Challenges Facing U.S. Healthcare

- Balancing Infinite Demand versus Finite Resources
- From Volume-Based (Do More-Bill More) Fee-for-Service to Value-Based Care
- From Reactive, Episodic Interventions in Advanced Disease to Proactive Identification of Disease Risk and Earlier Detection
- Improving Clinical Outcomes at Lower Cost and Optimizing Wellness
Biomedical Research and Healthcare Delivery: Ecosystems with Pervasive Embedded Inefficiencies Ripe for Creative Destruction

- slow translation of research for patient benefit
- unsustainable cost of care
- fragmented and uncoordinated duplication, waste and administrative bloat
- poor use of available information
- slow adoption of advanced IT systems relative to other sectors
- public dissatisfaction and intensified political engagement (Rx, IT)
- health data breaches, privacy violations: techlash
The Healthcare Ecosystem

- slow technology diffusion and wide variation in clinical care patterns
- disparities in access and availability of care
  - national (G20) and international (MIC, LIC)
The U.S. spends more on healthcare than any other OECD Country

The U.S. has the lowest life expectancy than any other OECD Country

Health is a One-Sided Marketplace

- patients receive and pay for a service without typically knowing the price beforehand
- no financial tools to spread cost overtime
  - e.g. mortgage, car loan
The US Healthcare System: Information Asymmetries

- patients (consumers) versus payers and providers
  - decisions about care selection and cost
- payers versus providers
  - cost control in care decisions
- patients and providers versus payers
  - coverage determinations, OOP-copays, pre-existing conditions
- patients and payers versus innovators and providers
  - transparency of cost and effectiveness (outcomes)
- innovators versus payers and providers
  - direct cost and indirect cost of integration into workflow
  - generalizability of RTC data to real world effectiveness (RWE)
The Demographics of an Aging Society: Clinical and Economic Challenges to U.S. Healthcare

- Wellness with longevity and high QOL
- OR
- Multiple co-morbidities and low QOL
The Growing Burden of Chronic Disease

- economic unsustainability of current care systems
- insufficient clinical resources and infrastructure
- cost of innovation (Rx prices as political target)
- future growth in public and political dissatisfaction with lack of progress in major solutions
The Growing Burden of Chronic Disease

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

• economic unsustainability of current care systems
• insufficient clinical resources and infrastructure
• cost of innovation (Rx prices as political target)
• future growth in public and political dissatisfaction with lack of progress in major solutions
Value

- clinical outcomes and QOL
  - QALY, DALY
  - socio-economic metrics: faster return to workplace/school
  - reduced demands on societal support services
- ‘downstream’ future cost/benefit calculus
  - reduced demand for future resource use versus
  - probability of increased resource use from suboptimal Rx efficacy/increased comorbidity risk
  - cost and management of longer-term Rx toxicity risks (cf. oncology)
Value

- disincentives for innovation uptake
- cost of adoption of new clinical protocols/HCP training
- institutional/HCP revenue loss from displacement of more expensive procedures/facilities utilization
Healthcare: A Complex, Multidimensional, Multi-stakeholder Ecosystem

Value and Sustainability

- innovation ecosystem
- care delivery ecosystem
- insurance ecosystem
- regulation and public policy
- access and affordability
- clinical decisions
- outcomes
- patient advocacy
- media/public perception
- political will
Infinite Demand and No Limits to Care

Welcome to the Age of One-Shot Miracle Cures That Can Cost Millions

MIT Technology Review

$2 million would save her life. Could you pay?

Should you?

