Precision Medicine, Learning Health Systems, and Improving Surveillance of Low Risk Prostate Cancer

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Outline

1. What is Precision Medicine?

2. Individualized Management of Low-Risk Prostate Cancer

3. Local and Multi-Cohort Implementation
Goal: Develop statistical framework to integrate all available data to inform clinical decision-making in a way that improves health outcomes.
Statistical Challenges in Precision Medicine
Statistical Challenges in Precision Medicine

• Heterogeneity
Statistical Challenges in Precision Medicine

- Heterogeneity
- Latent Health State Prediction
Statistical Challenges in Precision Medicine

• Heterogeneity
• Latent Health State Prediction
• Integrate Multiple Data Sources
Statistical Challenges in Precision Medicine

• Heterogeneity
• Latent Health State Prediction
• Integrate Multiple Data Sources
• Informative Missing Data Patterns
Statistical Challenges in Precision Medicine

- Heterogeneity
- Latent Health State Prediction
- Integrate Multiple Data Sources
- Informative Missing Data Patterns
- Data Visualization
Statistical Challenges in Precision Medicine

- Heterogeneity
- Latent Health State Prediction
- Integrate Multiple Data Sources
- Informative Missing Data Patterns
- Data Visualization
- Real-time Analysis
Outline

1. What is Precision Medicine?

2. Individualized Management of Low-Risk Prostate Cancer
   - Clinical Motivation
   - Statistical Model
   - Informative Missing Data Patterns
   - Results

3. Local and Multi-Cohort Implementation
Active Surveillance of Prostate Cancer
Active Surveillance of Prostate Cancer

• Majority of prostate tumors are indolent
Active Surveillance of Prostate Cancer

- Majority of prostate tumors are indolent
- Risk of permanent, significant side effects with surgery, radiation therapy
Active Surveillance of Prostate Cancer

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- AS is alternative to treatment
Active Surveillance of Prostate Cancer

• Majority of prostate tumors are indolent
• Risk of permanent, significant side effects with surgery, radiation therapy
• AS is alternative to treatment
• Key to success: Correctly differentiate between aggressive and indolent tumors
PSA (Every 6-12 Months)
Prostate Biopsy (Annually)

Age (years)

Biopsy Gleason

- 6
- 7+

PSA (ng/mL)
Prostate Biopsy (Annually)

- **Age (years)**
- **PSA (ng/mL)**
- **Biopsy Upgrade**
- **Biopsy Gleason**

![Diagram of prostate with cancer and normal tissue marked]

- Cancer
- Normal tissue

- Age range: 63 to 70 years
- Biopsy Gleason scores: 6 and 7+
Age (years)
PSA (ng/mL)
Biopsy Upgrade
Biopsy Gleason
6
6+
1
5
10

Active Surveillance at Johns Hopkins

- Prospective cohort study
- Started enrollment in 1995
- Over 1,300 patients
- Clearly defined enrollment criteria; monitoring and intervention protocols
### Individualized Risk Assessment of Prostate Cancer

**PCPTRC 2.0**

Enter Your Information

<table>
<thead>
<tr>
<th>Race</th>
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<tbody>
<tr>
<td>Age</td>
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<tr>
<td>PSA Level</td>
<td>ng/ml</td>
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<tr>
<td>Family History of Prostate Cancer</td>
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<td>Digital Rectal Examination</td>
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<tr>
<td>Prior Prostate Biopsy</td>
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</table>

Calculate Cancer Risk  
Clear Fields

**PCPTRC 2.0 and Adjusted Risk Calculators**

PCPTRC 2.0  
%freePSA  
Download the R Code

**PCPTRC 1.0 and Adjusted Risk Calculators**

PCPTRC 1.0  
BMI  
PCA3  
Finasteride  
%freePSA  
[-2]proPSA  
%freePSA and [-2]proPSA  
Prostate Volume and Number of Biopsy Cores  
AUA Symptom Score  
Finasteride with Volume  
Finasteride with AUA Symptom Score  
Download the R Code

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http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp
Individualized Decision Support for JH AS Patients
Individualized Decision Support for JH AS Patients

