ITR.ABC - A Single Step Reinforcement Learning Approach for Precision Medicine

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RDSA
right data
smart analytics

Outlines

Definition of Precision Medicine

Precision Medicine(Wiki)

Precision medicine is a medical model that proposes the customization of healthcare, with medical decisions, practices, and/or products being tailored to the individual patient. In this model, diagnostic testing is often employed for selecting appropriate and optimal therapies based on the context of a patient's genetic content or other molecular or cellular analysis. Tools employed in precision medicine can include molecular diagnostics, imaging, and analytics/software.

Summary

Making optimal healthcare decision for each individual patient based on this subject's context information.

Illustration Data

Table 1: An illustration dataset

ID	Y	A	X_1	X_2	X_3	$\cdots$
1	1.5	1	F	26	7.8	$\cdots$
2	1.2	2	M	28	8.2	$\cdots$
3	2.3	3	M	31	8.9	$\cdots$
4	0.9	2	F	35	9.4	$\cdots$
5	1.7	1	M	22	7.3	$\cdots$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$

Research Question

Based on these data, how can we treat a new patient?
In other words, how can we learn a treatment assignment rule that, if followed by the entire population of certain patients, would lead to the best outcome on average?

Three Key Components for Precision Medicine

Context based decision learning has data in 3 components:

- $X_1, X_2, \cdots, X_p$ is context information.
- A is a context action.
- Y is a reward.

Notes:

- This data structure differs from data for typical supervised and unsupervised learning.
- Examples on common mistakes about data collection for precision medicine ...

Other Examples: Car Purchase

Table 2: My Friends' Rating of Their First Cars

ID	Satisfaction	Car Type	Gender	Age	Mileage per Day	$\cdots$
1	90%	Focus	F	26	7.8	$\cdots$
2	85%	Corolla	M	28	8.2	$\cdots$
3	70%	Civic	M	31	8.9	$\cdots$
4	75%	Corolla	F	35	9.4	$\cdots$
5	60%	Civic	M	22	7.3	$\cdots$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$

Learning from these data, what car should I purchase?

Other Examples: Business Investment

Table 3: Previous Commercial Investments and Returns

Case ID	Return	Type	Month	Location	Share of Market	⋯
1	1.2	TV	Jan	MW	12.5	⋯
2	0.9	Radio	Oct	NE	18.2	⋯
3	1.4	Web	Nov	WE	12.9	⋯
4	1.3	Web	Dec	MW	10.4	⋯
5	1.2	Radio	Feb	SE	11.3	⋯
⋮	⋮	⋮	⋮	⋮	⋮	⋱

Learning from these data, what is our best way to invest in New England area if our product has 12% market share in this March?

Other Examples: Choice of Digital Biomarkers

Table 4: Choose Right Digital Biomarker for Alzheimer's Disease

ID	Accuracy	Digital Biomarker	State	Age	Gender	$\cdots$
1	70%	App No.1	Mild	63	F	$\cdots$
2	83%	App No.2	Moderate	72	F	$\cdots$
3	77%	App No.1	Mild	65	M	$\cdots$
4	62%	App No.3	Severe	86	M	$\cdots$
5	53%	App No.2	Moderate	77	F	$\cdots$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$

Learning from these data, which is the most accurate digital biomarker that we need to choose for a new patient based on this subject's characteristics? If we can only choose one digital biomarker for patients with mild Alzheimer's Disease which one we need to utilize?

Making Optimal Decision Based on Data

Broad applications, some examples:

- Treatment selection: which treatment is the best for this patient?
- Treatment transition: should we keep using the current treatment or consider an intensification?
- Business analytic: how to invest (among a few choices) to maximize the return?
- Recommendation system: which item should a system recommend to a customer to maximize profit?

All these problems are similar in terms of data format and analytic solutions. **Essentially, we focus on a problem of making the optimal decision based on data.**

So, what is a general framework to solve this?

Reinforcement Learning Framework

Later you will see that:

- This problem is a special case in reinforcement learning framework which is different from supervised learning (e.g. classification) and unsupervised learning (e.g. clustering).
- Traditional alternatives (e.g. linear regression) are not efficient to solve these problems.
- It is connected with supervised learning methods (e.g. support vector machines).
- It can be extended to multiple stage decision making to optimize treatment sequences (e.g. dynamic treatment regimes).

