4. Single Decision Treatment Regimes: Additional Methods

Classification analogy

Premise:

- The rule characterizing a regime $d \in \mathcal{D}$ can be likened to a *classifier*
- This allows work on classification and machine learning to be exploited
- Demonstrated by Zhang et al. (2012) and Zhao et al. (2012)

Generic classification problem

- Z = outcome or class label; here, $Z = \{0, 1\}$ (binary)
- X = vector of covariates or features taking values in $\mathcal{X}$, the feature space
- d is a classifier: $d : \mathcal{X} \rightarrow \{0, 1\}$
- $\mathcal{D}$ is a family of classifiers; e.g., with $X = (X_1, X_2)^T$
  - Hyperplanes of the form

$$d(X) = \mathrm{I}(\eta_{11} + \eta_{12} X_1 + \eta_{13} X_2 > 0)$$

  - Rectangular regions of the form

$$d(X) = \mathrm{I}(X_1 < \eta_{11}) + \mathrm{I}(X_1 \geq \eta_{11}, X_2 < \eta_{12})$$

Generic classification problem

Implementation:

- Training set: (X_i, Z_i), $i = 1, \ldots, n$
- Find classifier $d \in \mathcal{D}$ that minimizes
  - Classification error

$$\sum_{i=1}^{n} \{Z_i - d(X_i)\}^2 = \sum_{i=1}^{n} \mathrm{I}\{Z_i \neq d(X_i)\}$$

  - Weighted classification error

$$\sum_{i=1}^{n} w_i \{Z_i - d(X_i)\}^2 = \sum_{i=1}^{n} w_i \, \mathrm{I}\{Z_i \neq d(X_i)\}$$

for w_i, $i = 1, \ldots, n$, fixed, known weights

Generic classification problem

- This problem has been studied extensively by statisticians and computer scientists
- Is a form of *supervised learning*, an approach within the broad area of machine learning
- Many methods and software are available
- Recursive partitioning (CART): Rectangular regions
- Support vector machines (SVM): Hyperplanes (linear SVM), nonlinear SVM

Value search estimation, revisited

Zhang et al. (2012): $\mathcal{A}_1 = \{0, 1\}$, restricted class $\mathcal{D}_\eta$

- Elements $d_\eta = \{d_1(h_1; \eta_1)\}$, optimal restricted regime

$$d_\eta^{opt} = \{d_1(h_1; \eta_1^{opt})\}, \quad \eta_1^{opt} = \arg\max_{\eta_1} \mathcal{V}(d_\eta)$$

- AIPW estimator (3.44) for $\mathcal{V}(d_\eta)$ for fixed $\eta = \eta_1$

$$\widehat{\mathcal{V}}_{AIPW}(d_\eta) =$$
$$n^{-1} \sum_{i=1}^{n} \left[\frac{\mathcal{C}_{d_\eta,i} Y_i}{\pi_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\gamma}_1)} - \frac{\mathcal{C}_{d_\eta,i} - \pi_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\gamma}_1)}{\pi_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\gamma}_1)} \mathcal{Q}_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\beta}_1) \right]$$

$$\mathcal{C}_{d_\eta} = \mathrm{I}\{A_1 = d_1(H_1; \eta_1)\} = A_1 \mathrm{I}\{d_1(H_1; \eta_1) = 1\} + (1 - A_1)\mathrm{I}\{d_1(H_1; \eta_1) = 0\}$$
$$\pi_{d_\eta,1}(H_1; \eta_1, \gamma_1) = \pi_1(H_1; \gamma_1)\mathrm{I}\{d_1(H_1; \eta_1) = 1\} + \{1 - \pi_1(H_1; \gamma_1)\}\mathrm{I}\{d_1(H_1; \eta_1) = 0\}$$
$$\mathcal{Q}_{d_\eta,1}(H_1; \eta_1, \beta_1) = Q_1(H_1, 1; \beta_1)\mathrm{I}\{d_1(H_1; \eta_1) = 1\} + Q_1(H_1, 0; \beta_1)\mathrm{I}\{d_1(H_1; \eta_1) = 0\}$$

Value search estimation, revisited

Estimator for d_η^{opt}: $\widehat{d}^{opt}_{\eta,AIPW} = \{d_1(h_1; \widehat{\eta}^{opt}_{1,AIPW})\}$

- $\widehat{\eta}^{opt}_{1,AIPW}$ maximizes $\widehat{\mathcal{V}}_{AIPW}(d_\eta)$ in η_1

