping and genomic data

Clare Bycroft\textsuperscript{1,13}, Colin Freeman\textsuperscript{1,13}, Desislava Petkova\textsuperscript{1,12,13}, Gavin Band\textsuperscript{1}, Lloyd T. Elliott\textsuperscript{2}, Kevin Sharp\textsuperscript{2}, Allan Motyer\textsuperscript{3}, Damjan Vukcevic\textsuperscript{3,4}, Olivier Delaneau\textsuperscript{3,6,7}, Jared O’Connell\textsuperscript{8}, Adrian Cortes\textsuperscript{1,9}, Samantha Welsh\textsuperscript{10}, Alan Young\textsuperscript{11}, Mark Effingham\textsuperscript{10}, Gil McVean\textsuperscript{1,11}, Stephen Leslie\textsuperscript{3,4}, Naomi Allen\textsuperscript{11}, Peter Donnelly\textsuperscript{1,2,14} & Jonathan Marchini\textsuperscript{1,2,14}\textsuperscript{*}

FEATURES

BIOLOGY IN THE BANK

How an open-access trove of data on Britons is unlocking the genetics of disease, behavior, and physical traits

By Jocelyn Kaiser and Ann Gibbons

ENGINE OF PRODUCTIVITY

Published papers based on the UK Biobank’s bounty of health and genetics data are piling up fast, in part because the data are freely available.

- 2013
- 2014
- 2015
- 2016
- 2017
- 2018

Science 04 Jan 2019:
Vol. 363, Issue 6422, pp. 18-20
DOI: 10.1126/science.363.6422.18
Big Data and Social Determinants of Health (SDOH)

- lifestyle information on 280 million Americans
- "psychographic" analytics used in other sectors to ID/influence specific individuals
- claims to integrate 442 separate attributes to calculate an individual’s health risk score*
- ‘stealth’ entrant and complex consent and privacy issues

*M.L. Millenson (2018) NEJM Catalyst 5 June 2018
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’
Data Brokers and ‘Selling-On”

Nature (2017) 550, 174
National Security Implications of Genome Data on Populations

- Population Databanks
- Individual Profiles
- Foreign Access to Data
- Data Security
Big Biology and Biomedicine Meets Big Data

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

Integration of Large Scale, Multi-Disciplinary Datasets
Artificial Intelligence, Pattern Analysis and Medical Practice

“I don’t think any physician today should be practicing without artificial intelligence assisting in their practice. It’s just impossible otherwise to pick up on patterns, to pick up on trends to really monitor care.”

Bernard J. Tyson  
CEO, Kaiser Permanente  
Cited in Forbes: The Future of Work  
1 March 2017
“By far the greatest danger of artificial Intelligence is that people conclude too early that they understand it.”

Eliezer Yudkowsky
Machine Intelligence Research Institute, Berkeley
O’Reilly Artificial Intelligence Conference
May 2017
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
The Future of ‘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
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 Individuals

- 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 Emergence of Big Data Changes the Questions That Can Be Asked

- Isolated Data
- Complex Networked Data
- Complex Computational Data
A Pending Transition in Biomedical Research and Clinical Care Decisions?

- descriptive qualitative data
- hypothesis-driven inquiry

hypothesis-driven dominant

→

quantitative data
- large scale data mining
- automated analytics
- clinical decision support systems

data mining dominant
“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
Just What the Data Ordered

Machine Intelligence and Algorithms for Clinical Diagnosis and Treatment Decisions

Black Box Medicine?
Internal IBM Documents Reveal IBM Watson Recommended “Unsafe and Incorrect’ Cancer Treatment

- training used synthetic case histories versus RWE
- statistically underpowered training cohorts
  - 635 lung, 106 ovarian
- input from too few physicians (typically 1-2) on recommendations for each cancer type
- “raises serious questions about the process for building content and the underlying technology.”

Living in a World Where the Data Analytics and Interpretation Algorithms Are Obscure to the End User

- ceding decision authority to computerized support systems
- culturally alien to professionals in their claimed expertise domain but they accept in all other aspects of their lives
- who will have the responsibility for validation and oversight of critical assumptions used in decision tree analytics for big data?
  - regulatory agencies and professional societies?
  - humans?
  - machines?
Machine Learning (ML), Artificial Intelligence (AI) and Healthcare

- how will ML-AI algorithms/decision analytics be validated/regulated?
- how will ML-AI tools be integrated into current work flow?
- will radical reorganization/re-training be required?
- how will ML-AI platforms alter payment schemes?
Machine Learning (ML), Artificial Intelligence (AI) and Healthcare

- which clinical specialities/processes 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
“Explainable AI”
Keeping Humans in the Decision Loop

- need to better characterize the evolution of decision algorithms
- deconvolution of how and why machine learning algorithms reach flawed conclusions
- broad national security issues related to data integrity
- concern over AI-directed manipulation of social networks, advertising and personal data
- corruption of critical military and civilian systems and decision tools
The Future of Work and The Future Workforce
Major Transitions in Medical Education and Healthcare

1910 - present
(science-centric)

2000 - present
healthcare as a learning system (data-centric)

2015 - ?
mastery of escalating complexity and massive data (network-centric)
Major Opportunities (and Needs) in Education and Training in Complexity Science, Computing and Decision Science

- online interactive learning
- web-based collaboration tools
- multi-institutional education and training
- externships, public: private partnerships for future workforce preparation
Six “…ates” for Survival in a Data-Intensive Ecosystem

- navigate
- integrate
- authenticate
- collaborate
- innovate
- differentiate
The Future of Healthcare: Precision Medicine and Digital Medicine

- MultiOmic profiling
- Sensors, robotics
- Automation and computing
- Deep phenotyping and risk profiling
- Wearables, sensors, telemedicine
- Consumer patient engagement
- Social media and life style metrics
- Remote monitoring of health status
- New technology platforms
- The expanded care space
The Future of Healthcare: Precision Medicine and Digital Medicine

- New technology platforms
- The expanded care space
- Big Data
  - EHR
  - Population Health
  - Precision Medicine
  - Digital Medicine
  - ML-AI
- Multi-omics profiling
- Automation and computing
- Sensors, robotics
  - Wearables, sensors, telemedicine
  - Social media and lifestyle metrics
  - Consumer patient engagement
- Deep phenotyping and risk profiling
- Analytics for improved decisions and clinical outcomes at lower cost (value)
- Remote monitoring of health status
The Evolution of Data-Intensive Precision Medicine

- Technology Convergence and Acceleration
- Mapping Geno-Phenotype Complexity
- Topology of Biological Information Networks
- Big Data
- Data Security and Privacy
- Robotics and Human Machine Interactions
- Artificial Intelligence and Decision Support
- Ethics, Risk and Regulation
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
Ethics, Risk and Regulation

Slides Available @ [http://casi.asu.edu/presentations](http://casi.asu.edu/presentations)