Neuroscience in Intensive Care International Symposium (NICIS) – America

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March 3, 2017
40 year old man, no family history of life-threatening disease, tests “positive” in a routine screening exam

What is my disease state?

What action do I take to maintain healthy trajectory?

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**Data from population of “similar” people**

<table>
<thead>
<tr>
<th>Exam result</th>
<th>True disease status</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>15</td>
<td>985</td>
</tr>
<tr>
<td>Negative</td>
<td>5</td>
<td>8,995</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>9,980</td>
</tr>
</tbody>
</table>
Goals

• Inform each individual’s decision by population evidence, even with more complex measurements

  Population $\Leftrightarrow$ Individual

• Reference individual to an increasingly “otherwise similar” subset of the population

  Subset, Subset, Subset

• Focus on

  Trajectories
Per Capita Annual Medical Expenditures - OECD Countries

$1 trillion per year = BIG DATUM

$1 trillion
In Just 72 Hours, a Computer Learned How to Beat Nearly Anyone at Chess

20 Years Later, Humans Still No Match For Computers On The Chessboard
Common Health Questions

1. What is this person’s health state given current measurements?

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

3. What is the optimal choice of intervention for this person?

4. Is the intervention being used optimally in the health system population? How much does it improve the population’s health at what cost?
Plato’s Cave
inHealth examples

- **JH Prostate Cancer Active Surveillance** Cohort
  - Bal Carter, PI, Yates Coley

- **Etiology of Children’s Pneumonia**
  - Kate O’Brien, PI; Zhenke Wu

- **National Network of Depression** Centers
  - Peter Zandi, PI of Data/Analysis, Todd Fojo

- **Oncospace Project in Radiation Oncology**
  - Todd McNutt, Harry Quon, Sara Alcorn, Ted DeWeese

- **Scleroderma** Subsetting
  - Antony Rosen, Livia Rosen, Zhenke Wu

- **Tracking Systic Fibrosis** with novel skin chloride measure
  - Gary Cutting, Peter Searson, post-doc
JH Active Surveillance
Prostate Cancer Cohort
Bal Carter, PI
P(Aggressive PCa) = 8%
Risk of Upgrading on Biopsy

If you get your next biopsy today, what is the chance that the biopsy will show a higher grade?

Using information from men similar to you—men with a similar age, diagnosis, and PSA and biopsy history—we’ve estimated the chance that your next biopsy would show a more aggressive cancer.

If you get your next biopsy today, there is a 3% chance your cancer will be upgraded.
Predicted Prostate Cancer Outcomes

If 100 men with a similar age, diagnosis, and PSA and biopsy history had their prostate surgically removed today, what cancer grade would be found?

Click on a section of the pie chart to learn about longterm outcomes for men in each grade group or see outcomes for all 100 men like you.

If 100 men like you had their prostates surgically removed today, after 5 years...
Diagnosed with Prostate Cancer

- PSA
- PE Findings

- PSA
+ PE Findings

- PSA
- PE Findings

- Biopsy

Pre-diagnosis

Biopsy

Active Surveillance

Low Risk

Intermediate Risk

High Risk

Treatment

Diagnosis with Prostate Cancer

Metastatic

Non-metastatic

Hormone Sensitive

Castrate-resistant

Surgery & Radiation Tx

Surgery Tx Only

Radiation Tx Only

Re-occurrence

Cure

No Adverse Events

Incontinence

Impotence

Impotence & Incontinence

Re-occurrence

March 3, 2017
### Precision Medicine Centers of Excellence to Transform Healthcare

<table>
<thead>
<tr>
<th>Component</th>
<th>Prostate Cancer active surveillance example</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Frame unmet health/clinical need</td>
<td>Half of active surveillance prostatectomies yield indolent cancers</td>
</tr>
<tr>
<td>• Specify biomedical model</td>
<td>Predictors of indolence: PSA, past biopsies, family history,…?</td>
</tr>
<tr>
<td>• Wrangle relevant data into a cohort database (CDB) from which to learn through careful analysis</td>
<td>Brady Institute, Bal Carter Active Surveillance clinical cohort database with 1300 men</td>
</tr>
<tr>
<td>• Design and test users’ interface for population health manager, clinician and/or patient</td>
<td>PCORI ME-1408-20318</td>
</tr>
<tr>
<td>• Design and test curation</td>
<td>PCORI proposal</td>
</tr>
<tr>
<td>• Devise business model to sustain/improve tool</td>
<td>Partners</td>
</tr>
<tr>
<td>• Scale-up JHM “product” for national use</td>
<td>Partners</td>
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</tbody>
</table>
Gel Electrophoresis for 19 Scleroderma Patients
Individualized Health: Autoimmune Disease Sub-setting using Autoantibody Signature

Step I. Pre-Processing IP Data
- Band Detection
- Batch Effect Correction
- Gel Registration (De-Warping)

Step II. Discovery of Antibody Subsets
- Sera Subgrouping

A  B  C  D

Molecular Weight (kDa)
Health State/Trajectory ($\eta_{it}$) with Person-specific Indicator ($\delta_i$)
Health State/Trajectory ($\eta_{it}$) with Person-specific Indicator ($\delta_i$)
Effects of Exogenous (X) and Endogenous (Rx) Covariates on Health State/Trajectory with Person-specific Regression Coefficients ($\beta_i$)
Effects of Exogenous (X) and Endogenous (Rx) Covariates on Health State/Trajectory with Person-specific Regression Coefficients ($\beta_i$)
Observations ($Y$) that Inform about Health State through Coefficients ($\phi_i$)
Treatment Decisions Depend on **Past Measured** Outcomes through Parameters ($\zeta_i$)
Feb 24, 2017 Rob Kasdin discussion
Essential Infrastructure to Transform Medicine

- **Leadership** that creates a common vision for the future and investments to transform the current system
  - Johns Hopkins Founding Vision: Science ↔ Medicine
  - Precision Medicine Centers of Excellence

- **Business case**
  - Efficiencies from data-driven processes
  - Fee for service: attract and serve patients who travel to get the best medicine science can offer
  - Capitated business: save by not spending on services with little health value

- **Infrastructure** for modernized medical science/business
  - Data and analysis
  - Systems engineering solutions
  - Dissemination of modern “products”
MISSION: The mission of the PMCOE is to:

• offer optimal clinical care, based upon current scientific understanding, to each patient given his or her characteristics and preferences;

and

• continuously learn from each patient’s monitored experience to optimize her/his care and the care of patients who follow
PMCOEs Practice Science ⇔ Medical Care

(1) construct and continuously refine a **scientific framework** of the pathobiology to guide optimal clinical care

(2) **identify more homogeneous subsets of patients** with respect to their disease etiology and trajectory for whom clinical care can be optimized

(3) quantitatively model patient’s disease state, trajectory, and treatment benefits using **the best available measurements**

(4) **identify novel measures** that improve our capacity to monitor/predict patients’ health state, trajectory, and likely treatment benefits

(5) **continuously learn** from the accumulated evidence about how to better treat the current patient and future patients
Main ideas one again

- Individualized and population health - two sides of same data coin

- Use population data to improve assessment of individual’s health state trajectory, likely treatment benefit

- Improve individual’s and population health with novel measurements and analytic methods

- Modern version of sciences: biomedical + data advancing the vision of affordable health for all
References


Hopkins inHealth

Thank you