Algebra:

$$\frac{\mathcal{C}_{d_\eta} Y}{\pi_{d_\eta,1}(H_1;\eta_1,\gamma_1)} = \frac{[A_1 \mathrm{I}\{d_1(H_1;\eta_1)=1\} + (1-A_1)\mathrm{I}\{d_1(H_1;\eta_1)=0\}]Y}{\pi_1(H_1;\gamma_1)\mathrm{I}\{d_1(H_1;\eta_1)=1\} + \{1-\pi_1(H_1;\gamma_1)\}\mathrm{I}\{d_1(H_1;\eta_1)=0\}}$$

$$= \frac{A_1 Y}{\pi_1(H_1;\gamma_1)}\mathrm{I}\{d_1(H_1;\eta_1)=1\} + \frac{(1-A_1)Y}{\{1-\pi_1(H_1;\gamma_1)\}}\mathrm{I}\{d_1(H_1;\eta_1)=0\}$$

$$\frac{\mathcal{C}_{d_\eta} - \pi_{d_\eta,1}(H_1;\eta_1,\gamma_1)}{\pi_{d_\eta,1}(H_1;\eta_1,\gamma_1)}\mathcal{Q}_{d_\eta,1}(H_1;\eta_1,\beta_1)$$

$$= \frac{\{A_1 - \pi_1(H_1;\gamma_1)\}}{\pi_1(H_1;\gamma_1)} Q_1(H_1,1;\beta_1)\mathrm{I}\{d_1(H_1;\eta_1)=1\}$$

$$- \frac{\{A_1 - \pi_1(H_1;\gamma_1)\}}{1-\pi_1(H_1;\gamma_1)} Q_1(H_1,0;\beta_1)\mathrm{I}\{d_1(H_1;\eta_1)=0\}$$

Classification analogy

Define:

$$\psi_1(H_1, A_1, Y) = \frac{A_1 Y}{\pi_1(H_1)} - \frac{\{A_1 - \pi_1(H_1)\}}{\pi_1(H_1)} Q_1(H_1, 1), \tag{4.1}$$

$$\psi_0(H_1, A_1, Y) = \frac{(1 - A_1) Y}{1 - \pi_1(H_1)} + \frac{\{A_1 - \pi_1(H_1)\}}{1 - \pi_1(H_1)} Q_1(H_1, 0) \tag{4.2}$$

- Under SUTVA, NUC, positivity

$$E\{\psi_1(H_1, A_1, Y)|H_1\} = Q_1(H_1, 1), \quad E\{\psi_0(H_1, A_1, Y)|H_1\} = Q_1(H_1, 0)$$

- Thus

$$E\{\psi_1(H_1, A_1, Y) - \psi_0(H_1, A_1, Y)|H_1\} = C_1(H_1) = Q_1(H_1, 1) - Q_1(H_1, 0),$$

the contrast function (3.34)

Classification analogy

Thus, by all of this algebra: Can write

$$\widehat{\mathcal{V}}_{AIPW}(d_\eta) = n^{-1} \sum_{i=1}^{n} \Big[\widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) \mathrm{I}\{d_1(H_{1i}; \eta_1) = 1\} \\ + \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i) \mathrm{I}\{d_1(H_{1i}; \eta_1) = 0\} \Big]$$

- $\widehat{\psi}_1(H_{1i}, A_{1i}, Y_i)$ and $\widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)$ are (4.1) and (4.2) evaluated at (H_{1i}, A_{1i}, Y_i) with the fitted models $Q_1(H_1, 1; \widehat{\beta}_1)$, $Q_1(H_1, 0; \widehat{\beta}_1)$, and $\pi_1(H_1; \widehat{\gamma}_1)$ substituted
- Rewrite using $\mathrm{I}\{d_1(H_1; \eta_1) = 1\} = d_1(H_1; \eta_1)$, $\mathrm{I}\{d_1(H_1; \eta_1) = 0\} = 1 - d_1(H_1; \eta_1)$

Classification analogy

By further algebra: $\widehat{\mathcal{V}}_{AIPW}(d_\eta)$ can be expressed as

$$
\begin{aligned}
&\widehat{\mathcal{V}}_{AIPW}(d_\eta) \\
&= n^{-1}\sum_{i=1}^{n}\Big[\widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) d_1(H_{1i}; \eta_1) + \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)\{1 - d_1(H_{1i}; \eta_1)\}\Big] \\
&= n^{-1}\sum_{i=1}^{n}\Big[d_1(H_{1i}; \eta_1)\Big\{\widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) - \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)\Big\} + \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)\Big] \\
&= n^{-1}\sum_{i=1}^{n}\Big\{d_1(H_{1i}; \eta_1)\widehat{C}_1(H_{1i}, A_{1i}, Y_i) + \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)\Big\}
\end{aligned}
$$