• Predict true state, not biopsy result
Individualized Decision Support for JH AS Patients

- Predict true state, not biopsy result
- Continuously update model estimates as new patient data are observed
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3. Local and Multi-Cohort Implementation
True Prostate Cancer State

Biologic Variability

Measurement Error

True PSA

Observed PSA

Measurement Error

Biopsy Results
Latent Class
“True” Gleason score (6 vs. 7+)

True Prostate Cancer State

Biologic Variability

Measurement Error

True PSA

Observed PSA

Measurement Error

Biopsy Results
True Prostate Cancer State

Partially-Latent Observed after surgical removal

True PSA

Biologic Variability

Measurement Error

Observed PSA

Measurement Error

Biopsy Results
Biologic Variability

True PSA

Measurement Error

Observed PSA

True Prostate Cancer State

Time-varying Biomarker

Biopsy Results

Measurement Error
True Prostate Cancer State

Biologic Variability

Measurement Error

True PSA

Observed PSA

Measurement Error

Binary Outcome

Biopsy Results
Biologic Variability

True Prostate Cancer State

True PSA

Measurement Error

Observed PSA

Receive Biopsy

Measurement Error

Biopsy Results
True Prostate Cancer State

Biologic Variability

Measurement Error

True PSA

Observed PSA

Receive Biopsy

Biopsy Results

Measurement Error

Constant Assumption for Identifiability
Likelihood
Likelihood

Cancer State
Likelihood

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects
Likelihood

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects

Receive Bx | Covariates, Past PSA and Bx

Bx Gleason | Bx Received, Covariates, Cancer State

Bx: Biopsy
Bayesian Estimation:
Posterior Probability of True Gleason 7+

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects

Receive Bx | Covariates, Past PSA and Bx

Bx Gleason | Bx Received, Covariates, Cancer State

Bx: Biopsy
Likelihood

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects

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Bx Gleason | Bx Received, Covariates, Cancer State

Similar to Joint Latent Class Model of Lin et al. (2002) JASA

Bx: Biopsy
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True PSA

Measurement Error

Observed PSA

Receive Biopsy

Biopsy Results

Measurement Error

True Prostate Cancer State
Measurement Error

Biologic Variability

True PSA

Observed PSA

Receive Biopsy

Biopsy Results

True Prostate Cancer State

Measurement Error
Biologic Variability

Measurement Error

True PSA

Observed PSA

Receive Biopsy

Biopsy Results

Missing NOT At Random

True Prostate Cancer State
Likelihood

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects

\( \prod \) years

Receive Bx | Covariates, Past PSA and Bx, Cancer State

Bx Gleason | Bx Received, Covariates, Cancer State

Bx: Biopsy
True Prostate Cancer State

True PSA

Observed PSA

Biologic Variability

Measurement Error

Surgical Removal (Observe True State)

Biopsy Results

Measurement Error
True Prostate Cancer State

True PSA

Observed PSA

Surgical Removal (Observe True State)

Biopsy Results

Measurement Error

Biologic Variability
True Prostate Cancer State

Biologic Variability

Measurement Error

True PSA

Observed PSA

Surgical Removal (Observe True State)

Missing NOT At Random

Biopsy Results

Measurement Error
Likelihood

Cancer State

Individual Effects | Cancer State

PSA | Covariates, Individual Effects

\[ \prod \text{Receive Bx} | \text{Covariates, Past PSA and Bx, Cancer State} \]

\[ \prod \text{Bx Gleason} | \text{Bx Received, Covariates, Cancer State} \]

\[ \prod \text{Surgery} | \text{Covariates, Past PSA and Bx, Cancer State} \]

Bx: Biopsy
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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
<table>
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<tr>
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<th>Total Number Observations</th>
<th>Median # per patient</th>
<th>(25th, 75th)%ile # per patient</th>
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<td><strong>PSA</strong></td>
<td>10,425</td>
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<td>(6, 16)</td>
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<td><strong>Biopsy</strong></td>
<td>2,741</td>
<td>3</td>
<td>(1, 4)</td>
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<tr>
<td><strong>Years Follow-up</strong></td>
<td>4,980</td>
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<td>(3,8)</td>
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160 Biopsy Gleason 7+ 18% of patients  
<6% of all biopsies

