Leadership Challenges in Biomedical Innovation in an Era of Disruptive Change, Escalating Complexity and Pervasive Uncertainty

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The Health Ecosystem

- Public Health
- Population Health
- Global Risk Factors
- Individual Care
The US Healthcare Ecosystem

- The $4.1 trillion US health system (c. 20% GDP) is unmatched in the scale and diversity of organizations and functions.
- Over 450,000 entities involved in the development and delivery of highly specialized services to heterogeneous populations over their lifetimes.
- Health ranks highest in public and political expectations regarding access, availability, affordability and quality of care.
The US Health Ecosystem

- demographics of an aging society and increased chronic disease burden
  - 50% cost incurred in last six months of life
- disturbing increase in mental illness, SUD, suicide even before the COVID pandemic
- economically and clinically unsustainable
- imbalance between care-centric (sick care) versus health-centric (wellness) expenditures
- fee-for-service incentives for providers reward volume of care versus outcomes
- imbalance in investments in population focused health initiatives versus individual care
The US Health Ecosystem

- protracted and varied diffusion of new technologies into clinical practice
- wide variation in clinical practice
- poor coordination and continuity of care across the health/health care system
- large disparities in access to care
- inefficient integration and analysis of data to drive evidence-based/best practice protocols
The US Health Ecosystem

- urgent societal imperative to increase access to care, reduce cost and improve clinical outcomes
- need for greater recognition of social determinants of health (SDoH) in disease risk and access/cost of care
- fragility in preparedness/resiliency for unanticipated large-scale disruption (pandemic, cyber, grid collapse, supply chains)
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, data analytics, social media
- public and political expectations
  - access, availability, affordability and outcomes
  - reduce disparities and inequities
The Health Ecosystem

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Leaders as ‘Design Architects’

‘Design Thinking’ in an Era of Disruptive Change, Escalating Complexity and Uncertainty
Navigating Change

Complex Interactions Between Multiple Stakeholders with Different Incentives

Technical, Socio-Cultural, Economic and Political Change Drivers

Incremental Innovation Versus Disruptive (Radical) Innovation

threats

opportunities
Innovation

Disruptive Innovation

- new technical or commercial concepts that disrupts the status quo
- creation of entirely new markets for novel products/services
- competition on NEW VALUE PROPOSITIONS (intellectual/commercial/military)
- often unrecognized or dismissed by currently successful organizations (complacency)

Incremental Innovation

- small conceptual refinements and/or design of additional features into existing products and services
- competition on VOLUME between minimally differentiated products/services (market share)
Drivers of the Healthcare Innovation Ecosystem

- rapid adoption of disruptive technologies
- slow translational proficiency: scale and dependence on systems-based integration

- high research innovation
- low translational proficiency

- academia
- government
- healthcare
- computing and data science
- devices
- biopharma
- pharma
Drivers of the Healthcare Innovation Ecosystem

- **High investment levels per project (>$200M)**
  - Academia
  - Evidence-based healthcare
  - Computing and data science

- **Low investment levels per project (<$10M)**
  - Biopharma
  - Devices
  - Improved care delivery

- **Short R&D Cycles**
  - Government

- **Long R&D Cycles**
  - Pharma

- **R&D Cycles**

- **Investment levels per project**
  - High
  - Low
Precision Health and Digital Health: Inter-dependent Strategic Drivers in the Evolution of Healthcare Policies and Priorities
The Strategic Landscape for Biomedical Research and Health Services

- Technology convergence and cross-disciplinary/cross-sector networks
- More proficient use of data
- Escalating burden of chronic disease

- Biomedicine
- Engineering
- Computing
- New alliance networks

- Improve management of health risks
  - Outcomes
  - QOL
  - Lower cost

- Aging populations
- CV, diabetes, cancer, neurodegeneration
- SDoH disparities
- Mental illness
- SUD
- Suicide
The Strategic Landscape for Biomedical Research and Health Services

- technology convergence and cross-disciplinary/cross-sector networks
- more proficient use of data
- escalating burden of chronic disease

- remote health monitoring to identify/mitigate risk
- reduce (re)hospitalization
- the expanded care space and continuity of care
- SDoH and health disparities
- improve outcomes and QOL
The Strategic Landscape for Biomedical Research and Health Services

**Technology Convergence**

- Biomedicine
- Engineering
- Computing
- New Alliance Networks

**Precision Health**

- Defining disease at the molecular level
- Disease subtyping and optimum treatment selection
- Identify predisposition risks

**Digital Health**

- Telemedicine
- Remote health monitoring
- ML/AI for large data analytics
- Clinical decision support tools
- Empowered patients

**Escalating Chronic Disease Burden**

- Aging populations
- CV, diabetes, cancer, neurodegeneration
- SDoH disparities
- Mental illness SUD suicide
The Evolving Systemic Landscape in Health