- Predictor of the contrast function

$$\widehat{C}_1(H_{1i}, A_{1i}, Y_i) = \widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) - \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i)$$

Classification analogy

Result: Maximizing $\widehat{\mathcal{V}}_{AIPW}(d_\eta)$ in η_1 is equivalent to maximizing

$$n^{-1}\sum_{i=1}^{n} d_1(H_{1i};\eta_1)\widehat{C}_1(H_{1i},A_{1i},Y_i)$$

More algebra: Using $a = \mathrm{I}(a>0)|a| - \mathrm{I}(a\leq 0)|a|$ for any a and writing $d_{\eta_1,1i} = d_1(H_{1i};\eta_1)$, $\widehat{C}_{1i} = \widehat{C}_1(H_{1i},A_{1i},Y_i)$

$$\begin{aligned}
d_{\eta_1,1i}\widehat{C}_{1i} &= d_{\eta_1,1i}\mathrm{I}(\widehat{C}_{1i}>0)|\widehat{C}_{1i}| - d_{\eta_1,1i}\mathrm{I}(\widehat{C}_{1i}\leq 0)|\widehat{C}_{1i}| \\
&= \mathrm{I}(\widehat{C}_{1i}>0)|\widehat{C}_{1i}| - |\widehat{C}_{1i}|\{(1-d_{\eta_1,1i})\mathrm{I}(\widehat{C}_{1i}>0) + d_{\eta_1,1i}\mathrm{I}(\widehat{C}_{1i}\leq 0)\} \\
&= \mathrm{I}(\widehat{C}_{1i}>0)|\widehat{C}_{1i}| - |\widehat{C}_{1i}|\{\mathrm{I}(\widehat{C}_{1i}>0) - d_{\eta_1,1i}\}^2
\end{aligned}$$

Thus:

$$\begin{aligned}
d_1(H_{1i};\eta_1)\widehat{C}_1(H_{1i},A_{1i},Y_i) &= \mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)\geq 0\}|\widehat{C}_1(H_{1i},A_{1i},Y_i)| \\
&\quad - |\widehat{C}_1(H_{1i},A_{1i},Y_i)|\left[\mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)\geq 0\} - d_1(H_{1i};\eta_1)\right]^2
\end{aligned}$$

Classification analogy

Final result: Maximizing $\widehat{\mathcal{V}}_{AIPW}(d_\eta)$ in η_1 is equivalent to *minimizing* in η_1

$$n^{-1}\sum_{i=1}^{n}|\widehat{C}_1(H_{1i},A_{1i},Y_i)|\Big[\mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)>0\}-d_1(H_{1i};\eta_1)\Big]^2$$
$$=n^{-1}\sum_{i=1}^{n}|\widehat{C}_1(H_{1i},A_{1i},Y_i)|\mathrm{I}\Big[\mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)>0\}\neq d_1(H_{1i};\eta_1)\Big] \tag{4.3}$$

- A weighted classification error with
  - "Label" $\mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)\geq 0\}$ (Z_i)
  - "Weight" $|\widehat{C}_1(H_{1i},A_{1i},Y_i)|$ (w_i)
  - "Classifier" $d_1(h_1;\eta_1)$ (d)

Classification analogy

$$n^{-1}\sum_{i=1}^{n}|\widehat{C}_1(H_{1i},A_{1i},Y_i)|\text{I}\Big[\text{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)>0\}\neq d_1(H_{1i};\eta_1)\Big] \quad (4.3)$$

Intuitive interpretation:

- From (3.35), $d^{opt}\in\mathcal{D}$ satisfies

$$d_1^{opt}(h_1)=\text{I}\{C_1(h_1)>0\}$$

- The second term in (4.3) compares a predictor of the option selected by the global d^{opt} to that selected by a rule in $\mathcal{D}_\eta$
- The "weight" $|\widehat{C}_1(H_{1i},A_{1i},Y_i)|$ in (4.3) places greater importance on contributions from individuals for whom the absolute difference in expected outcomes for options 0 and 1 is large