67 received surgery 69 other treatment
24 none
<table>
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<tr>
<th>Biopsy Results</th>
<th>Pre-surgery Gleason</th>
<th>Post-Surgery Gleason</th>
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<tr>
<td></td>
<td>6</td>
<td>6</td>
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<tr>
<td></td>
<td>7+</td>
<td>7+</td>
</tr>
<tr>
<td>6</td>
<td>66 (69%)</td>
<td>30 (31%)</td>
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<tr>
<td>7+</td>
<td>17 (26%)</td>
<td>48 (74%)</td>
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<tr>
<td></td>
<td>(6 unknown)</td>
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<td>Pre-surgery Biopsy Gleason</td>
<td>Post-Surgery Gleason</td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------------</td>
<td></td>
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Sensitivity = 50% 62% 72%

Specificity = 71% 80% 88%
Specificity = 86% (77,93%) at Sensitivity = 62%

AUC = 0.67 0.75 0.83
Specificity = 77% 86% 93% at Sensitivity = 62%

AUC = 0.67 0.75 0.83

False Positive Rate

True Positive Rate

Last Biopsy

Specificity = 77% 86% 93% at Sensitivity = 62%
Observed Proportion Gleason $\geq 7$

Patient with Gleason $\geq 7$ on post-surgical analysis

Patient with Gleason = 6 on post-surgical analysis
Projected PSA Trajectory

Risk of Biopsy Gleason 7+

Probability of True Gleason 7+

6%

Biopsy Upgrade

No

Yes
Active Surveillance of Low-Risk Prostate Cancer - Decision Support Tool

Predicted True Prostate Cancer State

58.8% 23.8% 9% 8.4%

Gleason 6

3+4

4+3

8+

Likely PSA Trajectory

Future Risk of Grade Reclassification

PSA (ng/mL)

10

5

1

0

60

62

64

66

68

Age (years)

100%

75%

50%

25%

0%

60

62

64

66

68

Age (years)

Probability of Reclassification

Biopsy Performed

No Reclassification

No Biopsy Performed

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

This tool is designed for men with lower risk prostate cancer diagnoses who choose Active Surveillance (AS) instead of early treatment. In AS, serial PSA measurements and repeated biopsies are used to monitor disease state. Treatment is typically recommended after grade reclassification on biopsy, i.e. a biopsy with a Gleason score of 7 or higher. Here, we use PSA and biopsy measurements to predict a patient’s true underlying cancer state-- what would be observed if he were to have his prostate surgically removed. We draw a distinction between Gleason scores of 3+4 and 4+3 but combine Gleason scores of 8-10. (Few patients in AS have Gleason scores above 7.)

We also provide predictions of a patient’s anticipated PSA trajectory and risk of grade reclassification to inform expectations and decision-making. For example, patients and clinicians may decide to delay future biopsies if the likelihood of reclassification is low. Alternatively, clinicians may recommend a biopsy if future PSA values exceed what was expected. Darker shading in prediction intervals above indicate more likely values.

https://rycoley.shinyapps.io/dynamic-prostate-surveillance
Future Risk of Biopsy with Gleason 7+

Probability of Gleason 7+

Age (years)

No Biopsy Perfomed

Biopsy Perfomed
No Reclassification
Active Surveillance of Low-Risk Prostate Cancer - Decision Support Tool