Outlines

Notations

- There are N subjects from a large population.
- A_i is the treatment assignment (actions), where $i = 1, \cdots, N$.
- Y_i is the response assuming that larger Y_i is better (rewards).
- X_i is a vector of covariates.
- (Y, A, X) is the generic random variable of $\{(Y_i, A_i, X_i)\}$.
- $\mathcal{P}$ is the distribution of (Y, A, X).
- E is the expectation with respect to $\mathcal{P}$.
- Population space $\mathcal{X}$, i.e. $X_i \in \mathcal{X}$.
- $\mathcal{D}(\cdot)$ is a treatment recommendation based on covariates, i.e. $\mathcal{D}(\cdot) : \mathcal{X} \to \mathcal{A}$.
- $\mathcal{P}^{\mathcal{D}}$ is the distribution of (Y, A, X) given that $A = \mathcal{D}(X)$.

Modeling Assumptions

Assumption 1: Positivity $\exists\epsilon > 0, \Pr\{\Pr(A = a|X) \geq \epsilon, \forall a \in \mathcal{A}\} = 1.$

Assumption 2: Strong ignorability $\{Y(a) : a \in \mathcal{A}\} \perp A|X.$

Assumption 3: SUTVA $Y = \sum_{a=1}^{k} Y(a)I(A = a).$

SUTVA: Stable Unit Treatment Value Assumption. $Y(a)$ is the potential outcome if patient X takes treatment a.

Value Function

Define,

$$E^{\mathcal{D}}(Y) = \int Y d\mathcal{P}^{\mathcal{D}} = \int Y \frac{d\mathcal{P}^{\mathcal{D}}}{d\mathcal{P}} d\mathcal{P} = E\left[\frac{I\{A = \mathcal{D}(X)\}}{p(A|X)} Y\right],$$

where we use the fact that,

$$\frac{d\mathcal{P}^{\mathcal{D}}}{d\mathcal{P}} = \frac{p(y|x,a) I\{a = \mathcal{D}(x)\} p(x)}{p(y|x,a) p(a|x) p(x)} = \frac{I\{a = \mathcal{D}(x)\}}{p(a|x)}.$$

Our objective is to find $\mathcal{D}(\cdot)$ to maximize the following value function:

Value function

$$\mathcal{D}_o \in \underset{\mathcal{D} \in R}{\operatorname{argmax}} E^{\mathcal{D}}(Y) = E\left[\frac{I\{A = \mathcal{D}(X)\}}{p(A|X)} Y\right], \tag{1}$$

where R is a space of possible treatment recommendations.

Advantages of This Framework

- Y is able to handle binary, continuous, time to event data type.
- A is able to handle multiple treatments.
- X is able to incorporate variety of variables. For example, if X includes study ID, the framework can be used for meta analysis.
- $\Pr(A|X)$ allows treatment assignments depending on covariates. So it can handle both randomized control trials and observational studies.
- It has an objective function to evaluate different treatment assignments.

An Example to Build Intuition

Table 5: Example Data

ID	Y	A	X	$P(A\|X)$
1	1	1	1	0.5
2	2	1	2	0.5
3	3	1	3	0.5
4	4	1	4	0.5
5	5	1	5	0.5
6	3	2	1	0.5
7	3	2	2	0.5
8	3	2	3	0.5
9	3	2	4	0.5
10	3	2	5	0.5

Questions to think about: why is $P(A|X) = 0.5$? what do the responses look like?

Which Doctor is Better

Suppose we have two doctors and each of them has a treatment rule. Which doctor is a better one?

- Doctor Adam: give patients treatment 1 if $X \geq 2$, and treatment 2 otherwise, denoted as $\mathcal{D}_A(X)$.
- Doctor Barry: give patients treatment 1 if $X \geq 3$, and treatment 2 otherwise, denoted as $\mathcal{D}_B(X)$.