Classification analogy

Similarly: Analogous argument applies to

$$\widehat{\mathcal{V}}_{IPW}(d_\eta) = n^{-1} \sum_{i=1}^{n} \frac{\mathcal{C}_{d_\eta,i} Y_i}{\pi_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\gamma}_1)}$$

- Can be shown: The same formulation applies with

$$\psi_1(H_1, A_1, Y) = \frac{A_1 Y}{\pi_1(H_1)}, \quad \psi_0(H_1, A_1, Y) = \frac{(1 - A_1) Y}{1 - \pi_1(H_1)}$$

$$\begin{aligned} \widehat{C}_1(H_{1i}, A_{1i}, Y_i) &= \widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) - \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i) \\ &= \frac{A_{1i} Y_i}{\pi_1(H_{1i}; \widehat{\gamma}_1)} - \frac{(1 - A_{1i}) Y_i}{1 - \pi_1(H_{1i}; \widehat{\gamma}_1)} \end{aligned}$$

Classification analogy

Summary: Value (policy) search estimation of an optimal restricted regime d_η^{opt} by maximizing $\widehat{\mathcal{V}}_{IPW}(d_\eta)$ or $\widehat{\mathcal{V}}_{AIPW}(d_\eta)$ is equivalent to minimizing a weighted classification error

- Choice of classification approach dictates the restricted class $\mathcal{D}_\eta$.
- Can be implemented using off-the-shelf software and algorithms for classification problems
- E.g., for CART, SVM

However: This analogy does not circumvent the need to optimize a *nonsmooth* function of η_1

Demonstration

Decision function: Write $d_1(h_1;\eta_1) = \mathrm{I}\{f_1(h_1;\eta_1) > 0\}$

- E.g.

$$f_1(h_1;\eta_1) = \eta_{11} + \eta_{12}x_{11} + \eta_{13}x_{12}$$

- By algebra, can write

$$n^{-1}\sum_{i=1}^{n} |\widehat{C}_1(H_{1i}, A_{1i}, Y_i)| \mathrm{I}\Big[\mathrm{I}\{\widehat{C}_1(H_{1i}, A_{1i}, Y_i) > 0\} \neq d_1(H_{1i};\eta_1)\Big]$$

$$= n^{-1}\sum_{i=1}^{n} |\widehat{C}_1(H_{1i}, A_{1i}, Y_i)|\, \ell_{0\text{-}1}\Big(\Big[2\mathrm{I}\{\widehat{C}_1(H_{1i}, A_{1i}, Y_i) > 0\} - 1\Big] f_1(H_{1i};\eta_1)\Big)$$

in terms of the *0-1 loss function*

$$\ell_{0\text{-}1}(x) = I(x \leq 0)$$

Demonstration

$$n^{-1}\sum_{i=1}^{n}|\widehat{C}_1(H_{1i},A_{1i},Y_i)|\,\ell_{0\text{-}1}\Big(\Big[2\mathrm{I}\{\widehat{C}_1(H_{1i},A_{1i},Y_i)>0\}-1\Big]f_1(H_{1i};\eta_1)\Big)$$

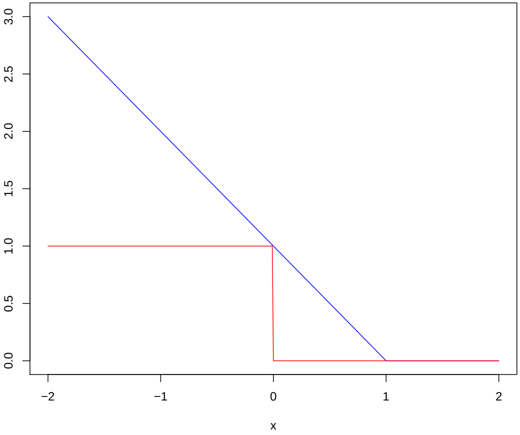
Source of difficulty: The 0-1 loss function is *nonconvex*

$$\ell_{0\text{-}1}(x) = I(x \leq 0)$$

- Optimization involving nonconvex loss functions is challenging; standard techniques cannot be used
- This problem has been well studied in the classification literature
- E.g., with SVM, replace $\ell_{0\text{-}1}(x)$ by a convex "surrogate" such as the *hinge loss function*

$$\ell_{hinge}(x) = (1-x)^{+}, \quad x^{+} = \max(0, x)$$

Hinge loss vs. 0-1 loss



Original formulation

Zhao et al. (2012): Approach based on the IPW estimator

$$\widehat{\mathcal{V}}_{IPW}(d_\eta) = n^{-1} \sum_{i=1}^{n} \frac{\mathcal{C}_{d_\eta,i} Y_i}{\pi_{d_\eta,1}(H_{1i}; \eta_1, \widehat{\gamma}_1)}$$

