Johns Hopkins *individualized* Health Initiative

Department of Epidemiology

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with

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Changing External Environment

Transforming biomedical and data science

Cancer Genome Landscapes

Bert Vogelstein, Nicholas Papadopoulos, Victor E. Velculescu, Shibin Zhou, Luis A. Diaz Jr., and Kenneth W. Kinzler
The Ludwig Center and The Howard Hughes Medical Institute at Johns Hopkins Kimmel Cancer Center, Baltimore, MD 21287, USA

Unaffordable health care combined with non-competitive outcomes

Total Per Capita Medical Expenditures for OECD Countries

$1 trillion
Population Patterns <=> Individual States

- 40 year old man with no family history of cancer tests “positive” in a screening test
- What to tell you patient?

Data from population of “similar” people

<table>
<thead>
<tr>
<th>Test result</th>
<th>Actual cancer status</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td>15</td>
<td>985</td>
<td>1000</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td>5</td>
<td>8995</td>
<td>9000</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>20</td>
<td>9980</td>
<td>10000</td>
</tr>
</tbody>
</table>
Extending the Population – Individual Connection to Emerging Health Data Types (Boole-a-Bayes)
JHU/JHHS Niche

Updated knowledge

Population

Evidence to address current hypotheses; Novel questions

Discovery JHU

Practice JHHS

Bioscience

Data science

Evidence to address current hypotheses; Novel questions

Public health

Population science research care

Clinical research
Johns Hopkins individualized Health Initiative
Hopkins inHealth - IDEA

“a unique partnership that combines the biomedical science, data science, and engineering assets of three Johns Hopkins Institutions:

• University
• Health System
• Applied Physics Laboratory

to discover and demonstrate how to better determine each individual's health state and guide the health trajectory in a manner tailored to his or her unique characteristics and circumstances.
Johns Hopkins *individualized* Health Initiative – Hopkins *inHEALTH*

**Cores**
- Health measurement
- Data and software solutions
- Statistical design and analysis
- Bioethics
- Dissemination

**Pilot Projects**
- Cancer screening
- Management of autoimmune diseases
- Cardiovascular disease diagnosis and treatment
- Genomics of cystic fibrosis
- Telomere biology and chronic diseases
- Myostatin in sarcopenia
- OncoSpace for head/neck cancer

**New Health Plan**
- **Scale and replicate**

**Improve Health at More Affordable Costs**

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People

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Ruth Faden, Berman Institute
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Sean Fahey, APL
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David Valle, SoM
Martha Sylvia, SoN
Scott Zeger, BSPH, Chair
inHealth as...

Witness the miracle that is... SuperGlue.
Next Gen Pilots in Discussion

1. Children’s obesity – Sara Bleich, Keisha Pollack
2. Brain image diagnosis – Mike Miller, Susumu Mori - Toshiba
3. African American children’s asthma – Kathy Barnes
5. Wearable health measurement devises - Ciprian Crainiceanu, Vadim Zipunnikov
6. Alzheimer’s disease progression – Marilyn Albert
Analytic Framework
Fundamental Questions in *Individualized Health*

1. What is the person’s health state given health measurements to date?

2. What is the person’s health “trajectory”?

3. Does a particular intervention improve health – on average; for a person with specific set of characteristics?

4. Is the intervention being used optimally? How much difference does it make to the population’s health?
Health State Trajectory ($\eta_{it}$) Characterized by Person-specific Indicator ($\delta_i$)
Health State Trajectory – Affected by Exogenous (X) and Endogenous (Rx) Covariates
Person-specific Regression Coefficients ($\beta_i$)
\[ \eta \]
What is the person’s health state given health measurements to date? $\mathbb{E}(\eta_{id} | Y_{it}, X_{it})$
What is the person's health "trajectory"?

\[
E(\beta_i, \delta_i | Y_{it}) = \ldots
\]
Benefit = \( E(\eta_{it} | Y_i, Rx=1) - E(\eta_{it} | Y_i, Rx=0) \)

or

\( E(\beta_i \delta_i | Y_i, Rx=1) - E(\beta_i \delta_i | Y_i, Rx=0) \)
Is the intervention being used optimally? If so, how much difference does it make to the population health?
inCAS - Individualized Cancer Screening

• Harness progress in the cancer biological sciences, leveraging the capacities of big data science, to develop
  – powerful tools for early cancer detection, and
  – overarching models of individualized cancer screening and prediction at Johns Hopkins,

so that each patient’s risk is assessed and managed in a way that is optimally effective for preventing cancer and/or its recurrence.

