Multivariate Functional Data Analysis

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Outline

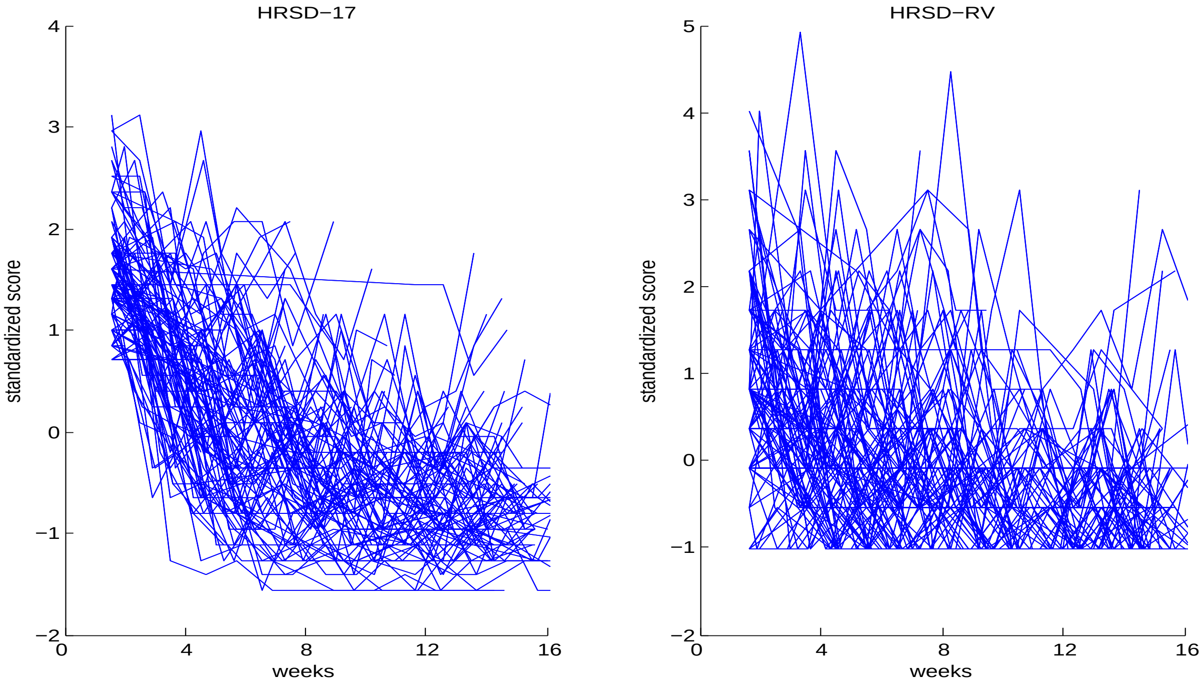
- Motivating example
- The model
- Estimation
- Example

Motivating Example

- Psychiatric study to compare psychotherapy to pharmacotherapy at the University of Pisa, Italy. Total of 103 acutely depressed subjects.

- Response variables: two subscales of the clinician-administered Hamilton Depression rating Scale.
  - HRSD-17 – measures anhedonia, sleep disturbance, agitation, anxiety, weight loss
  - HRSD-RV – measures reverse vegetative symptoms such as weight gain and hyperphagia

- Covariates: treatment group, lifetime depression spectrum


HRSD−17
standardized score
4
3
2
1
0
−1
−2
0
4
8
12
16
weeks
HRSD−RV
standardized score
5
4
3
2
1
0
−1
−2
0
4
8
12
16
weeks

The Model

$$\begin{aligned}
y_{i1}(t_{ij}) &= \boldsymbol{x}'_{ij}\boldsymbol{\mu_1}(t_{ij}) + \boldsymbol{z}'_{ij}\boldsymbol{g_{i1}}(t_{ij}) + \delta_{i1}(t_{ij}) \\
y_{i2}(t_{ij}) &= \boldsymbol{x}'_{ij}\boldsymbol{\mu_2}(t_{ij}) + \boldsymbol{z}'_{ij}\boldsymbol{g_{i2}}(t_{ij}) + \delta_{i2}(t_{ij}) \\
\vdots &= \vdots \\
y_{ip}(t_{ij}) &= \boldsymbol{x}'_{ij}\boldsymbol{\mu_p}(t_{ij}) + \boldsymbol{z}'_{ij}\boldsymbol{g_{ip}}(t_{ij}) + \delta_{ip}(t_{ij})
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\end{aligned}$$

- $\boldsymbol{\mu}_k(t) = (\mu_{k1}(t), \ldots, \mu_{kr}(t))'$ is an r-vector of fixed functions, $k = 1, \ldots, p$
- $\boldsymbol{g}_{ik}(t) = (g_{ik1}(t), \ldots, g_{iks}(t))'$ is an s-vector of random functions, $k = 1, \ldots, p$

The Model (Cont.)

$$\boldsymbol{y}_i(t_{ij}) = X_{ij}\boldsymbol{\mu}(t_{ij}) + Z_{ij}\boldsymbol{g_i}(t_{ij}) + \boldsymbol{\delta}_i(t_{ij}) \ ,$$