- new scientific and clinical concepts
- technology
- data and decisions
- organization of health services
- new participants
- new competencies
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
Molecular Classification of NSCLC and Identification of Single, Largely Non-Overlapping Oncogenic Alterations

Precision Health

- **(Epi)Genomics and MultiOmics Profiling**
- **Detection of Altered Molecular Signaling Networks in Disease: A New Taxonomy of Disease and Subtype Classification**
- **MDx Signatures of Disease Predisposition and Subtyping of Overt Disease for Optimum Rx Selection**

- terabytes per individual
- zettabyte – yottabyte population databases

The Challenge of Big (Messy) Data
Deep Phenotyping: “Much More Than Omics”

From Womb to Tomb: Systematic Integration of Diverse Health Data

SDoH, Lifestyle, Environment, Health Disparities
- 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.
Expanding the “Care Space” in Healthcare

Healthcare Beyond The Clinic

Remote Health Status Monitoring

Smartphones, Wearables, Devices and Digital Services

M4: Making Medicine More Mobile

AORTA: Always On, Real Time Access
Wearables and Mobile Devices: Key Drivers in Remote Health Monitoring and Care Delivery
Wellness Apps for Fitness, Diet and Exercise
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
- Device Registration
- Actuation Simulation
- Spender Simulator
- Replaceable Device Adhesion
- Injection Speed 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
Rapid Growth in Wearables, Sensors and Devices for In-Home Remote Health Status Monitoring
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
Telemedicine and Behavioral Health: Digital Psychiatry and Non-Pharmacologic Digital Therapeutics
Increased ED Behavioral Health Emergencies

- reported range of 8-25% of ED volume
- 70% of behavioral health patients also have one or more co-morbidities
- opioid-related visits tripled between 2005-19
- approx. 1 in 4 individuals with serious mental illness also have substance abuse disorder
- 60% of adolescents in community-based SUD treatment programs also meet diagnostic criteria for mental illness
- dramatic increase in mental health needs in COVID-19 pandemic
Computer Vision, Facial Recognition and New Digital Psychometrics in the Evaluation of Mental Illness

- eye movements
- facial dynamics
- stimulus response reaction and interaction speeds
- speech patterns (rhythm, tone, volume)
- semantic construction
- 256 lead EEG
- brain imaging functional MRI
- altered signal pathways

ML/AI analysis of individual multiparameter responses matched to large-scale analysis of video data banks of patients with clinically validated mental disorders
“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
Robot–Human Directed Interactions
- injury rehabilitation
- reduce apprehension/distraction in painful procedures
- anxiety, depression, PTSD, phobias
The Internet, Social Media and the Road to the Metaverse

- who knows why people do what they do?
  - the fact is that they do!
- the confessional of social media
- these actions can now be traced and measured with unprecedented precision
- with sufficient data the numbers reveal increasingly predictable behavior and individual risk patterns
- blurring of private and public spaces
- blurring of the real and the imaginary
- complex ethical and legal issues
  - consent, privacy, security, surveillance
### Metaverse Market Map

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Welcome to Metaverse World:

extended reality (XR): building the virtual sensorium

new virtual experiences:
Tamagotchi babies
The Neurobiology of Instant, Superficial, Repeated Gratification

Interactive multiplayer gaming and modulation of reward neurocircuitry

Virtual immersion and education in the most plastic phase in the development of human analytical skills and socialization
Health Effects of Ubiquitous Immersion and Dependencies in Digital Environments

- unknown long term socio-cultural implications of new sensory, cognitive and behavior patterns positively reinforced in digital ecosystems
  - individuals, institutions, society
  - the new evolutionary selection pressure? (digital Darwinian fitness)
The Co-Evolution of Precision Health, Digital Health: Building Learning Healthcare Information Systems

- Convergent Technologies
- Big Data
- The Expanded Care Space

- Computing and Automation
- MDx, Sensors, Robotics
- Biomedical Research and Clinical Medicine

- Population Databases
- Individual EHRs
- Data Science
- ML/AI

- Remote Patient Monitoring
- Consumer/Patient Engagement
- SDOH and Life Style Metrics

- Mapping the Complexity of Genophenotypic Relationships and Individual Risk(s)
- Risk Analysis, Analytics for Improved Decisions and Clinical Outcomes (Value)
- Longitudinal Monitoring of Individual Health Status
Now Comes the Hard Part!

