# Robust Estimation Individualised Treatment Rules Survival Data

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## Precision Medicine

**Motivation:** Patients with same disease exhibit different treatment responses

**RCT Data:**

- $N$ Small Sample Size
- $X_i$ medical history of patient $i$
- $A_i \in \{+1, -1\}$ Assigned treatment
- $Y(A = a)$ Observed outcome
- $Y(A \neq a)$ Counterfactual outcomes
- $\Delta$ Right-Censored Status

**Goal:** Find Optimal rule $\mathcal{D}*$ to maximize value func restricted mean survival time

$$D^* = \arg\max_{\mathcal{D}} E^D[Y]$$

## Treatment Rule Estimation

**Homogenous** "one-size-fits-all"

$$\arg\max_{D} E[Y(X, D)]$$

**Regression:** $Q(X, A, \beta)$ = hazard-based regression (e.g. Cox, AFT). if mis-pecified, convergance not guaranteed.

$$V_Q(d^*) = E\left\{\max_{a \in \mathbb{A}} Q(X, a; \beta)\right\}$$

**Inverse Probability Weighting:**

$$E[Y] = n^{-1} \sum_{i=1}^{n} \frac{Y_i}{\pi(A_i|X_i)}$$

## Outcome Weighted Learning

- Minimize Empirical Risk via SVM Classification. Minimize Assumptions
- Linear Decision Rule: Interpretability, Inference, & Rate of Converge $n^{-1/2}$

$$D^* \in \arg\max_{\mathcal{D}} E^D(Y)$$

1. **Outcome Weighted Learning (OWL)** Zhao et al. (2012)

$$V(D) = \mathbb{E}\left[Y \times \frac{\mathbb{I}(A = \mathcal{D}(X))}{\pi(A|X)}\right]$$

2. **Inverse Censoring Outcome (ICO)** Zhao et al. (2015) account for right-censored outcomes by weighting

$$V(D) = \mathbb{E}\left[\frac{\Delta_i T}{\hat{S}_c(Y|A, X)} \times \frac{\mathbb{I}(A = \mathcal{D}(X))}{\pi(A; X)})\right]$$

3. **Multistate (MSOWL)** Bakoyannis (2023) Fisher consistent estimates include censored data directly. Computational Cost: $\mathcal{O}(n^3)$; Divide & Conq $\mathcal{O}(n)$

$$V(D) = \mathbb{E}\left(\left[\int_0^\tau \frac{Y(t) I(C \geq (T_i \wedge t))}{S_c(\tilde{T} \wedge t))} dm(t)\right] \times \frac{\mathbb{I}(A_i = \mathcal{D}(X))}{\pi(A; X)}\right)$$

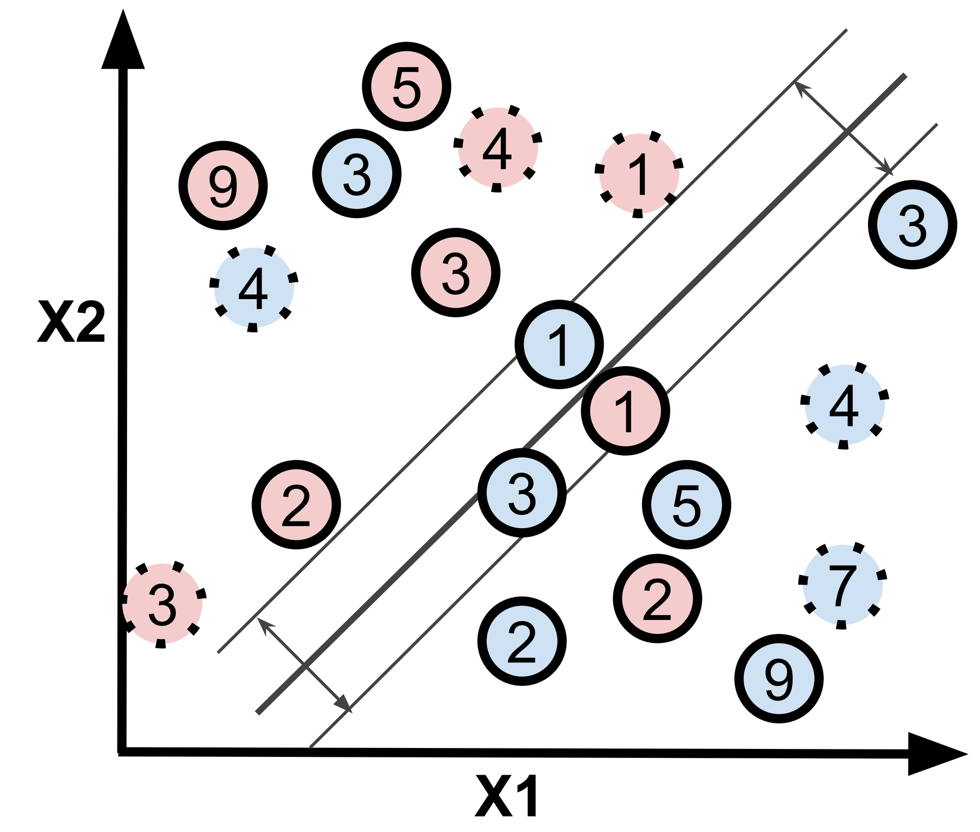


**Fig 1: OWL SVM** Dashed: Censored, Solid: Uncensored. Red/Blue: True Optimal Treatment. Numbers: Miss cost

## Real Clinical Data

- Douillard et al. (2010) Colorectal Cancer, Chemo vs immunotherapy.
- Immunotherapy delayed treatment response => Hazards Not Proportional.
- Preliminary results: MSOWL vs one-size-fits-all Progression-Free Survival

| | estimate | SE | ll | ul |
|---|---|---|---|---|
| V(dn) | 12.30 | 0.60 | 11.10 | 13.50 |
| V(1) | 11.60 | 0.40 | 10.70 | 12.40 |
| V(-1) | 11.20 | 0.50 | 10.30 | 12.10 |
| V(dn) - V(1) | 0.80 | NA | -0.30 | 1.80 |
| V(dn) - V(-1) | 1.10 | NA | -0.10 | 2.30 |

Table 6.3: PRIME PFS: Estimated Value (Months)

## Discussion

- Law of Total Probability => Consistency of IPW and Div&Conq
- Optimal ITR can outperform Homogenous Treatment value while sparing some patients from aggressive treatment
- Future: Multi-objective optimisation of aggressive treatment & adverse events

### References

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