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- $X_{ij} = I_p \otimes \boldsymbol{x}_{ij}'$, $Z_{ij} = I_p \otimes \boldsymbol{z}_{ij}'$.
- $\boldsymbol{\delta}_i(t_{ij}) = (\delta_{i1}(t_{ij}), \ldots, \delta_{ip}(t_{ij}))'$

Example

Assume 2 groups of subjects and a bivariate response ($p = 2$):

$\boldsymbol{x}_{ij} = (x_{ij1}, x_{ij2})'$, where $x_{ij1} = 1, \quad x_{ij2} = \begin{cases} 1 & \text{if} \quad \text{treatment} \\ 0 & \text{if} \quad \text{control} \end{cases}$

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$$\begin{aligned} y_{i1}(t_{ij}) &= (1 \quad x_{ij2}) \begin{pmatrix} \mu_{11}(t_{ij}) \\ \mu_{12}(t_{ij}) \end{pmatrix} + g_{i1}(t_{ij}) + \delta_{i1}(t_{ij}) \\ y_{i2}(t_{ij}) &= (1 \quad x_{ij2}) \begin{pmatrix} \mu_{21}(t_{ij}) \\ \mu_{22}(t_{ij}) \end{pmatrix} + g_{i2}(t_{ij}) + \delta_{i2}(t_{ij}) \end{aligned}$$

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\end{aligned}
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The Error Term

$\boldsymbol{\delta}_i(t)$ follows a multivariate Ornstein-Uhlenbeck (O-U) process, i.e.,

$$d\boldsymbol{\delta}_i(t) = -A\boldsymbol{\delta}_i(t) + Bd\boldsymbol{W}_i(t) \ .$$

- A and B are $p \times p$ matrices of full rank common to all $i = 1, \ldots, n$,
- $\boldsymbol{W}_i(t)$ is the p-dimensional Wiener process.
- Stationary if the EV of A have positive real parts.
- The stationary variance-covariance matrix Σ is the solution to

$$A\Sigma + \Sigma A' = BB'$$

The Error Term (Cont.)

In the stationary state, for $s < t$

$$\mathbb{C}\mathrm{ov}(\boldsymbol{\delta}_i(t), \boldsymbol{\delta}_i(s)) = \exp\{-A(t-s)\}\Sigma \ ,$$

so A controls how rapidly the influence of time s dies off by time $t > s$.

The Transition Density

Let $\Delta t_{ij} = t_{ij} - t_{i,j-1}\ j = 1, \ldots, m_i$, $t_{i0} = 0$.

The transition density of the O-U process is given by

$$p(\boldsymbol{\delta}_i(t_{ij}) | \boldsymbol{\delta}_i(t_{i,j-1}), \Delta t_{ij}) \propto |\Omega_{\Delta t_{ij}}|^{-1/2} \exp\left\{ -\frac{1}{2} \boldsymbol{\gamma}'_{t_{ij}} \Omega^{-1}_{\Delta t_{ij}} \boldsymbol{\gamma}_{t_{ij}} \right\} \ ,$$

where

$$\begin{aligned} \boldsymbol{\gamma}_{t_{ij}} &= \boldsymbol{\delta}_i(t_{ij}) - \exp(-A\Delta t_{ij}) \boldsymbol{\delta}_i(t_{i,j-1}) \\ \Omega_{\Delta t_{ij}} &= \Sigma - \exp(-A\Delta t_{ij}) \Sigma \exp(-A'\Delta t_{ij}). \end{aligned}$$

Nonparametric Function Estimation– Simple Example

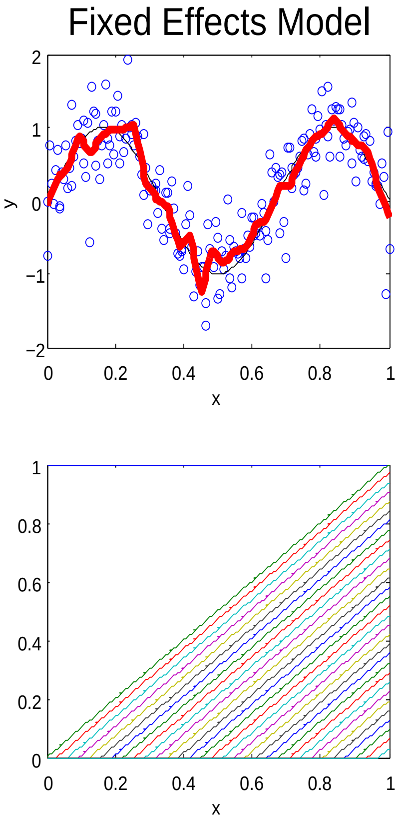
200 observations were generated from

$$y_i = \sin(3\pi x_i) + \epsilon_i, \quad , 0 \leq x_i \leq 1, \quad \epsilon_i \sim N(0, 0.4^2)$$

