Optimal Strategies for Active Surveillance of Men With Prostate Cancer

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Prostate Cancer (PCa)
- PCa is the 2nd most common cancer in American men
- American Cancer Society estimates about 29,430 deaths from PCa in 2018
- Early detection and treatment can mitigate the deterioration of patients’ health and improve survival rate
- Common treatments include radical prostatectomy, radiation therapy, and active surveillance
- Active surveillance is suited for low-risk cancer because it:
  - Has comparable survival rate with other treatments
  - Avoids treatment with significant side-effects

Active surveillance (AS) of PCa
- AS: periodically monitoring cancer using PSA or biopsy tests until it has progressed
- Testing infrequently could cause missed detection, but testing too frequently could cause significant harm from biopsies
- Research questions:
  - What is the optimal policy for when to biopsy?
  - When should biopsy be deferred for patients with low-risk PCa?

Partially Observable Markov Decision Process (POMDP) Model
- 5 states: C = low-risk cancer, P = progressed cancer, T = treatment, M = metastasized cancer, D = death
- Belief vector represent partially observable states of C and P:
  - \( \pi_n = P(P|P) \), the probability patient has progressed cancer in period n
- \( \pi_n \) is updated using Bayesian updating based on the observation in the current period
- Actions: wait (\( a_n = W \)), and biopsy (\( a_n = B \))
- Objective: maximize Quality Adjusted Life Years (QALY)
- We consider the following transition probabilities:

\[
P \rightarrow T \text{ happens immediately after } a \text{ biopsy result}
\]

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<tr>
<th>C</th>
<th>D</th>
<th>T</th>
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<td>( \alpha )</td>
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\( C, P \) are partially observable states

Optimality equations:
- Patient enters treatment immediately following a (+) biopsy

\[
\begin{align*}
\rho_{n}(r_n, W) + \sum_{i=1}^{3} P_i \rho_{n+1}(i, D) + (1 - \alpha) \beta \xi_{n+1}(P) R_{n+1}(M) \\
\end{align*}
\]

- Patient continues on to next period if the decision is to wait, or (-) biopsy result

\[
\begin{align*}
\rho_{n}(r_n, B) + \sum_{i=1}^{3} P_i \rho_{n+1}(i, D) + (1 - \alpha) \beta \xi_{n+1}(P) R_{n+1}(M) \\
\end{align*}
\]

- Another property of interest is the threshold policy:
  - A threshold policy exists if there is a probability \( \pi^* \), such that if the probability of having progressed cancer is above \( \pi^* \), then the optimal decision is to biopsy; otherwise, waiting is optimal

Results
- Used backward induction to generate values for optimality equation at every time period
- Create policy that will indicate whether it is optimal to wait or to biopsy for given belief vector at a given time period
- Figure 1 shows a graphical representation of reward function with respect to \( \pi_{n0} \) for \( n = 80 \)

\[
\begin{align*}
\text{Expected QALY} \times 100 \\
\end{align*}
\]

Conclusions
- There exists a Threshold Policy (\( \pi^* \)) at every time period, and this threshold increases with respect to age
- Patients over age 88 are suggested to discontinue surveillance because there is no benefit from treatment due to other cause mortality
- Threshold vs. time is most sensitive to \( \alpha_{M} \), \( \alpha_{P} \), \( \beta \), and \( \kappa \), and robust to the other values tested (\( \beta, f, \gamma, \alpha, \) and \( \beta \))

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