An Information Criterion for Marginal Structural Models

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Marginal Structural Models

Model marginal expectation as a function of time-varying exposure as a function of pre-defined time-varying treatment plans

- $E[Y_{X(t)}(t)] = f(X(t))$
- $Y_{X(t)}(t)$ potential outcome at time $t$
- $X(t)$ history of exposure $X$ to time $t$
- Let $Z$ denote a vector of covariates; $Z(t)$ represents $Z$ at time $t$, $Z(t)$ history to $t$.
- Interpretation: expected $Y(t)$ if all subjects followed $X(t)$. 
Marginal Structural Models - Simple Example

Model marginal expectation as a function of time-varying exposure as a function of pre-defined time-varying treatment plans

- $X_0$, $X_1$ two binary treatments
- Four possible treatment histories: $(0, 0), (1, 0), (0, 1), (1, 1)$
- an MSM models expected (average) outcome for each possible treatment history if ALL subjects were to follow that history
- e.g., $E[Y_{(1,1)}]$ is the average outcome if ALL subjects (possibly contrary to fact) were to receive $X_0 = 1, X_1 = 1$. 
Assumptions

- No unmeasured confounding

\[ Y_{X(t)}(t) \perp\!
\perp X(t) \mid X(t-1), Z(t) \]  \hspace{1cm} (1)

- Treatment at \( t \) is independent of potential outcomes given history of treatment and covariates;
- each treatment change is randomized given history

- Experimental treatment assumption - \( P(\overline{X}) \) is nonzero for all possible treatment histories.

- Every possible treatment history must have positive probability
Estimation

- Robins 1998, 1999, Hernán and Robins 2006: \( E[Y_{\overline{X}(t)}(t)] \) is the unique solution to the estimating equation

\[
E[q(\overline{x(t)))(Y - c(\overline{x(t)))}/w(t)]
\]

where

\[
w(t) = \prod_{i=0}^{t} P(X(i) = x(i) | \overline{X(i-1)}, \overline{Z(i)})
\]

ie inverse probability of treatment received given history of treatment and covariates, and \( q \) is any function.

- Requires model for \( w(t) \).
  - Robins 1998: \( \hat{w} \) must converge to \( w \) at rate \( n^{1/4} \).
Previous Work

Specification of model for $w$

- Must include confounders
- May include predictors of outcome
- Should not include predictors of treatment (instruments)
- Should account for time-modified confounders
- What about the outcome model?
Outcome Model

Specification of model for $Y$

- Typically some function of the exposure
- Most HIV examples have used $\text{cum}(X)$ - total amount of treatment received
- Has led to misconception that this functional form is part of the MSM!
- Functional form should reflect causal question under study
- What if uncertainty exists re causal question?
Outcome Model

- Could try multiple models
- How to evaluate/compare?
- Adjusted $R^2$?
- Some kind of information criterion?
Simple case: two time-point MSM

Let

- $\mathcal{X}$ denote a set of treatments that can be applied at any point in time, $x_1, x_2$ be a sequence of treatments
- $Y_{x_1, x_2}$ be a counterfactual outcome corresponding to a sequence of treatments, and
- $S = Y_{x_1, x_2}, (x_1, x_2) \in \mathcal{X}^2$ be the set of counterfactual outcomes corresponding to all possible treatment sequences.
- Let $X(t)$ denote the observed treatment at time $t$,
- $\bar{L}(t)$ denote the history of all covariates up to time $t$,
- $V \subset L(1)$ be some baseline covariates upon we which to condition.
Two time-point MSM

- Interested in estimating the conditional expectation of the counterfactual given $V$: $E[Y_{x_1,x_2}|V]$.
- If for each subject, we observed all counterfactual outcomes, $S$, one could fit a model $m(x_1, x_2, V)$ of $E[Y_{x_1,x_2}|V]$ directly.
- For example, $m(x_1, x_2, V) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$.
- Given a set of competing models that have been fit to the data, $\hat{m}_i, 1 \ldots I$, can we develop an information criterion?
QIC