- Assume that Y is bounded and $Y \geq 0$
- Can be developed as a special case of the above with

$$\psi_1(H_1, A_1, Y) = \frac{A_1 Y}{\pi_1(H_1)}, \quad \psi_0(H_1, A_1, Y) = \frac{(1 - A_1)Y}{1 - \pi_1(H_1)}$$

$$\begin{aligned}
\widehat{C}_1(H_{1i}, A_{1i}, Y_i) &= \widehat{\psi}_1(H_{1i}, A_{1i}, Y_i) - \widehat{\psi}_0(H_{1i}, A_{1i}, Y_i) \\
&= \frac{A_{1i} Y_i}{\pi_1(H_{1i}; \widehat{\gamma}_1)} - \frac{(1 - A_{1i}) Y_i}{1 - \pi_1(H_{1i}; \widehat{\gamma}_1)} \\
&= \frac{Y_i \{A_{1i} - \pi_1(H_1; \widehat{\gamma}_1)\}}{\pi_1(H_1; \widehat{\gamma}_1)\{1 - \pi_1(H_1; \widehat{\gamma}_1)\}}
\end{aligned}$$

As a special case

- With $Y \geq 0$

$$\mathrm{I}\{\widehat{C}_1(H_{1i}, A_{1i}, Y_i) > 0\} = \mathrm{I}(A_1 = 1) = A_1$$

- By considering $A_{1i} = 1$ and $A_{1i} = 0$

$$|\widehat{C}_1(H_{1i}, A_{1i}, Y_i)| = \frac{Y_i}{A_{1i}\pi_1(H_{1i}; \widehat{\gamma}_1) + (1 - A_{1i})\{1 - \pi_1(H_{1i}; \widehat{\gamma}_1)\}}$$

- Substitute in (4.3): Maximizing $\widehat{\mathcal{V}}_{IPW}(d_\eta)$ in η_1 is equivalent to minimizing

$$n^{-1} \sum_{i=1}^{n} \underbrace{\frac{Y_i}{A_{1i}\pi_1(H_{1i}; \widehat{\gamma}_1) + (1 - A_{1i})\{1 - \pi_1(H_{1i}; \widehat{\gamma}_1)\}}}_{\text{“Weight”}} \mathrm{I}\{A_{1i} \neq d_1(H_{1i}; \eta_1)\} \tag{4.4}$$

- “Label” A_{1i}, “Classifier” $d_1(h_1; \eta_1)$

Original formulation

Randomized study: With known

$$\pi_1(H_1) = P(A_1 = 1|H_1) = P(A_1 = 1) = \pi_1$$

- Recode options: $\mathcal{A}_1 = \{-1, 1\}$
- $d_1(h_1; \eta_1) = \text{sign}\{f_1(h_1; \eta_1)\}$ for decision function $f_1(h_1; \eta_1)$

Weighted classification error: (4.4) can be rewritten as

$$n^{-1} \sum_{i=1}^{n} \frac{Y_i}{A_{1i}\pi_1 + (1 - A_{1i})/2} \mathrm{I}\{A_{1i} \neq d_1(H_{1i}; \eta_1)\}$$

$$= n^{-1} \sum_{i=1}^{n} \frac{Y_i}{A_{1i}\pi_1 + (1 - A_{1i})/2} \mathrm{I}[A_{1i} \neq \text{sign}\{f_1(H_{1i}; \eta_1)\}]$$

- Involves the 0-1 loss function

$$\mathrm{I}[A_{1i} \neq \text{sign}\{f_1(H_{1i}; \eta_1)\}] = \mathrm{I}\{A_{1i} f_1(H_{1i}; \eta_1) \leq 0\} = \ell_{0\text{-}1}\{A_{1i} f_1(H_{1i}; \eta_1)\}$$

Outcome weighted learning (OWL)

Minimize:

$$n^{-1} \sum_{i=1}^{n} \frac{Y_i}{A_{1i}\pi_1 + (1 - A_{1i})/2} \ell_{0\text{-}1}\{A_{1i} f_1(H_{1i}; \eta_1)\}$$

Original OWL: Zhao et al. (2012)