Medicine is becoming hyper-personalized, hyper-accurate ... and hyper-unequal ...
Global Biopharmaceuticals: 
Highest R&D Investment as % Sales of Any Industry Sector

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Location</th>
<th>Rx Sales*</th>
<th>R&amp;D spend*</th>
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<tr>
<td>1</td>
<td>Pfizer</td>
<td>NEW YORK, NEW YORK [PFIZER.COM]</td>
<td>$45.302</td>
<td>$7.962</td>
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<tr>
<td>2</td>
<td>Roche</td>
<td>BASEL, SWITZERLAND [ROCHE.COM]</td>
<td>$44.552</td>
<td>$9.803</td>
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<td>3</td>
<td>Novartis</td>
<td>BASEL, SWITZERLAND [NOVARTIS.COM]</td>
<td>$43.481</td>
<td>$8.154</td>
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<td>4</td>
<td>Johnson &amp; Johnson</td>
<td>NEW BRUNSWICK, NEW JERSEY [JNJ.COM]</td>
<td>$38.815</td>
<td>$8.446</td>
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<td>5</td>
<td>Merck &amp; Co.</td>
<td>KENILWORTH, NEW JERSEY [MERCK.COM]</td>
<td>$37.353</td>
<td>$7.908</td>
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<td>6</td>
<td>Sanofi</td>
<td>PARIS, FRANCE [SANOFI.COM]</td>
<td>$35.121</td>
<td>$6.227</td>
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<td>7</td>
<td>AbbVie</td>
<td>NORTH CHICAGO, ILLINOIS [ABBVIE.COM]</td>
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<td>8</td>
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<td>$4.987</td>
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<td>9</td>
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<td>THOUSAND OAKS, CALIFORNIA [AMGEN.COM]</td>
<td>$22.533</td>
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<td>10</td>
<td>Gilead Sciences</td>
<td>FOSTER CITY, CALIFORNIA [GILEAD.COM]</td>
<td>$21.677</td>
<td>$3.897</td>
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</tbody>
</table>

What Does/Should Keep the Biopharmaceutical Industry C-Suite Up at Night?

- **market disruption**
  - disease subtypes and market segmentation

- **disruptive technologies**
  - pricing: public and political backlash

- **integrated care solution**
  - thinking beyond the pill

- **new business models**
  - value-based contracts

- **new vertical and horizontal relationship/collaboration**

- **new entrants (big tech)**

- **precision health**

- **digital health**
What Does/Should Keep the Biopharmaceutical Industry C-Suite Up at Night?

- Sustained high failure rates
- Continued cost escalation
- Small molecules vs. biologics
- Herd mentalities
- R&D productivity
What Does/Should Keep the Biopharmaceutical Industry C-Suite Up at Night?

BIG DATA

- Machine learning and AI
- New value propositions
- Privacy, security and ownership
- Real world evidence and data banks
Biopharmaceuticals

• one of the most efficient and cost-effective solutions to illness?

or

• overpriced and major contributor to rising healthcare costs (society) and the affordability crisis (society and individuals)?
“Unconscionable Rx Price Increases and Price Gouging”
Overly Simplistic Legislation and Emotions Run High
(State of the Union Address 4 Feb 2020)
The Politically Expedient Search for Unidimensional ‘Quick Fixes’ to Multi-dimensional Problems and the Law of Unintended Consequences

“For Every Complex Problem There Is an Answer That is Clear, Simple and Wrong.”

- H.L. Mencken
Pelosi Rx Pricing Bill Offers Big Savings, Big Drop In Drug Development – CBO

Pink Sheet (21 October 2019)
• cost shifting of financial risk to patients/consumers is the most publically visible endpoint in the opaque universe of ‘drug spend’

• adverse patient/consumer financial impact as the ‘lightning rod’ for public and political ire and negative image of both innovator and generic companies

• poor advocacy and communication of multi-dimensional complexity by biopharma-industry

• negative image reinforced by legacy and current marketing practices
• are financial returns on biopharmaceutical products excessive?

• is the biopharmaceutical industry receiving a ‘free ride’ by exploiting taxpayer-funded biomedical research?

• should medicines be viewed as an essential public social good and subject to provisions to ensure their availability and affordability?

• do individuals have a ‘right’ to unlimited healthcare services?
• how are Rx price(s) determined?

• what is a fair price to reward risk and sustain innovation?

