Establishing An Optimal Individualized Treatment Rule for Pediatric Anxiety with Longitudinal Modeling for Evaluation

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Background

An Individualized Treatment Rule (ITR) is a special case of dynamic treatment regimen when there is a single decision rule. This rule inputs information about a patient and recommends a treatment based on this information.

We propose a four-step analytic strategy:

Step 1. Split the data for training (70%) and evaluation (30%) • Ensure the two datasets are balanced by treatment assignment (CBT vs SRT) and baseline severity level (baseline PARS)

Step 2. Prune the 67 baseline covariates based on their potential for a qualitative interaction with treatment (score $U_j$), using a specialized variable screening algorithm for subset analysis with the training dataset (Gunter, et al. 2011)

• Let $A = (0, 1)$ denote treatment; let $R$ denote the outcome (PARS); let $a^* = \text{argmax}_a \hat{E}[R|A=a]$ be the best treatment on average
• For each covariate $X_j$ calculate the score $U_j$:

$D_j = (\max_a \log \frac{\hat{E}[R|X_j=x_{ij}, A=a]}{\hat{E}[R|X_j=x_{ij}, A \neq a]} - \min_a \log \frac{\hat{E}[R|X_j=x_{ij}, A=a]}{\hat{E}[R|X_j=x_{ij}, A \neq a]})$

$U_j = \frac{1}{2} \sum_{a=1}^{2} (\max_a \min_{\hat{p}_k \neq \hat{p}_k} \log \frac{\hat{E}[R|X_j=x_{ij}, A=a]}{\hat{E}[R|X_j=x_{ij}, A \neq a]})$

• Create a score plot of $U_j$ scores; select cut-off at inflection point

Step 3. Generate the optimal ITR with the screened covariates, using a data-driven approach known as “Decision List” with the training dataset (Zhang, et al. 2015)

• Used the covariates left to the green line (high potential for a qualitative interaction with treatment) in Figure 2
• Simple class of ITR based on “if-then-else” statements

Visualizations (Figure 4) of patients’ proportions recommended to CBT group versus SRT group based on ITR facilitates meaningful exchange between data scientists and clinical scientists

Step 4. Evaluate the optimal ITR vs. only providing PBO, only providing SRT, only providing CBT, and providing COMB , using longitudinal analysis with the evaluation dataset

• Estimate mean PARS (higher PARS means the child/adolescent has higher severity level in anxiety disorders) through week 0 (start of the treatment) to week 12 (end of the treatment)

• Compare the longitudinal trajectories of ITR vs. SRT, CBT, COMB

Discussion

The optimal ITR (Figure 3) suggests only 2 covariates are significant for customized treatment plans: 1) children’s physical symptoms caused by anxiety disorder (PSCAVE_E); 2) children’s self-measured coping ability for their anxiety (CCOMMEAN_1). The longitudinal trajectories indicate IRT has non-inferiority pattern compared with SRT, CBT, COMB.