- Restricted class $\mathcal{D}_\eta$ induced by linear or nonlinear SVM
- Replace 0-1 loss by the convex surrogate hinge loss function

$$\ell_{hinge}(x) = (1 - x)^+, \quad x^+ = \max(0, x)$$

- Minimize in η_1

$$n^{-1} \sum_{i=1}^{n} \frac{Y_i}{A_{1i}\pi_1 + (1 - A_{1i})/2} \{1 - A_{1i} f_1(H_{1i}; \eta_1)\}^+ + \lambda_n \|f_1\|^2 \quad (4.5)$$

- Flexible, highly parameterized representation of $f_1(h_1; \eta_1)$, penalty for overfitting

Outcome weighted learning

Remarks:

- Can take a similar approach (flexible $f_1(h_1; \eta_1)$, penalization) with the full AIPW formulation
- *Important:* Minimizing the original objective (4.4) and minimizing (4.5) with hinge loss substituted are different optimization problems and will lead to different $\widehat{\eta}_1^{opt}$ and thus different estimated optimal regimes
- Similarly for the AIPW formulation
- Simulation evidence: Suggests this might not be such a big deal in practice; resulting estimated optimal regimes perform well

Refinements and extensions of OWL: Zhou et al. (2017), Liu et al (2018)

4. Single Decision Treatment Regimes: Additional Methods

Flexibility vs. interpretability

Classification approach: Flexible representation

- Complex, highly parameterized estimated decision rules
- Pro: Can synthesize high-dimensional patient information and achieve performance close to a true optimal regime $d^{opt} \in \mathcal{D}$
- Con: Difficult to interpret, "black box," cannot glean scientific insights

Opposing view: Emphasize parsimony and interpretability

- Deliberately focus on $\mathcal{D}_\eta$ with rules that can be understood by clinicians and patients
- Pro: Accessibility, more readily accepted, can generate scientific insights
- Con: Optimal such regimes may not approach performance of $d^{opt} \in \mathcal{D}$

Decision rules as decision lists

Zhang et al. (2015): Focus on $\mathcal{D}_\eta$ with decision rules characterizing regimes in the form of a *decision list*

- Decision list: A sequence of if-then clauses
- "If" is a condition involving patient information that, if true, leads to selection of an option $a_1 \in \mathcal{A}_1$
- Natural for $\mathcal{A}_1$ with $m_1 \geq 2$ options

Example: Acute leukemia, $\mathcal{A}_1 = \{\mathrm{C}_1, \mathrm{C}_2\} = \{0, 1\}$

- Rule $d_1(h_1) = \mathrm{I}(\text{age} < 50 \text{ and WBC} < 10)$ as a list

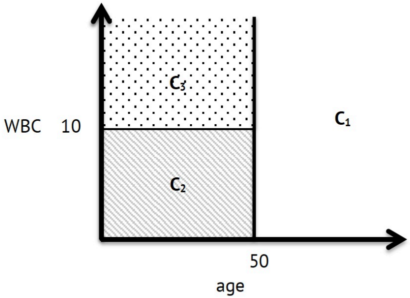
If age $<$ 50 and WBC $<$ 10 then C_2;

else C_1

Decision rules as decision lists

Fancier example: Acute leukemia, $\{C_1, C_2, C_3\}$

$$\begin{aligned} &\text{If age} < 50 \text{ and WBC} < 10 \text{ then } C_2; \\ &\text{else if age} \geq 50 \text{ then } C_1; \\ &\text{else } C_3 \end{aligned} \tag{4.6}$$



Decision rules as decision lists

Fancier still:

$$\begin{aligned} &\text{If age} < 50 \text{ and ECOG} < 2 \text{ then } \mathrm{C}_2;\\ &\text{else if WBC} \geq 20 \text{ then } \mathrm{C}_1;\\ &\text{else if PLAT} > 300 \text{ then } \mathrm{C}_1;\\ &\text{else } \mathrm{C}_3. \end{aligned} \tag{4.7}$$

Decision rules as decision lists

In general: Rule in form of decision list of length L_1

$$\begin{aligned}
&\text{If } c_{11} \text{ then } \mathrm{a}_{11};\\
&\text{else if } c_{12} \text{ then } \mathrm{a}_{12};\\
&\qquad\qquad \vdots\\
&\text{else if } c_{1L_1} \text{ then } \mathrm{a}_{1L_1};\\
&\text{else } \mathrm{a}_{10},
\end{aligned}$$