Example Continued

Table 6: Calculation Based on Table 5

ID	Y	A	X	$P(A\|X)$	$\mathcal{D}_A$	$\mathcal{D}_B$	$\mathcal{D}_A = A$	$\mathcal{D}_B = A$
1	1	1	1	0.5	2	2	0	0
2	2	1	2	0.5	1	2	1	0
3	3	1	3	0.5	1	1	1	1
4	4	1	4	0.5	1	1	1	1
5	5	1	5	0.5	1	1	1	1
6	3	2	1	0.5	2	2	1	1
7	3	2	2	0.5	1	2	0	1
8	3	2	3	0.5	1	1	0	0
9	3	2	4	0.5	1	1	0	0
10	3	2	5	0.5	1	1	0	0

Example Continued

Doctor Adam:

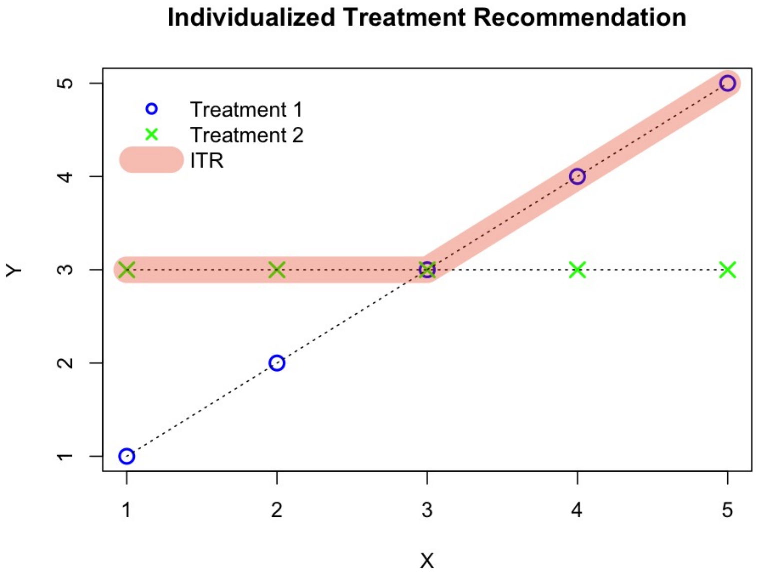
$$
\begin{aligned}
E^{\mathcal{D}_A}(Y) = \frac{1}{10}\Bigg(&\frac{0}{0.5}\times 1+\frac{1}{0.5}\times 2+\frac{1}{0.5}\times 3+\frac{1}{0.5}\times 4+\frac{1}{0.5}\times 5+\frac{1}{0.5}\\
&\times 3+\frac{0}{0.5}\times 3+\frac{0}{0.5}\times 3+\frac{0}{0.5}\times 3+\frac{0}{0.5}\times 3\Bigg)\\
= 3.4
\end{aligned}
$$

Doctor Barry:

$$
\begin{aligned}
E^{\mathcal{D}_B}(Y) = \frac{1}{10}\Bigg(&\frac{0}{0.5}\times 1+\frac{0}{0.5}\times 2+\frac{1}{0.5}\times 3+\frac{1}{0.5}\times 4+\frac{1}{0.5}\times 5+\frac{1}{0.5}\\
&\times 3+\frac{1}{0.5}\times 3+\frac{0}{0.5}\times 3+\frac{0}{0.5}\times 3+\frac{0}{0.5}\times 3\Bigg)\\
= 3.6
\end{aligned}
$$

Conclusion: Doctor Barry's rule is better than Doctor Adam's. Can we improve Doctor Barry's rule? How can we find the best rule?

Graphic Illustration



Thought Provoking Questions

- Both treatment 1 and treatment 2 have an average treatment effect as 3.0. But ITR generates average benefit value 3.6. Can algorithm beat a new molecule entity?

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- What if the treatment randomization ratio is not 1:1?

Thought Provoking Questions

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- Treatment 1 should not be only better than treatment 2. It has to be better with a non-trivial benefit margin. How can we handle this case?
- What if the treatment randomization ratio is not 1:1?
- What if we have multiple covariates? The rule can be complicated.
- What if we have multiple treatments?

Analysis results: how ITR creates more value.

This data analysis shows how ITR creates additional value for patients. We have 1978 patients from two treatment arms, and 2 important biomarkers are selected from 35 biomarkers.