• who profits and how much?

• how are value and access determined, by whom and for whom?

• how can affordability be balanced with incentives to sustain R&D investment in new Rx innovation?

• is the pace and cost of overall innovation outstripping our ability to afford certain categories of care?
Industry Critics

- sales and marketing 1.2 to 2.3X higher than R&D
- direct-to-consumer (DTC) advertising
  - drive up Rx use
  - high cost ‘glam-mercials’
  - notice everyone is healthy, active and affluent
- shift from print to TV to social media
  - identification of high prescriber MDs
  - identification of patients and new tools to ensure ‘brand stickiness’
  - first amendment rights upheld
Expensive DTC Campaigns
Hype Versus Hope: A Delicate Ethical Balance
Come and Be Cured by Us: (Go Elsewhere at Your Peril)!

WE CAN NOW SEE CANCER SO PRECISELY, WE CAN PREDICT ITS FUTURE.

MORE SCIENCE. LESS FEAR.

Memorial Sloan Kettering Cancer Center

WE SEE THROUGH CANCER'S DISGUISE.

And we're teaching patients' own immune systems to do likewise.

As the world leaders in cancer research, we have a unique opportunity to harness the power of the immune system to fight cancer.

DANA-FARBER CANCER INSTITUTE

Who will crack the cancer code?

It's the question that millions of people are asking. By piecing together every idea, continually refining our approach, and collaborating with innovators across the globe to explore cancer's true mechanisms, we can begin to identify cancer mechanisms and vulnerabilities, like PD-1 inhibitors and EGFR, that help stop us in the tracks to develop more targeted therapies. Together, we can find solutions to the toughest problems, because the more we learn, the more brave we become.

Attacking cancer is now personal.

Find your personalized treatment plan for your advanced cancer treatment. Get the latest on personalized treatments, more research, and the news you need to stay healthy. For more information or to schedule a visit: freemar.org or call 1-888-FREEMAR.

DID TRIPLE NEGATIVE BREAST CANCER TAKE THE LIFE OF ELIANA MARIN?

NO, NO, NO.

WE ARE COMING AT CANCER IN WAYS CANCER DOESN'T SEE COMING

We're not just fighting cancer. Now we're outsmarting it.

The Oregon Health & Science University

We can now see cancer so precisely, we can predict its future.

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the sale and pricing of biopharmaceuticals (and much else in healthcare) do not conform to free market principles

the pricing of drugs and all aspects of healthcare financing are shaped by myriad sectorial inefficiencies and perverse information asymmetries that render the true costs and profit distribution across the supply chain opaque

- Rx companies, wholesalers, PBMs, pharmacies, GPOs, payers, providers
- specialized services: dialysis
- geographies: MD office vs hospital; 340B legislation
Why Should Price Vary With Location?

- price for oncology drugs administered in hospital versus typically double price paid for community clinic
- Herceptin
  - hospital/hospital outpatient $5,350
  - independent clinic $2,740
- Avastin
  - clinic ($6,620), hospital ($14,100)
- incentive for trend for purchase of community clinics by hospital systems and reclassification as ‘hospital outpatient clinics’ and eligible for 340B discounts
Are Oncologists Financial Incentives Misaligned with Optimum Treatment?

- high cost of new oncology drugs (US) – $100K-250K/year
- estimated 80% annual income for community oncologists tied to Rx use
- no incentives to select less expensive Rx or palliative care
- physician/payer refuge in slow pace of change in SOC guidelines to incorporate obligate molecular diagnostic profiling for Rx selection
- unacceptable levels of use of new Rx regimen(s) in last two weeks of life
How Many Agents With the Same MOA Can the Market Support?

