Active Surveillance modeling and decision-making at Johns Hopkins

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November 19, 2015
Research sponsored by the Patrick C. Walsh Prostate Research Fund and PCORI Methods Grant “Bayesian Hierarchical Models for the Design and Analysis of Studies to Individualize Healthcare”
Active Surveillance of Prostate Cancer
Active Surveillance of Prostate Cancer

Key to Success:
Distinguish between indolent and lethal prostate cancer
Age (years)

PSA (ng/mL)

- 64
- 66
- 68
- 70
- 72

Reclassification

- No
- Yes

Biopsy Upgrading

- No
- Yes

Cancer

Normal tissue
Age (years)

PSA (ng/mL)

Reclassification

Yes

No

Biopsy Upgrading

Age (years)

PSA (ng/mL)
True Prostate Cancer State

Random Variability

Measurement Error

measurement Error

True PSA

Observed PSA

Biopsy Results

Measurement Error
Latent Class

“True” Gleason score (6 vs. 7+)

True Prostate Cancer State

Random Variability

True PSA

Measurement Error

Observed PSA

Biopsy Results
Gold standard
True state observed after surgical removal

True Prostate Cancer State

Random Variability

True PSA

Measurement Error

Observed PSA

Biopsy Results

Measurement Error

Gold standard
True state observed after surgical removal
Time-varying Biomarker

True Prostate Cancer State

Random Variability

True PSA

Measurement Error

Observed PSA

Biopsy Results

Measurement Error

Time-varying Biomarker
Discrete Time-to-Event

True Prostate Cancer Status

Random Variability

True PSA

Measurement Error

Observed PSA

Measurement Error

Biopsy Results

Discrete Time-to-Event
True Prostate Cancer State

Observed PSA

Observed PSA

Observed PSA

Biopsy Results

Biopsy Results

Individual-Level Random Effects

Time
True Prostate Cancer State

Biopsy Results

Observed PSA

Biopsy Results

Observed PSA

Observed PSA

Individual-Level Random Effects

Time
True Prostate Cancer State (Latent)

Observed PSA

Surgical Removal (Observe True State)

Biopsy Results

Missing at Random

(Rubin 1976; Little and Rubin 2014)
True Prostate Cancer State (Latent)

Observed PSA

Surgical Removal (Observe True State)

Biopsy Results

Missing NOT at Random

(Rubin 1976; Little and Rubin 2014)
True Prostate Cancer State (Latent)

Observation of PSA

Surgical Removal (Observe True State)

Biopsy Results

\[ \text{Pr (Surgical Removal } = 1 \mid \text{Time, Age, PSA, Previous Biopsy Results, Cancer State)} \]

(Rubin 1976; Little and Rubin 2014)
True Prostate Cancer State (Latent)

Observed PSA

Receive Biopsy

Biopsy Results

Missing at Random

(Rubin 1976; Little and Rubin 2014)
True Prostate Cancer State (Latent) ➔ Observed PSA ➔ Receive Biopsy ➔ Biopsy Results

Missing NOT at Random

(Rubin 1976; Little and Rubin 2014)
\[ \Pr(\text{Biopsy Performed} = 1 \mid \text{Time, Age, PSA, Previous Biopsy Results, Cancer State}) \]

(Rubin 1976; Little and Rubin 2014)
n=874

- Curative Intervention: n=318
- Death: n=19
- Lost to Follow-up: n=130
- Active: n=407
n=874

Curative Intervention
n=318

Death
n=19

Lost to Follow-up
n=130

Active
n=407

None due to Prostate Cancer
n=874

- Curative Intervention, n=318
- Death, n=19
- Lost to Follow-up, n=130
- Active, n=407

Most recent PSA or biopsy at least 2 years ago
n=874

Curative Intervention n=318

Death n=19

Lost to Follow-up n=130

Active n=407

Other Intervention n=151

Prostatectomy n=167
n=874

Curative Intervention n=318

Death n=19

Lost to Follow-up n=130

Active n=407

Prostatectomy n=167

Final Biopsy

<table>
<thead>
<tr>
<th>Post-Surgery Gleason</th>
<th>6</th>
<th>7+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>30</td>
</tr>
<tr>
<td>7+</td>
<td>17</td>
<td>48</td>
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</table>

(6 unknown)
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<tr>
<th></th>
<th>Total Number Observations</th>
<th>Median # per patient</th>
<th>(25th, 75th)%ile # per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>10,425</td>
<td>10</td>
<td>(6, 16)</td>
</tr>
<tr>
<td>Biopsy</td>
<td>2,741</td>
<td>3</td>
<td>(1, 4)</td>
</tr>
<tr>
<td>Years Follow-up (pre-RC)</td>
<td>4,980</td>
<td>5</td>
<td>(3, 8)</td>
</tr>
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- **160 Reclassifications**
  - 18% of patients
  - <6% of all biopsies

- **67 received surgery**
  - 69 other treatment
  - 24 none
Probability of True Gleason 7+

- Yes
- No

Probability Reclassification

- PSA (ng/mL)
- Age (years)

Projected PSA Trajectory

Risk of Biopsy Upgrade

- Biopsy Performed
- No Biopsy
Diagnosis

P(True Gleason 7+)

P(Biopsy Upgrade)

P(Lethal PCa)

P(True Gleason 7+)

Age (years)

PSA (ng/mL)

Age (years)
Adjusted for Informative Missingness
AUC = 0.75 (0.67, 0.83)

Unadjusted Model
AUC = 0.74 (0.64, 0.81)
Posterior P(Aggressive PCa)

Observed P(Aggressive PCa)

0.0 0.2 0.4 0.6 0.8 1.0

0.0 0.2 0.4 0.6 0.8 1.0

Patient with Gleason 7+ on post-surgery analysis

Patient with Gleason = 6 on post-surgery analysis

Observed Proportion with True Gleason 7+

Posterior P(True Gleason 7+)
Active Surveillance of Low-Risk Prostate Cancer - Decision Support Tool

https://rycoley.shinyapps.io/dynamic-prostate-surveillance
Dynamic Prediction Model

- Real-time predictions of cancer state for new patients
- Real-time updates of predictions for existing patients
- Over time, improve understanding of disease in the population by continuously updating model.
- Can incorporate new scientific knowledge, biomarkers
Hopkins inHealth

intelligent use of health information to individualize and integrate health care

http://hopkinsinhealth.jhu.edu/