Diagnosis
- PSA: 4
- Age: 60
- Year: 2010
- Year 1 PSA: 5
- Biopsy: No Grade Reclassification
- Year 2 PSA: 6
- Biopsy: No Biopsy
- Year 3 PSA: 5
- Biopsy: No Biopsy

https://github.com/aaronjfisher/in-clinic-updates-PSA
Coley et al. (2016) arXiv:1508.07511
“A Bayesian Hierarchical Model for Prediction of Latent Health States from Multiple Data Sources with Application to Active Surveillance of Prostate Cancer”

rycoley/prediction-prostate-surveillance
Outline

1. What is Precision Medicine?

2. Individualized Management of Low-Risk Prostate Cancer

3. Local and Multi-Cohort Implementation
• Assessment plan for outcomes and attitudes
• Assessment plan for outcomes and attitudes
• Real-time predictions for new patients, updates for existing patients
• Assessment plan for outcomes and attitudes
• Real-time predictions for new patients, updates for existing patients
• Over time, improve understanding of disease in patient population by continuously updating model
• Assessment plan for outcomes and attitudes
• Real-time predictions for new patients, updates for existing patients
• Over time, improve understanding of disease in patient population by continuously updating model
• Can incorporate new scientific knowledge, biomarkers
OSLER inHealth
(Open Source Learning Environment in R)

• Latent health state to predict
  • Constant and time-varying
  • Uni- and multivariate
  • Binary, categorical, ordered
• Multiple clinical data sources
• Informative missing data
• Interventions, treatment
Thank you!
Questions?

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False Positive Rate

True Positive Rate

0.0

0.2

0.4

0.6

0.8

1.0

Non-I.O.P. Specificity = 71% 81% 89%

I.O.P. Specificity = 77% 86% 93%

AUC = 0.67 0.75 0.83

AUC = 0.64 0.71 0.81

False Positive Rate

0.0 0.2 0.4 0.6 0.8 1.0

Non-I.O.P. Specificity = 71% 81% 89%
Observed Rate of Outcome

Posterior Probability of Outcome

Biopsy Performed

Grade Reclassification

Surgical Removal of Prostate

Observed Cancer State

- Aggressive (Gleason $\geq 7$)
- Indolent (Gleason = 6)
- Unobserved/No Surgery
1.2

log–OR of True State on Biopsy

log–OR of True State on Surgery

Flat Prior

Prior Mean OR for Main Effect on Surgery

Prior Mean OR for Interaction on Surgery

0.0

0.2

0.4

0.6

0.8

1.0

-1

0

1

-1

0

1

0

1

2

3

4

5
Informative Missing Data Approaches

Shared Parameter Model (Wu and Carroll 1988)
Random effect from mixed model related to censoring process

\[\text{[Censoring time | RE]} \ [\text{Response | RE}]\]

(Albert and Folkmann 2009)

Latent Class Drop-out Model (Roy 2003, 2007)
Discrete shared parameter: unobserved latent class

\[\text{[Latent class | censoring time]} \ [\text{Response | latent class}]\]
Real-Time Analysis with Importance Sampling
Real-Time Analysis with Importance Sampling

Start with:

- Posterior samples of population-level parameters
- Candidate samples of true state and random effects
Real-Time Analysis with Importance Sampling

Start with:  
- Posterior samples of population-level parameters
- Candidate samples of true state and random effects

Calculate:  
- Weights based on likelihood of posterior samples given newly observed data
Real-Time Analysis with Importance Sampling

Start with: Posterior samples of population-level parameters

Candidate samples of true state and random effects

Calculate: Weights based on likelihood of posterior samples given newly observed data