3,876 active IO agents in the current global drug development pipeline

https://www.nature.com/articles/d41573-019-00167-9
Policy Choices in Government Price Controls for Biopharmaceuticals

- median index pricing from G8 ‘basket’ prices
- expanded CMS negotiation of ‘best price’
- FDA to include value pricing metrics in comparable fashion to EU in regulatory approval
- inflation-based capitation
- reference pricing
- indication-based pricing
- march-in rights and compulsory licensing
- GoCo initiatives for public sector manufacturing (generics)
## Hypothetical Scenarios for Indication-Based Drug Pricing

<table>
<thead>
<tr>
<th>Drug and Indication</th>
<th>Median Survival Gain In Years</th>
<th>Current Monthly Price</th>
<th>Price Based On Indication With Most Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abraxane (Celgene)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic breast cancer</td>
<td>0.18</td>
<td>$6,255</td>
<td>$6,255</td>
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<tr>
<td>Non-small cell lung cancer</td>
<td>0.08</td>
<td>$7,217</td>
<td>$2,622</td>
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<tr>
<td>Pancreatic cancer</td>
<td>0.15</td>
<td>$6,766</td>
<td>$448</td>
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<td><strong>Tarceva (Roche/Astellas)</strong></td>
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<tr>
<td>First-line treatment metastatic non-small cell lung cancer</td>
<td>0.28</td>
<td>$6,292</td>
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<tr>
<td>Pancreatic cancer</td>
<td>0.03</td>
<td>$5,563</td>
<td>$1,556</td>
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<tr>
<td><strong>Erbitux (BMS/Lilly)</strong></td>
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<tr>
<td>Locally advanced squamous cell carcinoma of head/neck</td>
<td>1.64</td>
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<td>First-line treatment recurrent or metastatic squamous cell carcinoma of head/neck</td>
<td>0.23</td>
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<td><strong>Herceptin (Roche)</strong></td>
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<td>Adjuvant treatment breast cancer</td>
<td>1.99</td>
<td>$5,412</td>
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<td>Metastatic breast cancer</td>
<td>0.40</td>
<td>$5,412</td>
<td>$905</td>
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</table>

*Source: JAMA article by Peter Bach, Oct. 3, 2014*

Outcomes-Based Pricing: More Complicated Than It Might Seem

- pre-specified clinical outcomes
- robustness of efficacy endpoints
- design of observational/RCT protocols and registries
  - eligible patients
  - duration
- risk that administrative overhead and monitoring costs erode potential savings
- PhRMA proposal of safe-harbor from Federal anti-kickback penalties for manufacturer medication adherence programs
Reference Pricing

- uniform pricing of Rx deemed “clinically comparable”
- how should “clinically comparable” be defined?
- instructive precedents?
  - demise of antibiotic R&D
  - immuno-oncology drugs with apparent common MOA but different efficacy (Opdivo™ vs Keytruda™ in NSCLC)
Application of the Public Utility Model for Essential Public Goods Products to Pharmaceuticals

- water, electricity, gas, critical infrastructure
- regulated pricing plus periodic price increases
- commodity products/services with known performance characteristics and markets
- how would R&D risk (failure) be amortized in pricing of pharmaceuticals?
- what fraction of revenues would be reinvested to sustain next cycle of innovation
- competitiveness of US industry versus EU/PRC/FSU
How to Identify and Quantify the Contributions of Taxpayer-Funded Research to Commercial Products

- intellectual lineages of conceptual or technological advances are diffuse and diverse
- how to demarcate (and reward?) research done in overseas research laboratories
- biomedical R&D is increasingly dependent on innovations originating in industry
- reciprocal industry entitlement to recoup investments based on public funded research that cannot be reproduced or failed to fully characterize the proposed Rx target?
  - the reproducibility crisis in academic biomedical publications
Why Focus on Pharmaceutical R&D as a Beneficiary of Taxpayer-Funded Research and Exclude Other Industrial Sector Beneficiaries?