• Near term: Prostate cancer – Bal Carter, Ken Pienta - Brady
• Longer term: Additional cancers
• Leaders: Elizabeth Platz, Bal Carter
inMAD – Management of Autoimmune Disease

• Individualizing the management of autoimmune diseases, such as rheumatoid arthritis, lupus and scleroderma.

• Use clinical, immune, imaging, and patient self-reported data to monitor patient status and trajectory, and to thereby discover common disease trajectories among subgroups of patients for whom optimal treatment strategies are likely to differ.

• Combine prior pathobiological and clinical knowledge with emerging biomedical and patient-based measurements to define patient status and change.

• Leaders: Laura Hummers, Antony Rosen, Suchi Saria,...
inCARE – Cardiovascular Disease

• Develop, test, and disseminate a patient-centered, data-driven, cost-conscious, and continuously improving model of interventional cardiology (IC) care among Johns Hopkins patient populations.

• Develop automated information technology systems that will harness complex data, drawn from multiple sources, display relevant indicators, and provide evidence to help physicians make precise, real-time IC decisions.

• Identify subsets of patients who will benefit, and who are less likely to benefit, from specific IC procedures.

• Leaders: Julie Miller, Joao Lima
Long Term Model and Impact

Secondary Drivers

- Assess appropriateness of PCI and CABG
- Assess bleeding risk
- Assess risk of kidney injury
- Assess risk of death
- Assess mortality risk of PCI vs CABG
- Case-based peer-review of procedure appropriateness and angiographic outcomes
- Feedback peer-review outcomes to practitioner
- Encourage all practitioners to be reviewers
- Compare NCDR data with clinical record review to improve data integrity
- Support MD application to CMS for per member reimbursement plan
- Minimize per event

Primary Drivers

- Identify and recognize individual patient risks
- Minimize procedures that are inappropriate or of
- Individualized technical approach to PCI
- Engage informed patients in decision-making
- Improved practitioner application of guidelines
- Education of practitioners through active participation in peer-review process
- Modify individual operator practice patterns
- Minimize incentive to avoid doing beneficial procedures
- Minimize the financial incentives to do procedures

Aims

- Improve the health of patients with coronary artery disease treated with coronary angioplasty by reducing
  inappropriate procedures 50%
  complications by 20%
  use of high cost stents by 5%
  while reducing cost by 23%
  by March 2017
## Sample Real-time Decision Support

### Demographics
- **Medical Record Number**: 12345
- **Visit Number**: 22222
- **Last Name**: Doe
- **First Name**: John
- **Procedure Date**: 7/26/2013
- **Date of Birth**: 4/11/1952
- **Age**: 61
- **Gender**: Male
- **African-American**: Yes
- **Patient Source**: Outpatient
- **Height**: 5 ft 9 in
- **Weight (lbs)**: 210
- **Systolic BP (mmHg)**: 110

### Laboratory Values
- **Creatinine (mg/dl)**: 2.01
- **GFR**: 88
- **Hematocrit**: 45

### Historical Information
- **Diabetes**
- **Hypertension**
- **Peripheral Vascular Disease**
- **COPD**
- **Prior CABG**
- **Impaired Mobility**
- **Active Endocarditis**
- **LMWH Heparin in past 48 hrs**
- **PCI Indication**
  - No chest pain
  - Atypical chest pain
  - Stable angina
  - Unstable angina
  - Non-STEMI
  - STEMI

### Clinical Status
- **Urgency of Procedure**
  - Elective
  - Urgent
  - Emergent
  - Salvage

### Angiography
- **Left Main > 50%**
- **>= 2 Vessels with >= 70% stenosis**
- **3 vessel CAD**
- **Device Diameter >= 3 mm**
- **Device length >= 30 mm**
- **IABP**

### Cardiac Surgery Information
- **Surgical Procedure**
  - CABG only
  - Single non-CABG
  - 2 Procedures
  - 3 Procedures
- **Contrast Volume (ml)**: 100
- **Number of Lesions Treated**: 2

### Appropriateness Calculator
- **Appropriateness**
  - Appropriate
  - Uncertain
  - Inappropriate

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Courtesy: T. Aversano
Clinical Summary
Primary Sx: Chest Pain
Angina Class
Other Sx: Dyspnea
Co-morbid conditions: COPD, Renal Failure, Diabetes, PVD