Perform: Apply weights to candidate/posterior samples

Obtain: Posterior prediction of cancer state
\[
L \left( \rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \tilde{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{s=0} \mid \eta_i, i = n_{s=0} + 1, \ldots, n; (Y_i, X_i, Z_i), (B_i, U_i), (R_i, V_i), (S_i, W_i), i = 1, \ldots, n \right) \\
= \prod_{i=1}^{n} \rho^{\eta_i} (1 - \rho)^{1-\eta_i} f(Y_i \mid X_i, Z_i, \beta, \xi, \tilde{b}_i, \sigma^2) g(\tilde{b}_i \mid \mu_{\eta_i}, \Sigma_{\eta_i}) \\
\prod_{j=1}^{J_i} P(B_{ij} = 1 \mid \eta_i, U_{ij}, \nu)^{B_{ij}} P(B_{ij} = 0 \mid \eta_i, U_{ij}, \nu)^{1-B_{ij}} \\
(\prod_{j=1}^{J_{S_i}} P(R_{ij} = 1 \mid \eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0 \mid \eta_i, V_{ij}, \gamma)^{1-R_{ij}})^{B_{ij}} \\
\prod_{j=1}^{J_{S_i}} P(S_{ij} = 1 \mid \eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0 \mid \eta_i, W_{ij}, \omega)^{1-S_{ij}}.
\]
\[
L(\rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \tilde{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{S=0}) |
\]
\[
= \prod_{i=1}^{n} \rho^{\eta_i} (1 - \rho)^{1-\eta_i} f(Y_i|X_i, Z_i, \beta, \xi, \tilde{b}_i, \sigma^2) g(\tilde{b}_i|\mu_{\eta_i}, \Sigma_{\eta_i})
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\[
= \prod_{j=1}^{J_i} P(B_{ij} = 1|\eta_i, U_{ij}, \nu)^{B_{ij}} P(B_{ij} = 0|\eta_i, U_{ij}, \nu)^{1-B_{ij}}
\]
\[
(P(R_{ij} = 1|\eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0|\eta_i, V_{ij}, \gamma)^{1-R_{ij}})^{B_{ij}}
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\[
= \prod_{j=1}^{J_{S_i}} P(S_{ij} = 1|\eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0|\eta_i, W_{ij}, \omega)^{1-S_{ij}}.
\]
\[
(5)
\]
Prior: Beta(1,1)
Individual Effects | Cancer State

\[ L \left( \rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \bar{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{S=0} \right) \]

\[ = \prod_{i=1}^{n} \rho^{\eta_i} (1 - \rho)^{1-\eta_i} f(Y_i | X_i, Z_i, \beta, \xi, \bar{b}_i, \sigma^2) g(\bar{b}_i | \mu_{\eta_i}, \Sigma_{\eta_i}) \]

\[ \prod_{j=1}^{J_i} P(B_{ij} = 1 | \eta_i, U_{ij}, \nu)^{B_{ij}} P(B_{ij} = 0 | \eta_i, U_{ij}, \nu)^{1-B_{ij}} \]

\[ \left( P(R_{ij} = 1 | \eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0 | \eta_i, V_{ij}, \gamma)^{1-R_{ij}} \right)^{B_{ij}} \]

\[ \prod_{j=1}^{J_{Si}} P(S_{ij} = 1 | \eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0 | \eta_i, W_{ij}, \omega)^{1-S_{ij}}. \]

(5)

PSA | Covariates, Individual Effects

Priors: Minimally Informative Multivariate Gaussian (mean effects)
Scaled Inverse Wishart (covariance) (with Uniform scale)
Minimally Informative Multivariate Gaussian (other coefficients)
Uniform (measurement error)
\[
L(\rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \tilde{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{S=0}) \]

\[
\eta_i, i = n_{S=0} + 1, \ldots, n; (Y_i, X_i, Z_i), (B_i, U_i), (R_i, V_i), (S_i, W_i), i = 1, \ldots, n
\]

\[
= \prod_{i=1}^{n} \rho^\eta_i (1 - \rho)^{1-\eta_i} f(Y_i|X_i, Z_i, \beta, \xi, \tilde{b}_i, \sigma^2) g(\tilde{b}_i|\mu_{\eta_i}, \Sigma_{\eta_i})
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\[
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(\prod_{j=1}^{J_{S_i}} P(R_{ij} = 1|\eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0|\eta_i, V_{ij}, \gamma)^{1-R_{ij}})^{B_{ij}}
\]

\[
\prod_{j=1}^{J_{S_i}} P(S_{ij} = 1|\eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0|\eta_i, W_{ij}, \omega)^{1-S_{ij}}.
\]