- Driving Precision Health and Large Scale Data Analytics into Routine Clinical Practice

- New Incentives and New Delivery Models

- New Participants and New Business Models
More Than Just Technology

Clinical-Centric Needs
- integration of new work processes
- no risk to income (HCPs), profitability (private sector)
- continuing training curricula and CME

Patient (Caregiver)-Centric Needs
- increased convenience, acceptance and adherence to treatment
- telemedicine and interactive systems
- empowerment

Payor Needs
- the bottom line and margins
- reduce direct care costs
- optimize use of finite and expensive resources (Facilities, Equipment, Personnel, Training)
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
Managing Big Data in Biomedicine Will Not Be a Simple Extrapolation from Current Practices

Co-Evolution of Professional Competencies With Advanced Computing and Automated Clinical Decision Systems
Welcome to The World of Biomedical Research and Healthcare Information Systems
Biomedical Data: Vast, Growing Rapidly but Poorly Used

- inadequate standardization
- fragmented, incomplete, inaccurate data and uncertain provenance
- incompatible data formats as barrier to data integration and sharing
- static, episodic snapshots of individual health status versus integrated longitudinal health history
- obstacles to EHR integration of new data classes multi-Omics; wearables; IoMT; RHM
- legislative barriers to data transfer based on well intentioned privacy protections (HIPAA)
- organizational, economic and cultural barriers to open data sharing
- major impediments to research productivity, optimum clinical decisions and continuity-of-care for patients
Data Security and Protection of Health Information
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
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
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
The Emergence of 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”

- Feature Extraction and Classification
- Context Analysis
- Persistent Context
- Relevance Mapping
- Learning Systems
- Situational Awareness
- Rapid, Robust Decisions
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
Machine Learning (ML) and Artificial Intelligence (AI):
Massive Infusion of Private-Sector Funding and Entrepreneurial Activities

https://mattturck.com/data2021/
Machine Intelligence and Algorithms for Clinical Diagnosis and Treatment Decisions

Black Box Medicine?
The ML Adoption of AI Platforms in Clinical Medicine

- from current applications in image analysis to comprehensive assembly and interpretation of multifactorial "deep phenotyping" data to build 'signatures' of individual health status and risk
Precision Health and Digital Health: Evolving Inter-Dependencies

Individual Data

- Population Data

Deep Phenotyping:
- multiOmics
- clinical history- EHR/PHR
- socio-behavioral data
- remote health monitoring
- environmental exposures

Integration and analysis of large-scale diverse data
Exabyte and zettabyte data tsunami
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
How Will Healthcare ML-AI Algorithms/Decision Analytics Be Validated and Regulated?

- Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)
- REPORT ON RISKS AND BENEFITS TO HEALTH OF NON-DEVICE SOFTWARE FUNCTIONS
- Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan

(Images of regulatory reports and frameworks from the FDA)
Validation of ‘Black Box’ ML/AI Algorithms

- regulatory frameworks for ML/AI platforms used for clinical decisions for patient care
  - ‘software as medical device’
- “interpretable AI”
  - uncoupling of learned intermediary from comprehension of how the output(s) for decision opinion(s) were derived
- getting ready for “primetime”?  
  - generative adversarial networks and transformer platforms
- general artificial intelligence (GAI)
  - ChatGPT, RYTR, and DALL-E
ChatGPT Generative AI Passed All Three Parts of the US Medical Licensing Examination (Dec. 2022) Without Prior Training on Medical Dataset

Performance of ChatGPT on USMLE: Potential for AI-Assisted Medical Education Using Large Language Models

Tiffany H. Kung, Morgan Cheatham, ChatGPT, Arielle Medenilla, Czarina Sillos, Lorie De Leon, Camille Elepaño, Maria Madriaga, Rimel Aggabo, Giezel Diaz-Candido, James Maningo, Victor Tseng

doi: https://doi.org/10.1101/2022.12.19.22283643
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

- how will ML-AI platforms alter payment schemes?

- what new malpractice liabilities will emerge by failure to use/interpret ML-AI platforms?
Unidimensional “Quick Fixes”

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

- Peter Drucker
DNR: Is the Current Healthcare System Terminal?
Living In The Infocosm
Burgeoning Information and An Expanding Metaverse

- boundaries between traditional expertise domains increasingly blurred
- entirely new domains emerge, dissolve and re-emerge in reconfigured form at ever faster rates
- escalating complexity of mapping, multi-dimensional strategic spaces
- ML/AI platforms embedded in all aspects of healthcare
“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
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)
New Patterns of Learning
Asleep at the Wheel: Ignoring Healthcare Challenges of Increasing Complexity and Urgency

- dysfunctional national governance, lack of bipartisanship and legislative paralysis
- ideological extremism
- the rise of anti-science, anti-expert populism
- legislative technical illiteracy and the retreat from complexity
- the corrosive role of social media in fueling social and political division
- the myopia of short-term, cosmetic quick fixes and kicking the problem down the road
Asleep at the Wheel: Ignoring Healthcare Challenges of Increasing Complexity and Urgency

- aging demographics and the chronic disease burden cost access, availability and affordability
- mental health
- SUD and lack of border security
- cybersecurity and data protection
- preparedness for highly disruptive biosecurity events (pandemics) or other major disasters
- novel threats from dual-use technologies and complex ethical and legal issues
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
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- Public Policy: Ethics, Risk and Regulation
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