We assume that the weight model \( w \) is correctly specified, and that it is constant across candidate \( m_i \).
In the full (partially unobserved) data, we propose

\[
QIC(\hat{m}) = 2p - \frac{1}{n} \sum_{i=1}^{n} \sum_{x_1, x_2 \in X^2} (Y_{(x_1, x_2),i} - \hat{m}(x_1, x_2, V_i))^2,
\]

where \( p \) is the number of free parameters in the model.
With only the observed data, we choose the model that maximizes the inverse-probability weighted quasi-likelihood information criterion:

\[
QIC_W(\hat{m}) = 2p - \frac{1}{n} \sum_{i=1}^{n} \frac{(Y_i - \hat{m}(X(1)_i, X(2)_i, V_i))^2}{P(X_i(2)=x_i(2)|L_i(2), X_i(1))P(X_i(1)=x_i(1)|L_i(1))} \tag{4}
\]
It is straightforward to show that

\[ QIC_W(\hat{m}) = QIC(\hat{m}) \]

in the two time-point setting. This extends easily to more complicated models.
Simulations - Design

- 4 time points $i = 1, \ldots, 4$
- Treatment $T_i$, confounder $L_i$ generated as:
  - $L_1 \sim N(10, 1)$
  - $T_i \sim Bin(p_i)$ where $p_i$ a function of $L_i$ and $T_{i=1}$
- $Y$ Normal, function of $T_i$. 
Simulations - Design

- 5 scenarios (others under consideration)
- 3 sample sizes
- Fit "full", "null", and "reduced" model (including only $T_1$ and $T_2$)
Simulations - Results

- Simpler models: $QIC_w$ selects correct or over-fit model, adj. $R^2$ under-fit
- More complex models: $QIC_w$ selects correct model, adj. $R^2$ under-fit
  - When all coefficients nonzero, $QIC_w$ selects correct model 85-100% of the time
  - Adj. $R^2$ selects reduced model most of the time
- Performance improves with sample size.
PROBIT

- Breastfeeding promotion intervention
- 17,045 subjects
- Followed at 0, 1, 2, 3, 6, 9, 12 months
- All mothers intended to breastfeed
- We considered models for weight at 12 mos as a function of breastfeeding duration
Considered four models ($M =$ months breastfed)

- **Linear** $E[Y_{12}] = \beta_0 + \beta_1 \times M$
- **Quadratic** $E[Y_{12}] = \beta_0 + \beta_1 \times M + \beta_2 M^2$
- **Cubic** $E[Y_{12}] = \beta_0 + \beta_1 \times M + \beta_2 M^2 + \beta_3 M^3$
- “saturated” model with dummy variable for each time point
Results

Figure: Plot of weight as function of months BF; shaded area confidence band for saturated model
## Results II

<table>
<thead>
<tr>
<th>Model</th>
<th>No. parms</th>
<th>$QIC_w$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated</td>
<td>7</td>
<td>16,776</td>
</tr>
<tr>
<td>Linear exposure</td>
<td>2</td>
<td>16,784</td>
</tr>
<tr>
<td>Quadratic exposure</td>
<td>3</td>
<td>16,786</td>
</tr>
<tr>
<td>Cubic exposure</td>
<td>4</td>
<td>16,775</td>
</tr>
</tbody>
</table>
CD4 and HIV treatment

- Selected a model with a piecewise linear function
- linear from 0-1 year, and linear after 1 year.
- Is this best model?
# Results

<table>
<thead>
<tr>
<th>Model</th>
<th>No. parms</th>
<th>$QIC_w$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Intercept</td>
<td>1</td>
<td>931.77</td>
</tr>
<tr>
<td>2. Intercept and time a</td>
<td>5</td>
<td>496.94</td>
</tr>
<tr>
<td>3. Model 2 + linear exposure</td>
<td>6</td>
<td>482.11</td>
</tr>
<tr>
<td>4. Model 2 + curvilinear exposure</td>
<td>7</td>
<td>481.57</td>
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<tr>
<td>5. Model 2 + 2-part linear exposure</td>
<td>7</td>
<td>480.92</td>
</tr>
<tr>
<td>6. Model 2 + per visit (Saturated model)</td>
<td>25</td>
<td>516.58</td>
</tr>
</tbody>
</table>
Conclusions

- QIC appears to provide useful information for model selection
- Simulations: selects richer model
- Examples: chooses interesting models/provides insight
Limitations

- Proof (and simulations) assume weight model correctly specified
- No joint modeling/information criterion
- Assumes IPTW fitting of models
Future Work

- Joint modeling of weight and outcome: optimization criteria?
- Targeted Maximum Likelihood?
- Machine-learning orientation?
Thanks!

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