Hypertension Management: A Value of Information Perspective

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Presentation:
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Agenda

✓ Background

✓ Problem Statement

✓ Methods (Prediction and Optimization)

✓ Results and Discussions
Hypertension (HTN)

- A chronic medical condition in which the blood pressure (BP) in vessels elevates to a level higher than its normal range.
  - major Public health issue worldwide;
  - highly prevalent with serious consequences (One billion in the world and $\frac{1}{3}$ in the US)

Mechanism
Importance of HTN Control

The **leading risk for death** in North America (WHO)

77% of first stroke events occur among patients with HTN
HTN Control

➢ Good news
  ✓ HTN can be controlled with promising benefits

➢ Bad news
  ✓ Only a few hypertensive patients have their BP under control
    • In the US, less than half of patients with HTN have it controlled!
Reasons for The Poor Control of HTN?

1. HTN is **asymptomatic**
   - silent killer
   - solution: keep track of BP

2. BP is complex; fluctuates both in the short- and long-terms.
   - very difficult consistent and reliable measurement of BP.

3. Traditional BP measurement is **noisy**
   - Obscuring the true underlying BP.

4. 1,2,3 => profound **subjectivity** in clinical decision-making!
   - physician inertia:
     - Physician’s failure to adequately adjust treatment (i.e., add medication) in response to elevated BP
   - “humanistic” issue related to “physician behavior” or judgment bias
     - “to err is human!”

Solution:
- increase the accuracy of:
  - measurement
  - predictions

med. literature
BP Measurements

Measurement

1. Traditional approach (gold standard)
   ✓ peripheral BP
   ✓ noisy: *inaccurate*

2. New technologies
   ✓ e.g., tech. based on ultrasound
   ✓ Applanation Tonometry or Automated Office BP (AOBP)
   ✓ *noise-free or at least less noisy*
   ✓ more costly (staff, time, technology, etc.)

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low adoption of these technologies → uncertainty over their benefits vs cost!

Value of Information (VOI)
comparing our best decisions: in the presence and absence of information
HTN Control

1. Measurement
   1. Systolic BP (SBP): usually on quarterly basis

2. Treatment
   • Medication therapy through a class of medications called *antihypertensives*
   • Usually combination therapy (i.e., multiple medications)

Five common classes of antihypertensives:

1. **Beta Blockers**
2. **ACEI** (Angiotensin-Converting-Enzyme Inhibitor)
3. **ARBs**: Angiotensin II Receptor Blockers
4. **Diuretic** (aka. thiazide)
5. **CCBs** (Calcium Channel Blockers)
Problem Statement

- How HTN can be controlled considering:
  - Measurement uncertainty
    - underestimation vs. overestimation
  - Intervention trade-off
    - Optimal course actions (medication therapy)
    - too early (unnecessary medication side-effects) vs. too late (risk of CVD)

- From analytics perspective
  - How to effectively marry predictive analytics and prescriptive analytic → VOI?

  focus of today’s presentation
How BP Evolves in the short- and long-term?

1. Everyone has a mean BP ($\theta_t$): changes over time and is unobservable → basis for physician’s medication decision

2. In the short-term (e.g., daily), one’s BP observation ($b_t$) varies according to a Normal distribution with
   ✓ mean = $\theta_t$
   ✓ variances = person’s short-term BP variability ($\sigma_b^2$) + measurement noise ($\tau^2$)

3. In the long-term (e.g., quarterly), $\theta_t$ changes according to a Normal distribution such that:
   ✓ mean at $t + 1$ = mean at $t$ + known/deterministic changes (such as change due to aging and medications)
   ✓ variance = person’s long-term BP variability ($\sigma_{\theta}^2$)
The Framework for Prediction and Decision-Making

1. **Observation**
   - Underlying BP (hidden) $\theta_t$
   - BP Observation $b_t$ at $t-1$

2. **Prediction/Learning**
   - Prediction/belief:
     $$\pi_t(\theta_t) = N(\mu_t, \sigma_t^2)$$
   - Prediction beliefs: $\mu_t$: best prediction of $\theta_t$
   - $\sigma_t^2$: uncertainty around prediction

3. **Decision-Making**: choose action $a_t$ optimally

- Noise-free BP measurement (new tech)
- Noisy BP measurement (traditional tech.)