Table 7: *HbA1c Reduction Before and After Following ITR.* Patients with baseline fasting insulin $\geq$ 61.12pmol/L and baseline HbA1c $\geq$ 8.1% (A_o^1) are recommended to take Pioglitazone, otherwise (A_o^0) patients are recommended to take Gliclazide. After following ITR, the overall HbA1c reduction changes from -1.287% to -1.473%. Notes: ITR is our proposed method which is referred to as Individualized Treatment Recommendation.

	Original		Follow ITR		
	-1.287		-1.473		
	Gliclazide	Pioglitazone		Gliclazide	Pioglitazone
Mean	-1.271	-1.303	A_o^1	-1.394	-1.864
			A_o^0	-1.19	-0.932

Outlines

Key Insights on Solving ITR

Three connections:

1. Maximization and minimization of the value function.
2. Classification and loss functions.
3. ITR and weighted classifications.

From Maximization to Minimization

Original objective function

$$\mathcal{D}_o \quad \in \quad \underset{\mathcal{D} \in R}{\text{argmax}}\, E^{\mathcal{D}}(Y) = E\left[\frac{I\{A = \mathcal{D}(X)\}}{p(A|X)} Y\right]. \tag{2}$$

Making connections:

$$E\left\{\frac{Y}{p(A|X)}\right\} - E\left[\frac{I\{A = \mathcal{D}(X)\}}{p(A|X)} Y\right] \quad = \quad E\left[\frac{I\{A \neq \mathcal{D}(X)\}}{p(A|X)} Y\right],$$

New objective function

$$\mathcal{D}_o \quad \in \quad \underset{\mathcal{D} \in R}{\text{argmin}}\, E^{\mathcal{D}}(Y) = E\left[\frac{I\{A \neq \mathcal{D}(X)\}}{p(A|X)} Y\right]. \tag{3}$$

Empirical Evaluation

Objective function

$$\mathcal{D}_o \quad \in \quad \underset{\mathcal{D} \in R}{\operatorname{argmin}}\, E^{\mathcal{D}}(Y) = E\left[\frac{I\left\{A \neq \mathcal{D}(X)\right\}}{p(A|X)} Y\right].$$

When we have data, we can evaluate the objective function as,

Empirical evaluation

$$D_o \quad = \quad \underset{D \in R}{\operatorname{argmin}}\, n^{-1} \sum_{i=1}^{n} \frac{Y_i}{p(A_i|X_i)} I\left\{A_i \neq \mathcal{D}(X_i)\right\}. \tag{4}$$

Classification and Loss Function

Roughly speaking, A good classifier has smaller errors (we will discuss regularization later).

Classification objective function

$$D_o \quad = \quad \operatorname*{argmin}_{D \in R} n^{-1} \sum_{i=1}^{n} I\left\{A_i \neq \mathcal{D}(X_i)\right\}.$$

Classification and Loss Function

Roughly speaking, A good classifier has smaller errors (we will discuss regularization later).

Classification objective function

$$D_o = \underset{D \in R}{\operatorname{argmin}} \, n^{-1} \sum_{i=1}^{n} I \left\{ A_i \neq \mathcal{D}(X_i) \right\}.$$

If we compare our ITR objective function as below,

ITR objective function

$$D_o = \underset{D \in R}{\operatorname{argmin}} \, n^{-1} \sum_{i=1}^{n} \frac{Y_i}{p(A_i|X_i)} I \left\{ A_i \neq \mathcal{D}(X_i) \right\}.$$

A GREAT Connection

Outcome Weighted Learning

Therefore, our ITR problem can be considered as a weighted classification problem!

So, we can make it connected with SVM, tree, gradient boosting methods as ...

- ITR.SVM
- ITR.SVM.DC
- ITR.BR
- ITR.Tree
- ITR.CS
- ITR.Boosting
- ...

Today, we are going to show you an exciting development based on multicategory angled based classifier as **ITR. ABC**.

