Subset, Subset, Subset

Toward Individualized Healthcare

Scott L. Zeger with Yates Coley (post-doctoral fellow)
Professor of Biostatistics, Bloomberg School
Director, Johns Hopkins Individualized Health Initiative
Financial Disclosures/Unapproved Use

- I have no financial relationships with a commercial entity that is relevant to the content of this presentation.

- I will not reference unlabeled or unapproved uses of drugs or other products.
Objectives

By the conclusion of this talk, you will be able to:

1. Describe the goal of individualized health: *Subset, subset, subset*
2. Recall William Osler’s vision for medicine: “*Variability is the ...*”
3. Understand that Bayes Theorem can be used predict a patient’s health status and trajectory from his data and population data, thereby better informing clinical decisions
4. Be inspired to pursue your own vision for individualized health and know a few ways Hopkins inHealth can support you.

Join *inHealth* at help://hopkinsinhealth.jhu.edu/
Case Presentation: 53 year old male, contacted by his physician with health–relevant data update

It's your doctor—he just got an alert that you're having a second helping of pie.
At a moment of opportunity (crisis), be guided by core principles – What would William Osler say?

“Variability is the law of life, and as no two faces are the same, so… no two individuals react alike and behave alike under the abnormal conditions which we know as disease.”

– William Osler
Hopkins inHealth – Achieve Olser’s vision to be better “subset” and treat patients

• Explain meaningful variation by:
  – Novel measurements
  – Novel analysis of existing data

• Identify subsets of patients and optimal treatments for each group

• Develop and disseminate tools for others to use
Novel Measurements

AR-V7 and Resistance to Enzalutamide and Abiraterone in Prostate Cancer

Emmanuel S. Antonarakis, M.D., Changxue Lu, Ph.D., Hao Wang, Ph.D., Brandon Luber, Sc.M., Mary Nakazawa, M.H.S., Jeffrey C. Roeser, B.S., Yan Chen, Ph.D., Tabrez A. Mohammad, Ph.D., Yidong Chen, Ph.D., Helen L. Fedor, B.S., Tamara L. Lotan, M.D., Qizhi Zheng, M.D., Angelo M. De Marzo, M.D., Ph.D., John T. Isaacs, Ph.D., William B. Isaacs, Ph.D., Rosa Nadal, M.D., Channing J. Paller, M.D., Samuel R. Denmeade, M.D., Michael A. Carducci, M.D., Mario A. Eisenberger, M.D., and Jun Luo, Ph.D.
71 year old man in Brady Institute Prostate Cancer Active Surveillance – Dr. Bal Carter
With which group would this PSA trajectory be more consistent?
### Probability of biopsy grade given true prognostic grade group

<table>
<thead>
<tr>
<th>Biopsy Grade</th>
<th>5-6</th>
<th>3+4</th>
<th>4+3</th>
<th>8</th>
<th>9-10</th>
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<tbody>
<tr>
<td>True 5-6</td>
<td>75%</td>
<td>24%</td>
<td>9%</td>
<td>2%</td>
<td>4%</td>
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<tr>
<td>True 3+4</td>
<td>20%</td>
<td>55%</td>
<td>32%</td>
<td>18%</td>
<td>8%</td>
</tr>
<tr>
<td>True 4+3</td>
<td>4%</td>
<td>18%</td>
<td>46%</td>
<td>31%</td>
<td>19%</td>
</tr>
<tr>
<td>True 8</td>
<td>0.7%</td>
<td>2%</td>
<td>8%</td>
<td>31%</td>
<td>11%</td>
</tr>
<tr>
<td>True 9-10</td>
<td>0.4%</td>
<td>0.1%</td>
<td>5%</td>
<td>18%</td>
<td>58%</td>
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(Epstein et al., 2012)
### Biopsy True

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>5-6</th>
<th>3+4</th>
<th>4+3</th>
<th>8</th>
<th>9-10</th>
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<td>0.4</td>
<td>0.1</td>
<td>5</td>
<td>18</td>
<td>58</td>
</tr>
</tbody>
</table>
Diagnosis

P(Gleason 7+)

49%

Age (years)

PSA (ng/mL)

64 66 68 70 72

# Positive Cores = 1
% Positive = 20%

Probability Reclassification

Age (years)

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Diagnosis

5 Years Follow-up

P(Gleason 7+)

49%

4%

PSA (ng/mL)

Age (years)

PSA (ng/mL)

Age (years)

# Positive Cores = 1
% Positive = 20%

No Change in Biopsy Characteristics

Probability Reclassification

Age (years)

Probability Reclassification

Age (years)

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Bayes Theorem

Pr(Hypothesis | Data) = \frac{Pr(Data | Hypothesis) \times Pr(Hypothesis)}{Pr(Data)}

How probable is it that an individual has Gleason 7+ given their observed PSA and biopsy results?