Telcoms  |  GPS  |  Computing  |  Internet  |  Social Media
---|---|---|---|---
![Satellite](image1.png)  |  ![GPS Satellite](image2.png)  |  ![Computer Network](image3.png)  |  ![Smartphone](image4.png)  |  ![Facebook Logo](image5.png)

Novel Materials  |  Geophysics  |  Robotics  |  3D printing  |  Biotechnology
---|---|---|---|---
![Airplane](image6.png)  |  ![Seismic Wave](image7.png)  |  ![Robot](image8.png)  |  ![3D Printer](image9.png)  |  ![DNA Structure](image10.png)
R&D Costs Continue To Increase In An Increasingly Cost-Sensitive Market

The Imperative to Improve the Efficiency of the R&D Process

Precision Medicine and Implications for Biopharmaceutical R&D and Pricing
R&D Composite Success Rate in 2018 by Therapeutic Area

Source: OQVIA Pipeline Intelligence, Mar 2019; IQVIA Institute
Failure of Investigational Drugs in Clinical Trials

- 50% fail on insufficient efficacy
- 30% fail on safety issues
  - 8% on known concerns
  - 22% on new unexpected AEs
- 20% fail on lack of differentiation
  - 16% on inadequate efficacy
  - 4% on safety profile
Addressing the Biopharmaceutical Industry’s Principal Pain Point

- amortization of cost of failed trials in pricing of successful agents
  - political liabilities
- lack of predictive tools to differentiate responder (R) and non-responder (NR) patients
  - growing payer pressure for value-based reimbursement for guaranteed therapeutic outcomes
  - waste/risk from futile therapy in NR cohorts
The Promise of Immunotherapy: Is Widespread Adoption Economically Feasible?

- unit Rx cost (> $100K)
- indirect care cost
- escalating cost of combination Rx regimens (> $200K)
- extravagant cost of cell-based therapies ($500K - $1.5 million)
- complex clinical management challenges and compatibility with community oncology services

40-80% patients fail to respond even with I/O – I/O combinations
Performance-Based Contracts and Pricing: The Inevitable Future Landscape for Cancer Therapy?

- robust identification of responders and non-responders
- companion diagnostics and labeling requirements
- performance-based outcomes and premium pricing
A Pricing and Reimbursement Dichotomy
Conflicts and Contrasts in Reimbursement Policies and Clinical Utilization of Molecular Diagnostics (MDx) and Therapeutics (Rx) in Oncology

- **MDx and Multi-Omics Profiling**
- **SOC Rx guidelines**
- **Disease Subtyping and ID of Rx-Responsive Cohorts**
- **High Cost Rx Without Subset Profiling**

Precision Diagnosis and Rational Treatment Selection

Propagation of Therapeutic Regimens With Variable Response Rates
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.

---

Bryan Bollier

Bloomberg Businessweek

December 14 - December 20, 2015

BAD BLOOD
Secrets and Lies in a Silicon Valley Startup
John Carreyrou
Drug Discovery

- the low hanging fruit have been picked
- major unmet medical needs:
  - late-onset chronic diseases
  - mental illness
- identification of new targets or Rx action
  - mapping underlying perturbations in molecular signaling networks (wiring diagrams)
  - GxE: interplay between genes (G) and environment (E) in disease predisposition risk and progression patterns
The Search for New Drug Targets: Mapping Disease–Associated Perturbations in Molecular Information Networks

- ‘It’s the Network, stupid!’

- most major diseases involve complex perturbations at multiple points in the network or hits on key control nodes
Understanding Perturbations in Molecular Signaling Networks and Rx Target Identification

'Single Hit' Diseases
- single target or master control target
- foreign target (m/organisms)
- replacement therapy (insulin)
- no/low interpatient variation

'Multi-Hit' Diseases
- varied ‘excursions’ from physiological topologies
- variable GxG interactions
- GxE (SDoH) interactions
  - high inter-patient variation
Genetic Overlap Between Stroke and Related Vascular Traits at 32 Genome Loci for Stroke Profiled in 520,000 Subjects