Learning/Prediction is needed

- Two prediction/learning strategies:
  - **Surprise-Induced Learning (SIL)**
    accounts for judgment bias
    learner $l = SIL$
  - **Kalman Filtering (KF)**
    optimal learner (learning benchmark)
    learner $l = KF$

Optimal decisions compute outcomes

Compare best outcomes $\rightarrow$ VOI

Prediction/belief:
$$\pi_t^l(\theta_t) = N(\mu^l_t, \sigma_{t,l}^2)$$
The Problem

Timeline of decision and events

Learning

Optimization

We model both to capture the entire decision-making process
KF Learning

- KF characterized the parameters of belief about \( \theta_t \), i.e., \( \pi^K_F (\theta) \) as follows:

\[
\begin{align*}
\mu^K_F &= K_t b_t + (1 - K_t) \mu_{t-1}^K \\
\sigma^2_{t,KF} &= (1 - K_t) \zeta_t \\
K_t &= \frac{\zeta_t}{\phi^2 + \zeta_t} \\
\zeta_t &= \sigma^2_{t-1,KF} + \sigma^2_\theta
\end{align*}
\]

- \( K_t \in [0,1] \) is called Kalman gain which identifies the relative contribution of the new evidence \( b_t \) in building the new belief.

- new belief/prediction= convex combination of old prediction and the new observation

- does not account for any subjectivity (hence bias) in predictions
**Surprise Induced Learning (SIL):** a modified Bayesian updating!

- Conventional Bayesian Updating → very similar to KF!

\[
\pi_t^B(\theta_t) \equiv \pi_t^B(\theta) = \mathcal{N}(\mu_t^B, \sigma_{t,B}^2)
\]

\[
\begin{align*}
\mu_t^B &= \rho_t b_t + (1 - \rho_t) \mu_{t-1}^B \\
\sigma_{t,B}^2 &= (1 - \rho_t) \sigma_{t-1,B}^2 \\
\rho_t &= \frac{\sigma_{t-1,B}^2}{\sigma_{t-1,B}^2 + \phi^2}
\end{align*}
\]

- The **issue:**
  - Conventional Bayesian updating assumes stationary mean → belief convergence!

  *Not reacting to the new observation*
SIL Strategy: a modified traditional Bayesian Updating!

➢ To resolve the issue:

✓ We introduce the notion of **surprise**, as:

\[
s_t = \begin{cases} 
1, & \text{if } |\mu_{t-1} - b_t| \geq \Delta \\ 
0, & \text{otherwise} 
\end{cases}
\]

**surprise** ~ observing unexpected events

*Signal for BP regimen change*

When surprise occurs, we impose a **shock** to the belief/prediction system by resetting the belief updating mechanism such that:

• maximum belief uncertainty (we are in a surprise state)
• maximum weight to new observations → **surprise triggers attention**
• minimum weight to the prior belief
SIL Strategy

\[ \pi^\text{SIL}_t(\theta) = \mathcal{N}(\mu^\text{SIL}_t, \sigma^2_{\text{SIL}}) \]

parameters

\[ \begin{align*}
\mu^\text{SIL}_t &= \rho_t b_t + (1 - \rho_t) \mu^\text{SIL}_{t-1}; \\
\sigma^2_{\text{SIL}} &= (1 - \rho_t) \sigma^2_{\text{SIL}_{t-1}} & \text{if } s_t = 0 \\
\mu^\text{SIL}_t &= \rho_1 b_t + (1 - \rho_1) \mu^\text{SIL}_{t-1}; \\
\sigma^2_{\text{SIL}} &= (1 - \rho_1) \sigma^2_{\text{SIL}_0} & \text{if } s_t = 1
\end{align*} \]

\[ \rho_t = \frac{\sigma^2_{\text{SIL}_{t-1}}}{\sigma^2_{\text{SIL}_{t-1}} + \phi^2} \]

\[ \rho_1 = \frac{\sigma^2_{0,\text{SIL}}}{\sigma^2_{0,\text{SIL}} + \phi^2} \]

surprise-free event

surprising event
**SIL Strategy**

- Δ: characterizes the physician’s learning behavior → physician’s characteristics → commitment to belief
  - physician with low Δ → undercommitment to belief
    - experiences more frequent surprises,
    - lower expectation for change → perceiving even small changes as unexpected,
    - assigns larger weights to the new observations → overestimating evidence
  - physician with high Δ → overcommitment to belief
    - becomes surprised less frequently,
    - higher expectations for change, → ignoring larger changes
    - with time, she assigns higher weights to her own belief → underestimating evidence
    - Captures the so-called physician inertia (a key obstacle in HTN treatment recently mentioned in the EU Guideline for HTN control)

- Both cases indicate sub-optimal learning behaviors.