Would we expect to see these PSA and biopsy results if an individual had leason 7+?
Decision Support Tool

Prognosis for Active Surveillance Patients

These plots show your anticipated PSA trajectory (left) and risk of reclassification (right) based on your diagnostic characteristics. Green bands represent uncertainty in these estimates.

- Date of birth: 1940-01-01
- Date of diagnosis: 2000-01-01
- Prostate volume (g): 50
- Number positive cores: 1
- Maximum % positive core: 100
- Clinical stage T1C

http://rycoley.shinyapps.io/prediction-app

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Boole - Bayes

George Boole 1815–1864

Thomas Bayes 1701–1761
# Hopkins inHealth Spring Seminar Series

<table>
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<tr>
<th>Topic</th>
<th>Speaker</th>
<th>Date</th>
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<tr>
<td>Overview</td>
<td><strong>Scott Zeger</strong>, Professor of Biostatistics and Director of Hopkins inHealth</td>
<td>March 6</td>
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<tr>
<td>Data Systems</td>
<td><strong>Chris Chute</strong>, Professor of Health, Policy and Management and BDP</td>
<td>March 20</td>
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<tr>
<td>Organizational Models</td>
<td><strong>Earl Steinberg</strong>, CEO of xG Health Solutions</td>
<td>April 6</td>
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<td>Culture Change</td>
<td><strong>Peter Pronovost</strong>, Professor of Critical Care Medicine and Director of Armstrong Institute</td>
<td>April 27</td>
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<td>Future of the Academic Health Center</td>
<td>TBN</td>
<td>TBD in May</td>
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<td>Bioethics</td>
<td><strong>David Katzelnick</strong>, Assoc. Prof. of Psychiatry, Mayo</td>
<td>February 9</td>
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<tr>
<td></td>
<td><strong>Nancy Kass</strong>, Prof. Bioethics, Berman Institute <strong>Todd McNutt</strong>, Assoc. Prof. of Radiation Oncology <strong>Dan Ford</strong>, SOM Vice Dean for Clinical Investigation</td>
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To support faculty, Hopkins inHealth can:

1. Consult on best design and implementation of your inHealth projects: bioethics, data, sta.s.cs, project management, and dissemination.

2. Match start-up funds; leverage other sources of investment.

3. Support grant writing.

## inHealth People

<table>
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<th>Group</th>
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<tr>
<td>Steering Committee</td>
<td>Sommer, Nelson, Brown, Faden, Wyskiel, Reel, Searson, Kinzler, Valle, Fox, Pronovost, DeWeese, Wirtz</td>
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<tr>
<td>Leadership</td>
<td>Rosen, Zeger, Cooke, Pienta, Phelan, Hill</td>
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<tr>
<td>Cancer</td>
<td>Carter, Nelson, Platz, Kinzler, <strong>Coley</strong>, Joshu, Rao</td>
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<td>Cardiology</td>
<td>Miller, Aversano, Naiman, Liang, <strong>Schoenthaer</strong>, Benson, Stoll,</td>
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<td>Autoimmune disease</td>
<td>Hummers, Wigley, Saria, Bingham, <strong>Schulam</strong></td>
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<tr>
<td>Radiation Oncology</td>
<td>DeWeese, Wong, McNutt, Robertson, <strong>Alcorn</strong>, Charu</td>
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<td>Bioethics</td>
<td>Kass, Faden</td>
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<td>Data science</td>
<td>Rosenblum, Stewart, <strong>Wu</strong>, Rosner, Ogburn, Hackman, <strong>Diaz</strong>, Varadahn, Fisher</td>
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<td>Dissemination</td>
<td>Hair</td>
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<tr>
<td>Management/Development</td>
<td>Calvin, Cornelison, Rentschler, Klicos, Bowden</td>
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</tbody>
</table>
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http://hopkinsinhealth.jhu.edu/

to

MAKE REAL OSLER’S VISION FOR JOHNS HOPKINS MEDICINE