<table>
<thead>
<tr>
<th>Locus</th>
<th>Stroke subtype</th>
<th>Related vascular trait</th>
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<tbody>
<tr>
<td>CASZ1</td>
<td>LAS</td>
<td>White-matter hyperintensities on brain MRI</td>
</tr>
<tr>
<td>WNT2B</td>
<td>CES</td>
<td>Carotid plaque</td>
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<tr>
<td>TSPAN2</td>
<td>LAS</td>
<td>Coronary artery disease</td>
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<tr>
<td>PMF1–SEMA4A</td>
<td>CES</td>
<td>Atrial fibrillation</td>
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<td>RGS7</td>
<td>CES</td>
<td>Systolic BP</td>
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<tr>
<td>KCNK3</td>
<td>CES</td>
<td>Diastolic BP</td>
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<td>TM4SF4–TM4SF1</td>
<td>CES</td>
<td>LDL levels</td>
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<tr>
<td>PITX2</td>
<td>CES</td>
<td>HDL levels</td>
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<td>ANK2</td>
<td>CES</td>
<td>Venous Thromboembolism</td>
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<td>SH3PXD2A</td>
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<td>MMP12</td>
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<td>TBX3</td>
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<td>LRCH1</td>
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<tr>
<td>FURIN–FES</td>
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<tr>
<td>ILF3–SLC44A2</td>
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<tr>
<td>SMARCA4–LDLR</td>
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</table>

An Ugly but Fundamental Question:
Is Unifocal Rx Modulation of Complex Network Dysregulation in Advanced Chronic Diseases Feasible or a Delusion?

- “too disrupted for homeostatic reset?”
- multi-point/multi-module/multi-subnetwork dysregulation
- low feasibility of multi-Rx intervention against multiple targets
- even lower probability of design of promiscuous multi-target action in a single Rx molecule
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 Subtypes

Data from TCGA (Sanchez-Vega et al.\textsuperscript{178}, Ellrott et al.\textsuperscript{179} and Hoadley et al.\textsuperscript{180}), Imielinski et al.\textsuperscript{92} and Kadara et al.\textsuperscript{133} ($n = 741$)

Data from MSK-IMPACT (Jordan et al.\textsuperscript{15}) and FoundationOne (Frampton et al.\textsuperscript{15}) panels ($n = 5262$)
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
Still Two Largely Separate Worlds

- Precision medicine
- Routine healthcare delivery and SOC

Slow incremental adoption of technological advances

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

Research and early clinical adopters (largely oncology)

- $100-125* billion (estimated)
- $3.6 trillion (19% GDP)

*Includes investment in investigational Rx candidates
The Dangers of Techno-Optimism

Product 1998

- Drug
- Package insert

Medicine 2008

- Databases, applications
- Smart cards
- Diagnostics
- Counseling
- Genetic profiling
- Disease management protocols, patient information

Molecular medicine and information-based targeted healthcare.
Precision Medicine and Digital Medicine: Evolving Inter-Dependencies

Individual Data

- "digital siblings and imputed phenotypes"
  - matching individual profiles to ‘best fit’ data cohorts
  - integration and analysis of large scale, diverse data categories
  - to identify risk and selection of optimum treatment regimens

Population Databanks
Precision Medicine, Disease Subtyping and Market Segmentation into Ever Smaller Niche Domains

- from ‘all-comer’ RTC to stratified trials of Rx-target positive patients
- cost and time to find eligible patients
- narrow regulatory labeling
- increased ROI risks
- oncology: short-lived Rx eligibility with rapid emergence of Rx resistance

Data from MSK-IMPACT (Jordan et al. [20]) and FoundationOne (Frampton et al. [21]) panels (n = 5262)
The “Geno-Enviro-Pheno’ Triad

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

Behavior

Environment
Precision Medicine and Digital Medicine: Evolving Inter-Dependencies

Individual Data

Population Databanks

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

integration and analysis of large scale, diverse data categories

$3.2$ trillion
Social Determinants of Health (SDoH):
Invasion of the Body Trackers: 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
• 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
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
Smart Devices for Automated Drug Delivery and Improved Therapeutic Adherence

Propeller Health

Gecko (now Teva)

CapMedic

Biocorp Insair

Help patients get onboard with onbody injections

Aterica
Veta
EpiPen

Onbody Trainers
- Sonic Generator
- Actuation Simulation
- Spandy Simulator
- Replaceable Device Adhesion
- Injection Speed Simulator

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
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."