**Question:** Is there an optimal Δ?

**Answer:** Yes! The one which minimizes prediction error or maximizes outcomes!
Data Setting at the Montreal General Hospital

Two sets of data

1. Noise-Free Environment
   ✓ Patients undergoing meticulous BP measurements in the clinic
   ✓ Quarterly visits
   ✓ Using Automated Office Blood Pressure (AOBP) technology

2. Noisy Environment
   ✓ For the same patient
   ✓ At the same day of clinic visit
   ✓ Undergoing 24hr BP measurement, every 20-30min
     • Called 24hr BP measurement or Ambulatory BP Monitoring (ABPM)
Characterizing Optimal Decision Making Through Optimization

- Markov Decision Procession (MDP)
  - Choosing optimal medication decisions to maximize the expected quality adjusted life years of patients over the problem horizon

- Key component:
  - **States**: information needed for making decisions and characterizing the evolution of system → patient’s BP mean (either we know it or we learn it)

- Both learning strategies used in our study are **Markovian, sequential, and recursive** → ideal for MDP

- States in SIL strategy:
  - Best prediction about patient’s BP mean → \( \mu^\text{SIL}_t \)
  - Number of office visits since last surprise \( n_t = \{0, 1, \ldots, N\} \)
    - one-to-one relationship to \( \sigma^2_t \)
    - measures belief strength
    - surprise state
Optimization Framework

We develop three MDP models:

- **Under Noise-Free Measurement:**
  1. Under noise-free measurement, called $\text{MDP}^0$.

- **Under Noisy Measurement:**
  2. Under noisy measurement but KF learning strategy, called $\text{MDP}^{\text{KF}}$.
  3. Under noisy measurement but SIL learning strategy, called $\text{MDP}^{\text{SIL}}$. 
Optimal Policies for $MDP^{SIL}(\Delta^*)$

Theorem 5. Suppose that As.1-4 - As4-4 hold for $t = 1, 2, ..., T$. Then, at each period $t$ and for fixed levels of $\mu_t$ and $m_t$, there exists an optimal policy $a^*_t(\mu_t, n_t, m_t)$ which is nondecreasing in $n_t$. In other words, there is a threshold $n^*_t$ such that:

$$a^*_t(\mu_t, n_t, m_t) = \begin{cases} i^-, & n_t < n^*_t \\ i^+, & n_t \geq n^*_t \end{cases}$$

(4.25)

\[\text{Optimal Policy for Prescribing in [ACIE]}\]
Value of Information (VOI) Analysis

- **Definitions:**
  - $v^0$: value function under perfect information (i.e., noise-free)
  - $v^l$: value function under imperfect information, learner $l$ (i.e., noisy)

\[ VOI = v^0 - v^l: \text{ in terms of Total QALY gained} \]

\[ RVOI = \frac{v^0 - v^l}{v^l}: \text{ in terms of } \% \text{ Total QALY gained} \]
VOI Decomposition: Important Lessons

More specifically:
- $v^0$: the value function under perfect information.
- $v^{KF}$: the value function under imperfect information, yet KF-learner (learning benchmark)
- $v^*$: the value function under imperfect information, yet $\Delta^*$-learner
- $v^l$: the value function under imperfect information, yet $\Delta^{l\neq*}$-learner

Therefore:

$$VOI^l = v^0 - v^l = (v^0 - v^{KF}) + (v^{KF} - v^*) + (v^* - v^l)$$

price paid for information
(net value of information)
value of new technology

price paid for optimal learning strategy

price paid for optimal learning behavior

Conclusion:
- not all the price we pay is because of not knowing the truth (which can be learned/predicted),
- we also pay for our sub-optimal learning strategy (predictive models) or suboptimal learning behavior!

In our study: $VOI = VOI^l(\sigma_\theta, \sigma_b, \tau, j); \ l:\text{learner/physician}, j:\text{patient’s baseline risk}$
Conclusions:

- The new technology is valuable!
- Its value depends on:
  - Patient: risk profile and her BP variability
  - Measurement technology: current traditional devices
  - Physician: those who are not good learners pay more!

Not all the price we pay for information (because of lack of knowledge) is because of the information itself (that we tend to know or predict); we also pay for our suboptimal learning strategies (predictive models) or suboptimal learning behaviors!

- not choosing the best predictive models/methods
- not using the predictive models in the best possible way
Thank You!