- Summarized as $\{(c_{11}, \mathrm{a}_{11}), \ldots, (c_{1L_1}, \mathrm{a}_{1L_1}), \mathrm{a}_{10}\}$
- For example, in (4.7), $L_1 = 3$, $c_{11} = \{$ age < 50 and ECOG $< 2\}$, and $\mathrm{a}_{11} = \mathrm{C}_2$
- Options can be repeated in different clauses
- $L_1 = 0$ corresponds to a static regime

Basic formulation

Can mathematize: Define

$$\mathcal{T}_1(c_{1\ell}) = \{h_1 : \; c_{1\ell} \text{ is true } \}, \quad \ell = 1, \ldots, L_1$$

$$\mathcal{R}_{11} = \mathcal{T}_1(c_{11})$$

$$\mathcal{R}_{1\ell} = \left\{ \cap_{j<\ell} \mathcal{T}_1(c_{1j})^c \right\} \bigcap \mathcal{T}_1(c_{1\ell}), \quad \ell = 2, \ldots, L_1,$$

$$\mathcal{R}_{10} = \bigcap_{j=1}^{L_1} \mathcal{T}_1(c_{1j})^c$$

- Each $\mathcal{R}_{1\ell}$, $\ell = 0, \ldots, L_1$, represents the conditions that must be satisfied for an individual to receive option $a_{1\ell}$
- For the diligent student: Determine the sets $\mathcal{R}_{11}$, $\mathcal{R}_{12}$, $\mathcal{R}_{13}$, and $\mathcal{R}_{10}$ for the example in (4.7)
- Clearly: A given h_1 can belong to at most one set $\mathcal{R}_{1\ell}$, $\ell = 0, 1, \ldots, L_1$

Basic formulation

Treatment regime: Decision rules of form

$$d_1(h_1) = \sum_{\ell=0}^{L_1} a_{1\ell}\, I(h_1 \in \mathcal{R}_{1\ell}). \tag{4.8}$$

- Characterized by $\{(c_{11}, a_{11}), \ldots, (c_{1L_1}, a_{1L_1}), a_{10}\}$

Zhang et al. (2015): For parsimony and interpretability, restrict to $c_{1\ell}$ involving at most 2 components of h_1

- For h_1 with p_1 components, $j_1 < j_2 \in \{1, \ldots, p_1\}$, restrict to $\mathcal{T}_1(c_{1\ell})$ of any of the forms

$$\begin{array}{ll}
\{h_1:\ h_{1j_1} \leq \tau_{11}\} & \{h_1:\ h_{1j_1} \leq \tau_{11} \text{ or } h_{1j_2} \leq \tau_{12}\} \\
\{h_1:\ h_{1j_1} \leq \tau_{11} \text{ and } h_{1j_2} \leq \tau_{12}\} & \{h_1:\ h_{1j_1} \leq \tau_{11} \text{ or } h_{1j_2} > \tau_{12}\} \\
\{h_1:\ h_{1j_1} \leq \tau_{11} \text{ and } h_{1j_2} > \tau_{12}\} & \{h_1:\ h_{1j_1} > \tau_{11} \text{ or } h_{1j_2} \leq \tau_{12}\} \\
\{h_1:\ h_{1j_1} > \tau_{11} \text{ and } h_{1j_2} \leq \tau_{12}\} & \{h_1:\ h_{1j_1} > \tau_{11} \text{ or } h_{1j_2} > \tau_{12}\} \\
\{h_1:\ h_{1j_1} > \tau_{11} \text{ and } h_{1j_2} > \tau_{12}\} & \{h_1:\ h_{1j_1} > \tau_{11}\},
\end{array} \tag{4.9}$$

Regimes

Restricted class $\mathcal{D}_\eta$: Define η_1 to be a collection

$$\{(c_{11}, a_{11}), \ldots, (c_{1L_1}, a_{1L_1}), a_{10}\}$$

with conditions $c_{1\ell}$ as in one of the $\mathcal{T}_1(c_{1\ell})$ in (4.9)

- A rule as in (4.8) can be written as $d_1(h_1; \eta_1)$, and $\mathcal{D}_\eta$ comprises all regimes with rules of this form
- Feature: Do not need to collect all patient variables up front; can ascertain as needed, useful if some are expensive or burdensome to collect

A decision rule can be represented with more than one list:

- For a decision list with $\eta_1 = \{(c_{11}, a_{11}), \ldots, (c_{1L_1}, a_{1L_1}), a_{10}\}$ and decision rule $d_1(h_1; \eta_1)$, there may exist another decision list with $\eta_1' = \{(c_{11}', a_{11}'), \ldots, c_{1L_1'}', a_{1L_1'}'), a_{10}'\}$ and decision rule $d_1(h_1; \eta_1')$ such that $d_1(h_1; \eta_1) = d_1(h_1; \eta_1')$ for all h_1 but $L_1 \neq L_1'$ or $L_1 = L_1'$ but $c_{1j} \neq c_{1j}'$ or $a_{1j} \neq a_{1j}'$ for some $j = 1, \ldots, L_1$

Nonuniqueness

Example: (4.6) and alternative

If age $<$ 50 and WBC $<$ 10 then C_2;

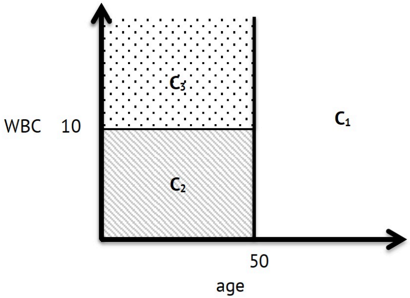
else if age $\geq$ 50 then C_1;

else C_3

If age $\geq$ 50 then C_1;

else if WBC $<$ 10 then C_2;

else C_3



Optimal regime

Value of a regime: For any regime $d_\eta \in \mathcal{D}_\eta$, $\mathcal{V}(d_\eta)$ is the same regardless of which version of d_η is considered

- Optimal regime d_η^{opt}

$$d_1(h_1; \eta_1^{opt}), \quad \eta_1^{opt} = \arg\max_{\eta_1} \mathcal{V}(d_\eta)$$

- Suggests: If there are equivalent versions of d_η^{opt}, estimate the version that is least costly/burdensome to implement
- Value search: Maximize $\widehat{\mathcal{V}}_{AIPW}$ on Slide 171 subject to targeting the version of an optimal regime minimizing a measure of "cost"
- Cost: If $\mathcal{N}_{1\ell}$ = cost of measuring components of h_1 necessary to check $c_{11}, \dots, c_{1\ell}$, expected cost

$$N_1(d_\eta) = \sum_{\ell=1}^{L_1} \mathcal{N}_{1\ell} P(H_1 \in \mathcal{R}_{1\ell}) + \mathcal{N}_{1L_1} P(H_1 \in \mathcal{R}_{10})$$

- Zhang et al. (2015): Describe a computational algorithm

4. Single Decision Treatment Regimes: Additional Methods

Extensive literature

Numerous approaches: We highlight two additional approaches to estimation of an optimal regime

- *Regression-based estimation:* To mitigate concern over parametric model misspecification, represent

$$Q_1(h_1, a_1) = E(Y|H_1 = h_1, A_1 = a_1)$$

  nonparametrically,, e.g., using generalized additive models, support vector regression, random forests, etc, to obtain a nonparametric estimator $\widehat{Q}_1(h_1, a_1)$
- Use $\widehat{Q}_1(h_1, a_1)$ as the fitted model and thus obtain

$$\widehat{d}^{opt}_{Q,1}(h_1) = \arg\max_{a_1 \in \mathcal{A}_1} \widehat{Q}_1(h_1, a_1)$$

Extensive literature

- *Alternative form of value search:* Because for d_η in a restricted class $\mathcal{D}_\eta$

$$\mathcal{V}(d_\eta) = E\left[Q_1(H_1, 1)\mathrm{I}\{d_1(H_1; \eta_1) = 1\} + Q_1(H_1, 0)\mathrm{I}\{d_1(H_1; \eta_1) = 0\}\right]$$

maximize in η_1

$$\widehat{\mathcal{V}}(d_\eta)$$

$$= n^{-1} \sum_{i=1}^{n} \left[\widehat{Q}_1(H_1, 1)\mathrm{I}\{d_1(H_1; \eta_1) = 1\} + \widehat{Q}_1(H_1, 0)\mathrm{I}\{d_1(H_1; \eta_1) = 0\}\right]$$

- As above, $\widehat{Q}_1(h_1, a_1)$ is a nonparametric estimator for $Q_1(h_1, a_1)$
- But here $\widehat{Q}_1(h_1, a_1)$ is used only to ensure faithful representation of the value and not to define the optimal regime estimator directly

4. Single Decision Treatment Regimes: Additional Methods

References

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