HIPPA-Compliant Intelligent Agents
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
VR/AR and Neuromodulation

- promote behavior change via altered sensory inputs and feedback
- mental illness: PTSD, physical rehabilitation, substance abuse and pain control
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
The Precision Medicine: Digital Medicine Convergence

- The expanded care space
- New combination product classes and services
- New cross-sector industry alliances and engagement
Meeting the Needs of the Expanded Care Space
Created by the Precision Medicine: Digital Medicine Convergence

- mobile
- in-home
- social media analysis
- improved continuity in care
- earlier detection of risk and mitigation

the expanded care space

new product classes, services and new industry alliances/entrants

- Dx-Rx
- Dx-Rx-Ix
- Dx-Rx-Device
- DigRx
- brain-computer interactions
- intelligent agents
Creative Destruction and Disruptive Innovation

- 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
Technology Innovation and Creative Destruction

**Emergence at Margin of an Existing Domain**

- Biotechnology
  - 1980-present

**Emergence by Convergence of Previously Separate Domains**

- Multi-Omics and precision medicine
- Big data, AI, and digital medicine
Amazon and Healthcare
The Next Competitor for Amazon?

Walgreens

Microsoft
Economies of Scale and Convenience Come to Primary Care
CVS Launch of Transform Oncology Care™ (December 2019)

- genome sequencing at diagnosis
- align therapeutic selection to NCCN guidelines
- automatic prior authorization approval
- faster patient access to Rx including high cost specialty Rx
Now Comes the Hard Part!

Driving Precision Medicine and Large Scale Data Analytics into Routine Clinical Practice

New Incentives and New Delivery Models

New Participants and New Business Models
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 Big Data Challenge
Data Standards, Validation, Provenance and Security

I-3
1. infrastructure
2. investment
3. intelligent systems

V-7
1. volume
2. velocity
3. variety
4. veracity
5. visualization
6. virtualization
7. VALUE!

D-3
1. dynamic
2. distributed
3. decision-support
Data Brokers and ‘Selling-On’

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

By REBECCA ROBBINS @rebeccadrobinson / SEPTEMBER 26, 2019
Big Tech: Big Provider Linkups Fuel HIPAA Privacy Debate
National Security Implications of Genome Data on Populations

Population Databanks

Foreign Access to Data

Individual Profiles

Data Security

iCarbonX

华大基因

BGI
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
AAIH Founding Members: Unified Vision for Healthcare
Leading IT and Tech Corporations / AI Companies / Pharma Corporations
Advanced AI in Healthcare and Drug Discovery
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
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
Assessing and referring adult cancers

by Will Stahl-Timmins

Abdominal features (discomfort or pain)

- Abdominal pain
  - Rectal bleeding
  - Weight loss
  - Age 60+
  - Colorectal cancer excluded
- Upper abdominal pain
  - Weight loss
  - Age 60+
  - Colorectal cancer excluded
- Dyspepsia
  - Weight loss
  - Treatment resistant
  - Thrombocytosis
  - Nausea
  - Vomiting
  - Age 60+

Abdominal features (distension or mass)

- Rectal or abdominal mass
- Upper abdominal mass, consistent with enlarged:
  - Gall bladder
  - Liver
  - Stomach
- Hepatosplenomegaly
  - Spleen size
  - Fever
  - Night sweats
  - Breathlessness
  - Obesity
  - Weight loss
  - Abdominal distension
  - Persistent
  - Frequent
  - Exsanguination
  - Age 60+
  - Asymptomatic
  - Pelvic/abdominal mass
  - Not obviously urinary fluid
  - Asymptomatic
  - Irregular bowel syndrome symptoms
  - Last 12 months
  - Age 60+
  - Change in bowel habit
  - Unexplained
  - Age 60+
  - Constipation
  - Weight loss
  - Age 60+

