Optimizing Surveillance of Low-Risk Prostate Cancer

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Active Surveillance of Prostate Cancer
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Key to Success:
Distinguish between indolent and potentially lethal prostate cancer
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Key to Success:
Distinguish between indolent and potentially lethal prostate cancer

Statistical Question: What is the probability that my prostate cancer may become aggressive?
True Prostate Cancer Status

Random Variability

True PSA

Measurement Error

Observed PSA

Measurement Error

Biopsy Results

Measurement Error
Latent Class

- Indolent
- Aggressive

True Prostate Cancer Status

Random Variability

Measurement Error

Biopsy Results

Measurement Error

True PSA

Observed PSA
Gold standard
Pathologic analysis observed in subset

True Prostate Cancer Status

Random Variability

True PSA

Measurement Error

Observed PSA

Biopsy Results

Measurement Error
Time-varying Biomarker

True Prostate Cancer Status

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

Measurement Error

True PSA

Observed PSA

Biopsy Results

Measurement Error

Discrete Time-to-Event
True Prostate Cancer Status

Biopsy Results

Observed PSA

Biopsy Results

Observed PSA

Observed PSA

Individual-Level Random Effects

Time
True Prostate Cancer Status

Biopsy Results

Observed PSA

Observed PSA

Observed PSA

Observed PSA

Individual-Level Random Effects

Time
Observed PSA

Biopsy Results

Biopsy Results

True Prostate Cancer Status

Time
\[ L_i \propto P(\text{Cancer State}_i) \]

\[ \times f(\text{PSA}_i | X_i, Z_i, \text{Random Effects}_i) g(\text{Random Effects}_i | \text{Cancer State}_i) \]

\[ \times \prod_j P(\text{Biopsy Upgrade}_{ij} | W_{ij}, \text{Cancer State}_i) \]
We then proceed as above to get a re-weighted posterior for the latent variables of patient $k$.

$$L_i \propto P(\text{Cancer State}_i)$$

$$\times f(\text{PSA}_i | X_i, Z_i, \text{Random Effects}_i) g(\text{Random Effects}_i | \text{Cancer State}_i)$$

$$\times \prod_j P(\text{Biopsy Upgrade}_{ij} | W_{ij}, \text{Cancer State}_i)$$

Pooled Logistic Regression
\[ L_i \propto P(\text{Cancer State}_i) \]

\[ \times f(\text{PSA}_i | X_i, Z_i, \text{Random Effects}_i) \times g(\text{Random Effects}_i | \text{Cancer State}_i) \]

\[ \times \prod_j P(\text{Biopsy Upgrade}_{ij} | W_{ij}, \text{Cancer State}_i) \]

**Stratified Mixed Effects Model**
We then proceed as above to get a re-weighted posterior for the latent variables of patient $k$.

$$L_i \propto P(\text{Cancer State}_i) \times f(\text{PSA}_i | X_i, Z_i, \text{Random Effects}_i) g(\text{Random Effects}_i | \text{Cancer State}_i) \times \prod_j P(\text{Biopsy Upgrade}_{ij} | W_{ij}, \text{Cancer State}_i)$$
We then proceed as above to get a re-weighted posterior for the latent variables of patient $k$.

Partially-latent class

\[
L_i \propto P(\text{Cancer State}_i) \\
\times f(\text{PSA}_i | X_i, Z_i, \text{Random Effects}_i) g(\text{Random Effects}_i | \text{Cancer State}_i) \\
\times \prod_j P(\text{Biopsy Upgrade}_{ij} | W_{ij}, \text{Cancer State}_i)
\]

Bayesian Estimation:
Posterior Probability of Lethal Cancer
Active Surveillance of Low-Risk Prostate Cancer - Decision Support Tool

Diagnosis

PSA
4

Age
60

Year 1
PSA
5

Biopsy
No Grade Reclassification

Year 2
PSA
6

Biopsy
No Biopsy

Year 3
PSA
5

Biopsy
No Biopsy

Submit

Probability of Aggressive Prostate Cancer

Likely PSA Trajectory

Future Risk of Reclassification

Predictions given submitted data: probability of aggressive prostate cancer (top), PSA trajectory (bottom left), and risk of grade reclassification on future biopsy (bottom right).

https://rycoley.shinyapps.io/dynamic-prostate-surveillance
Related Research

- Informative Missingness
  - Shared Parameter Model

- Rapid Updating of Bayesian Posteriors
  - Importance Sampling

- Multi-cohort Modeling
Research sponsored by the Patrick C. Walsh Prostate Research Fund
Goals:

- Promote research that will discover new ways to better define, measure, and communicate each person’s unique health state and health trajectory.
- Create and disseminate novel tools that can be used in health practice to improve clinician and patient decision-making.

http://hopkinsinhealth.jhu.edu/
Posterior P(Aggressive PCa) vs Observed P(Aggressive PCa)

Patient with Gleason > 6 on post-surgery analysis

Patient with Gleason = 6 on post-surgery analysis