Receive Bx | Covariates, Past PSA and Bx, Cancer State

Prior: Minimally Informative Multivariate Gaussian
\[ L(\rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \tilde{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{s=0}) \]
\[ \eta_i, i = n_{s=0} + 1, \ldots, n; (Y_i, X_i, Z_i), (B_i, U_i), (R_i, V_i), (S_i, W_i), i = 1, \ldots, n) \]
\[ = \prod_{i=1}^{n} \rho^{\eta_i} (1 - \rho)^{1-\eta_i} f(Y_i|X_i, Z_i, \beta, \xi, \tilde{b}_i, \sigma^2) g(\tilde{b}_i|\mu_{\eta_i}, \Sigma_{\eta_i}) \]
\[ \prod_{j=1}^{J_i} P(B_{ij} = 1|\eta_i, U_{ij}, \nu)^{B_{ij}} P(B_{ij} = 0|\eta_i, U_{ij}, \nu)^{1-B_{ij}} \]
\[ (P(R_{ij} = 1|\eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0|\eta_i, V_{ij}, \gamma)^{1-R_{ij}})^{B_{ij}} \]
\[ \prod_{j=1}^{J_s} P(S_{ij} = 1|\eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0|\eta_i, W_{ij}, \omega)^{1-S_{ij}}. \]

Bx Gleason | Bx Received, Covariates, Cancer State

Prior: Minimally Informative Multivariate Gaussian
\[ L(\rho, \beta, \xi, \sigma^2, \nu, \gamma, \omega; (\mu_k, \Sigma_k), k = 0, 1; \tilde{b}_i, i = 1, \ldots, n; \eta_i, i = 1, \ldots, n_{S=0} | \]

\[ \eta_i, i = n_{S=0} + 1, \ldots, n; (Y_i, X_i, Z_i), (B_i, U_i), (R_i, V_i), (S_i, W_i), i = 1, \ldots, n \]

\[ = \prod_{i=1}^{n} \rho^{\eta_i} (1 - \rho)^{1-\eta_i} f(Y_i|X_i, Z_i, \beta, \xi, \tilde{b}_i, \sigma^2) g(\tilde{b}_i|\mu_{\eta_i}, \Sigma_{\eta_i}) \]

\[ \prod_{j=1}^{J_i} P(B_{ij} = 1|\eta_i, U_{ij}, \nu)^{B_{ij}} P(B_{ij} = 0|\eta_i, U_{ij}, \nu)^{1-B_{ij}} \]

\[ (P(R_{ij} = 1|\eta_i, V_{ij}, \gamma)^{R_{ij}} P(R_{ij} = 0|\eta_i, V_{ij}, \gamma)^{1-R_{ij}})^{B_{ij}} \]

\[ \prod_{j=1}^{J_{S_i}} P(S_{ij} = 1|\eta_i, W_{ij}, \omega)^{S_{ij}} P(S_{ij} = 0|\eta_i, W_{ij}, \omega)^{1-S_{ij}} \]

(5)

Surgery | Covariates, Past PSA and Bx, Cancer State

Prior: Minimally Informative Multivariate Gaussian
Probability of True Gleason 7+ in Johns Hopkins AS Cohort
Regression Model for Patient-Specific Probability of True Gleason 7+
Network of Active Surveillance Cohorts

Johns Hopkins Active Surveillance

CANARY PASS
Network of Active Surveillance Cohorts

Separate modeling approach:
- No information shared across sites
- No sense of generalizability
Comparing Johns Hopkins and Canary Cohorts

1. Underlying risk
2. Inclusion criteria
3. Biopsy and PSA protocols
4. Biopsy reclassification criteria
5. Drop-out to treatment
Comparing Johns Hopkins and Canary Cohorts

Inoue and Etzioni (2014)
Comparing Johns Hopkins and Canary Cohorts

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Comparing Johns Hopkins and Canary Cohorts

1. Underlying risk
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4. Biopsy reclassification criteria
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Proportion of Cohort with True Gleason 7+
Network of Active Surveillance Cohorts

- Johns Hopkins Active Surveillance
- CANARY PASS
- New AS Cohort
Why a time constant cancer state?

- True state observed at most once
- Data insufficient to model both grade progression and misclassification
- 65-70% upgrading from misclassification
- Rate of progression sensitive to priors
- Modified interpretation of true state

Inoue et al. (2014) *Statistics in Medicine*