Abdominal features (bowel transit symptoms)

- Women
  - Change in bowel habit
  - Unexplained
  - Age 60+
  - Diarrhoea
  - Constipation
  - Weight loss
  - Age 60+

Abdominal features (Upper gastrointestinal symptoms)

- Nausea
  - Vomiting
  - Thrombocytosis
  - Weight loss
  - Reflux
  - Age 60+
  - Upper abdominal pain
  - Age 60+
  - Reflux
  - Weight loss
  - Age 60+

Dysphagia

Bleeding

- Rectal bleeding
  - Abdominal pain
  - Change in bowel habit
  - Weight loss
  - Low haemoglobin
  - Anaemia

Haemoptysis

Haematemesis

Musculoskeletal

- Back pain
  - Persistent
  - Bone pain
  - Unexplained fracture
  - Age 60+
  - Weight loss

Neurological

- Loss of central neurological function
  - Progressive
  - Sub-acute

Fatigue

Weight loss

Appetite loss

Multiple possibilities

Assess for additional features to clarify most likely cancers

Possible cancers

- Non-Hodgkin's lymphoma
- Colorectal
- Stomach
- Ovarian
- Oesophageal
- Gall bladder
- Liver
- Leukaemia
- Mesothelioma
- Myeloma
- Lung
- Pancreatic
- Brain/CNS

Primary care investigation

- Testing for occult blood in faeces
- CT scan/ Ultrasound
- Upper GI endoscopy
- Direct access
- Ultrasound
- Full blood count
- Measure serum CA125
- Chest x ray
- MRI scan/ CT scan

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

Isolated Data

Complex Networked Data

Complex Computational Data
Just What the Data Ordered

Machine Intelligence and Algorithms for Clinical Diagnosis and Treatment Decisions

Black Box Medicine?
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
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
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

• 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
New Patterns of Learning
DNR: Is the Current Healthcare System Terminal?

Denial

Negativity

Resistance
“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
China is catching up to the United States on funding for research and development.

**World R&D**
- **US**: $2.2 Trillion, **25%**
- **PRC**: 23%

**ACGR**
- **US**: 4.3%
- **PRC**: 17%
Threats to the U.S. Research Enterprise: China’s Talent Recruitment Plans

STAFF REPORT

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

UNITED STATES SENATE
The Arrest of Charles Lieber,
Chair, Dept. of Chemistry, Harvard University
(28 January 2020)
Global Biosecurity
A Neglected Consequence of Comfort and Compliancy
The Challenge of Legislative Technical Literacy in an Era of Escalating Complexity

• 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
• novel threats from dual-use technologies and complex ethical and legal issues
ON THE ROAD TO SUCCESS,
THERE ARE NO SHORTCUTS.

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OUR MOST VALUABLE
RESOURCE SITS
63 FEET AHEAD.
Unidimensional “Quick Fixes”

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

- Peter Drucker
“Strategic Design Spaces”
Exploring the Architecture and Dynamics of Complex Networks

Precision Medicine, Biotechnology, Synthetic Biology

Population Demographics and Disease Burden

IoT: Ubiquitous Sensing and Sensor Networks

Big Data Analytics, Machine Learning

Escalating Complexity

New Patterns of Technology Convergence, Evolution and Adoption

New Knowledge Networks

New Participants

New Organizational Models

“Bio-Space”

“Unmet Need Space”

“Connected and Monitored Space”

“Decision Space”

“Opportunity Space”
The Evolution of Data-Intensive Precision Health

- 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
The Evolution of Data-Intensive Precision Health

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

- Data Security and Privacy
- Robotics and Human Machine Interactions
- Artificial Intelligence and Decision Support
- Public Policy: Ethics, Risk and Regulation