Outlines

A k-Regular Polyhedron in a $\mathbb{R}^{k-1}$ Euclidean Space

A simplex W with k vertices $\{W_1, \cdots, W_k\}$ in a $(k-1)$-dimensional space,

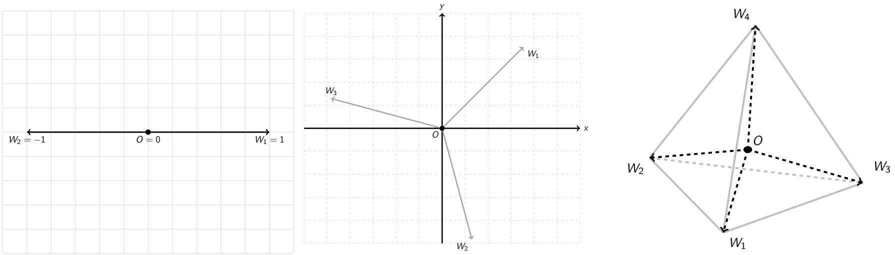
$$W_j = \begin{cases} (k-1)^{-1/2}\mathbf{1}_{k-1}, & j = 1, \\ -(1+k^{1/2})/\{(k-1)^{3/2}\}\mathbf{1}_{k-1} + \{k/(k-1)\}^{1/2} e_{j-1}, & 2 \le j \le k, \end{cases}$$

where $\mathbf{1}_i$ is a vector of 1 with length equal to i, and e_i is a vector in $\mathbb{R}^{k-1}$ such that its every element is 0, except the ith element is 1.

Properties:

- The centre of W is at the origin.
- Each W_j has Euclidean norm 1.
- The angles between any two directions $\angle(W_i, W_j), \forall i \ne j$ are equal.
- Every vector in $\mathbb{R}^{k-1}$ generate k different angles with respect to $\{W_1, \cdots, W_k\}$, and all these angles are in $[0, \pi]$.

Illustration of $\{W_i\}$ When $k = 2, 3, 4$.



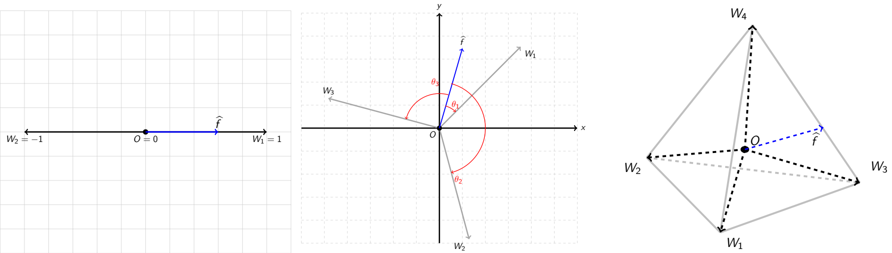
(a) $k = 2$ (b) $k = 3$ (c) $k = 4$

Remark: When $k = 3$, $\{W_i, i = 1, 2, 3\}$ are the vertices of an equilateral triangle, and when $k = 4$, $\{W_i, i = 1, 2, 3, 4\}$ are the vertices of a regular tetrahedron.

Angle Based Classifier

- Let W_j represent class j.
- Our method is to map x to $\widehat{f}(x) \in \mathbb{R}^{k-1}$.
- $\mathcal{A}$ is the class spaces as $\mathcal{A} = \{1, 2, \cdots, k\}$, and $a_i \in \mathcal{A}$ which is the class membership of subject i.
- We predict $\widehat{a}$ to be the class whose corresponding angle is the smallest, i.e. $\widehat{a} = \arg\min_j \angle(W_j, \widehat{f})$, where $\angle(\cdot, \cdot)$ denotes the angle between two vectors.
- Minimizing the angle is equivalent to maximize $\langle f(x_i), W_{a_i} \rangle$.

Angle Based Classifier Illustration



(a) $k = 2$ (b) $k = 3$ (c) $k = 4$

- $k = 2$, $W_1 = 1$ and $W_2 = -1$.
- $k = 3$ (equilateral triangle),
  $W_1 = \left(\frac{1}{\sqrt{2}}, \frac{1}{\sqrt{2}}\right)$, $W_2 = \left(\frac{\sqrt{3}-1}{2\sqrt{2}}, -\frac{\sqrt{3}+1}{2\sqrt{2}}\right)$, $W_3 = \left(-\frac{\sqrt{3}+1}{2\sqrt{2}}, \frac{\sqrt{3}-1}{2\sqrt{2}}\right)$.
- $k = 4$ (regular tetrahedron),
  $W_1 = \left(\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}\right)$, $W_2 = \left(\frac{1}{\sqrt{3}}, -\frac{1}{\sqrt{3}}, -\frac{1}{\sqrt{3}}\right)$, $W_3 = \left(-\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}, -\frac{1}{\sqrt{3}}\right)$, $W_4 = -\left(\frac{1}{\sqrt{3}}, -\frac{1}{\sqrt{3}}, \frac{1}{\sqrt{3}}\right)$.