Risk Summary for PCI:
Bleeding = high (5.8%)
Death: Moderate 1.6%
Renal failure: low
Emergency CABG

Objective Data Summary
Creatinine = 1.8 mg/dl
BUN = 45 mg/dl
INR = 1, PTT = 22 sec
Stress Test: Bruce, positive 3 min, CP, 2 mmST depression II, III, AVF
Imaging: inferior ischemia, SSS

Angiographic Summary
PCI Appropriateness: 7
SYNTAX Score: 17
Surgical risk
DES v BMS Restenosis Risk:
DES 3.4%
BMS 6.2%

Patient’s Risk for PCI
- Restenosis Risk
- Kidney Injury Risk
- Bleeding Risk

Patient Specific
AUC : PCI: Appropriate

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Courtesy: T. Aversano
inCYF – Cystic Fibrosis

• Near term: Develop integrated, individualized profile to optimize CF patient management and research including sophisticated phenotyping, genetic/genomic data, biomarkers, environmental variables, and response to individualized treatments

• Longer term: Produce a model for integrated and individualized patient care informed by the biomedical resources of JHU (SOM, BBE, APL, Computational biology groups, basic science, etc.) that generates research opportunities and optimizes patient management.

• Leaders: Garry Cutting, Bill Guggino, Rachel Karchin
inHealth Pilot: Individualized treatment tracts using CF as a model

Diagnosis
- Clinical Genomics Center
- Stratification based on genes
  - Basic Science (Physiology/Bioengineering)
  - Molecular therapy
  - Translational Science (ICTR/Genetic Translational Tech Core)
- Stratification based on environment
  - Welch Center
- Management
  - Genetics and Public Policy Center/Berman Institute
  - Health promotion
  - Disease prevention
- Learning Communities for Health
  - Hopkins CF Center

Outcomes
- Biome Sequencing
- Org. Models for Affordable Health
- Data Science for Health
- Health promotion

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inTEL – Telomere Diseases

• Goal: individualized treatment of telomere-related diseases, bringing telomere biology into the clinic
• Initial steps
  – Building one-of-a-kind clinical research infrastructure
  – Improving diagnosis and clinical decision making
  – Developing treatments for challenging age-related diseases
• Leaders: Mary Armanios, Carol Greider
Hopkins-based Telomere Length Test for Individualizing Clinical Decisions

An intervention

Blood draw

Patient

Mononuclear cells

Telomere length measurement by flowFISH

Treatment A
Long Telomeres

Telomere Length Specific Treatment

Treatment B
Short Telomeres

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Scope of Research and Clinical Care in the Johns Hopkins Telomere Center
inSAR – Age-Related Sarcopenia

• Goal: individualized treatment of age-related sarcopenia, define path for sarcopenia clinical trials

• Approach:
  – Focus on the myostatin pathway; assess activity in patient biopsies
  – Define parameters for assessing efficacy of myostatin-affecting drugs, paving the way for clinical trials

• Project still in formative stages, key meeting at end of June

• Leaders: Se-Jin Lee, Jeremy Walston
inOncoSpace – Radiation Treatment Design

• Goal: individualized radiation treatment of cancer
• Approach:
  – OncoSpace – multi-center data-driven decision support tool for radiation oncologists
  – Implement and test across 5 institutions
  – Expand paradigm to all of oncology
  – Expand to EPIC-based health systems
• Leaders: Ted DeWeese, John Wong, Todd McNutt
Sample automated radiation planning result

<table>
<thead>
<tr>
<th></th>
<th>Brain (Gy) (max)</th>
<th>Brainstem (Gy) (max)</th>
<th>Cord4mm (Gy) (max)</th>
<th>L inner ear (Gy) (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>original</td>
<td>61.25</td>
<td>54.58</td>
<td>41.75</td>
<td>57.18</td>
</tr>
<tr>
<td>re-plan</td>
<td>56.33</td>
<td>46.48</td>
<td>37.89</td>
<td>43.72</td>
</tr>
<tr>
<td>R inner ear (Gy) (mean)</td>
<td>40.57</td>
<td>66.58</td>
<td>61%</td>
<td>63.74</td>
</tr>
<tr>
<td>re-plan</td>
<td>38.38</td>
<td>63.78</td>
<td>59%</td>
<td></td>
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