Angle Based Classifier

With ℓ a convex monotone decreasing function, we have our angle based classifier as,

$$\underset{f \in \mathcal{F}}{\text{minimize}} \quad \frac{1}{n}\sum_{i=1}^{n} \ell\{\langle f(x_i), W_{a_i} \rangle\} + \lambda J(f). \tag{5}$$

Example ($k = 2$)

For a binary case, i.e. $k = 2$, $\langle f(x_i), W_{a_i} \rangle = af(x_i)$,

- When $\ell(\cdot)$ is a deviance loss, $\ell(z) = \log\{1 + \exp(-z)\}$, equation (5) is a logistic regression.
- When $\ell(\cdot)$ is a hinge loss, $\ell(z) = (1 - z)_+$, equation (5) is the support vector machine.

Fisher Consistency

Let $f^*(\cdot)$ be a classifier, and a function $g(\cdot,\cdot)$ is a map $g\{f^*(x), i\}$ from $x \in \mathcal{X}$ and $i \in \mathcal{A}$ to $\mathbb{R}$. The classification of x is $\widehat{a} = \arg\max_{\forall i} g\{f^*(x), i\}$. In our angle based classifier, $g\{f^*(x), i\} = \langle f^*(x), W_i \rangle$.

Definition (Fisher consistency)

A classifier $f^*(\cdot)$ is called Fisher's consistence if it satisfies that, $\forall x$,

$$\underset{\forall i}{\operatorname{argmax}} \Pr(A = i | X = x) = \underset{\forall j}{\operatorname{argmax}} \, g\{f^*(x), j\}.$$

Theorem (Fisher consistency for ABC)

The angle-based classifier from is Fisher consistency if ℓ is a convex, the derivative ℓ' exists and $\ell'(x) < 0, \forall x$.

Original objective function,

$$D_o \quad = \quad \underset{D \in R}{\operatorname{argmin}}\, n^{-1} \sum_{i=1}^{n} \frac{Y_i}{p(A_i|X_i)} I\left\{A_i \neq \mathcal{D}(X_i)\right\}.$$

ITR.ABC objective function,

$$\underset{f \in \mathcal{F}}{\text{minimize}} \quad \frac{1}{n} \sum_{i=1}^{n} \frac{Y_i}{\Pr(A_i|X_i)} \ell\{\langle f(x_i), W_{a_i}\rangle\} + \lambda J(f).$$

Theorem (Fisher consistency for ITR.ABC)

A classifier $f^*(\cdot)$ is called Fisher's consistence if it satisfies that, $\forall x$,

$$\underset{\forall j}{\operatorname{argmax}} \langle f^*(x), W_j\rangle \quad = \quad \underset{\forall j}{\operatorname{argmax}}\, E(Y|A=j,x)$$

ITR.ABC is Fisher consistency if ℓ is a convex, the derivative ℓ' exists and $\ell'(x) < 0, \forall x$.

Illustration Data: Survival Outcome with Censoring

Table 8: *An illustration dataset: with censoring.* $Y = T \wedge C$ and $\Delta = I(T \leq C)$.

ID	Y	Δ	Trt	X_1	X_2	X_3	$\cdots$
1	1.5	1	1	F	26	7.8	$\cdots$
2	1.0	0	2	M	28	8.2	$\cdots$
3	2.3	1	3	M	31	8.9	$\cdots$
4	0.8	0	2	F	35	9.4	$\cdots$
5	1.7	1	1	M	22	7.3	$\cdots$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$

Research Question

When some survival times are censored, based on these data, how we can learn a treatment assignment rule that, if followed by the entire population of certain patients, would lead to the best outcome on average.

Because,

$$E(T|A,X) = E\left[E\left\{\frac{T \cdot I(C > T)}{S_C(T|A,X)}\middle|A,X,T\right\}\right] = E\left\{\frac{\Delta \cdot Y}{S_C(Y|A,X)}\middle|A,X\right\},$$

we have,

$$\begin{aligned} L(\mathcal{D}) &\triangleq E\left[\frac{I\{A \neq \mathcal{D}(X)\}}{p(A|X)}T\right] \\ &= E\left[\frac{I\{A \neq \mathcal{D}(X)\}}{p(A|X)}E(T|A,X)\right] \\ &= E\left[\frac{I\{A \neq \mathcal{D}(X)\}\Delta Y}{p(A|X)S_C(Y|A,X)}\right]. \end{aligned} \tag{6}$$

Intuitive motivations

What if my model is wrong ...

- We often assume independent and noninformative censoring in analyzing survival outcomes (e.g. Cox model).
- Therefore, censoring event time and survival event time can be modeled separately.
- When event times or censoring times are rare, we may not be very confident to model both event time and censoring time right.
- It will be great that my method is right, if I can get at least one model is correct although I am not sure which one is correct.
- Let us use notations with superscript m to denote a proposed model (which may not be the true model).
- Now we propose our doubly robust estimator as ...

Doubly Robust Estimator

$$L^m(\mathcal{D}) \triangleq E\left(\left[\frac{\Delta \cdot Y}{S_C^m(Y|A,X)} + \int E^m(T|T>t,A,X)\right.\right.$$
$$\left.\left.\left\{\frac{dN_C(t)}{S_C^m(t|A,X)} + I(Y \geq t)\frac{dS_C^m(t|A,X)}{S_C^m(t|A,X)^2}\right\}\right]\frac{I\left\{A \neq \mathcal{D}(X)\right\}}{p(A|X)}\right) \tag{7}$$

Theorem (Doubly Robust)

We have $L^m(\mathcal{D}) = L(\mathcal{D})$, if one of the following two condition holds,

1. $S_C^m(t|A,X) = S_C(t|A,X)$,
2. $E^m(T|T>t,A,X) = E(T|T>t,A,X)$.

ITR.Survival

Original objective function,

$$D_o = \underset{D \in R}{\operatorname{argmin}} \, n^{-1} \sum_{i=1}^{n} \frac{T_i}{p(A_i|X_i)} I\left\{A_i \neq \mathcal{D}(X_i)\right\}.$$

ITR.ABC objective function,

$$\underset{f \in \mathcal{F}}{\text{minimize}} \quad \frac{1}{n} \sum_{i=1}^{n} \frac{T_i}{\Pr(A_i|X_i)} \ell\{\langle f(x_i), W_{a_i} \rangle\} + \lambda J(f).$$

Definition (ITR.Survival)

$$L_n^m(f) \triangleq \frac{1}{n} \sum_{i=1}^{n} \left(\left[\frac{\Delta_i \cdot Y_i}{S_C^m(Y_i|A_i, X_i)} + \int E^m(T|T > t, A_i, X_i) \left\{ \frac{dN_C(t)}{S_C^m(t|A_i, X_i)} + I(Y_i \geq t) \frac{dS_C^m(t|A_i, X_i)}{S_C^m(t|A_i, X_i)^2} \right\} \right] \frac{\ell\{< f(x_i), W_{a_i} >\}}{p(A|X)} \right) + \lambda J(f)$$

Fisher Consistency for ITR.Survival

Theorem (Fisher consistency for ITR.Survival)

A classifier $f^*(\cdot)$ is called Fisher's consistence if it satisfies that, $\forall x$,

$$\underset{\forall j}{\operatorname{argmax}} \langle f^*(x), W_j \rangle = \underset{\forall j}{\operatorname{argmax}} \, E(T | A = j, x)$$

ITR.Survival is Fisher consistency if ℓ is a convex, the derivative ℓ' exists and $\ell'(x) < 0, \forall x$.

Summary

1. Precision Medicine
2. Individualized Treatment Recommendation Framework
3. ITR and Outcome Weighted Learning
4. ITR.ABC