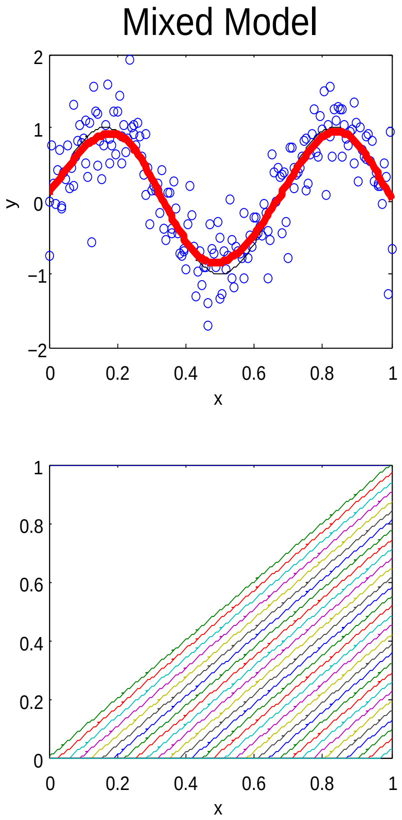
Model:

$$y_i = \beta_0 + \beta_1 x_i + \sum_{k=1}^{30} u_k (x_i - \kappa_k)_+ + \epsilon_i, \quad \epsilon_i \sim N(0, \sigma_\epsilon^2)$$

- Low rank truncated line basis functions.
- Fixed effects: βs and us fixed.
- Mixed effects: βs fixed, $u_1, \ldots, u_{30} \overset{iid}{\sim} N(0, \sigma_u^2)$.



Fixed Effects Model



Mixed Model

Nonparametric Function Estimation (Cont.)

We estimate

$\mu_{kl}(t)$ and $g_{ikm}(t), k = 1, \ldots, p, l = 1, \ldots, r, m = 1, \ldots, s, i = 1, \ldots, n$

by cubic splines using low-rank radial basis functions (French et al., 2001, Ruppert et al., 2003):

Write $\mu_{kl}(t_{ij}) = \boldsymbol{\phi}'_{ij}\boldsymbol{\beta}_{kl} + \boldsymbol{\psi}'_{ij}\boldsymbol{v}_{kl}$ and $g_{ikm}(t_{ij}) = \boldsymbol{\phi}'_{ij}\boldsymbol{w}_{ikm} + \boldsymbol{\psi}'_{ij}\boldsymbol{u}_{ikm}$.

Nonparametric Function Estimation (Cont.)

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$\mu_{kl}(t)$ and $g_{ikm}(t), k = 1, \ldots, p, l = 1, \ldots, r, m = 1, \ldots, s, i = 1, \ldots, n$

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- Place K knots $\kappa_1, \ldots, \kappa_K$ at sample quantiles of t_{ij}.

Nonparametric Function Estimation (Cont.)

We estimate

$$\mu_{kl}(t) \quad \text{and} \quad g_{ikm}(t), k = 1, \ldots, p, l = 1, \ldots, r, m = 1, \ldots, s, i = 1, \ldots, n$$

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- Place K knots $\kappa_1, \ldots, \kappa_K$ at sample quantiles of t_{ij}.
- Let $\boldsymbol{\phi}'_{ij} = (1 \quad t_{ij})$, $\boldsymbol{\xi}'_{ij} = (|t_{ij} - \kappa_1|^3, \ldots, |t_{ij} - \kappa_K|^3)$,
- Compute $\Lambda_K = [|\kappa_k - \kappa_{k'}|^3]_{1 \le k, k' \le K}$ and $\boldsymbol{\psi}'_{ij} = \boldsymbol{\xi}'_{ij}\Lambda_K^{-1/2}$ (via SVD)

Prior Distributions

Priors on the basis function coefficients:

1. Flat priors on $\boldsymbol{\beta}_{kl}$.
2. $\boldsymbol{v}_{kl} \overset{ind}{\sim} N(\mathbf{0}, \sigma^2_{v_{kl}} I_K)$
3. $\boldsymbol{w}_{ikm} \overset{ind}{\sim} N(\mathbf{0}, \text{diag}(\sigma^2_{w_{km0}}, \sigma^2_{w_{km1}}))$.
4. $\boldsymbol{u}_{ikm} \overset{ind}{\sim} N(\mathbf{0}, \sigma^2_{u_{km}} I_K)$.

Priors on the variance components:
independent $IG(a_i, b_i)$, e.g., $p(\sigma^2_{v_{kl}}) \propto (\sigma^2_{v_{kl}})^{-(a_1+1)} \exp(-b_1/\sigma^2_{v_{kl}})$

Prior Distributions (Cont.)

Prior on A:

- Let $A = S\Psi S^{-1}$, where

$$S = \begin{pmatrix} 1 & s_{12} & s_{13} & \dots & s_{1p} \\ s_{21} & 1 & s_{23} & \dots & s_{2p} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ s_{p1} & s_{p2} & s_{p3} & \dots & 1 \end{pmatrix}$$

  and $\Psi = \text{diag}(\psi_1, \dots, \psi_p)$, $\psi_i > 0$, $i = 1, \dots, p$.

- $s_{ij} \sim N(0, \sigma_s^2)$, $\log \psi_i \sim N(0, \sigma_\psi^2)$

Prior Distributions (Cont.)

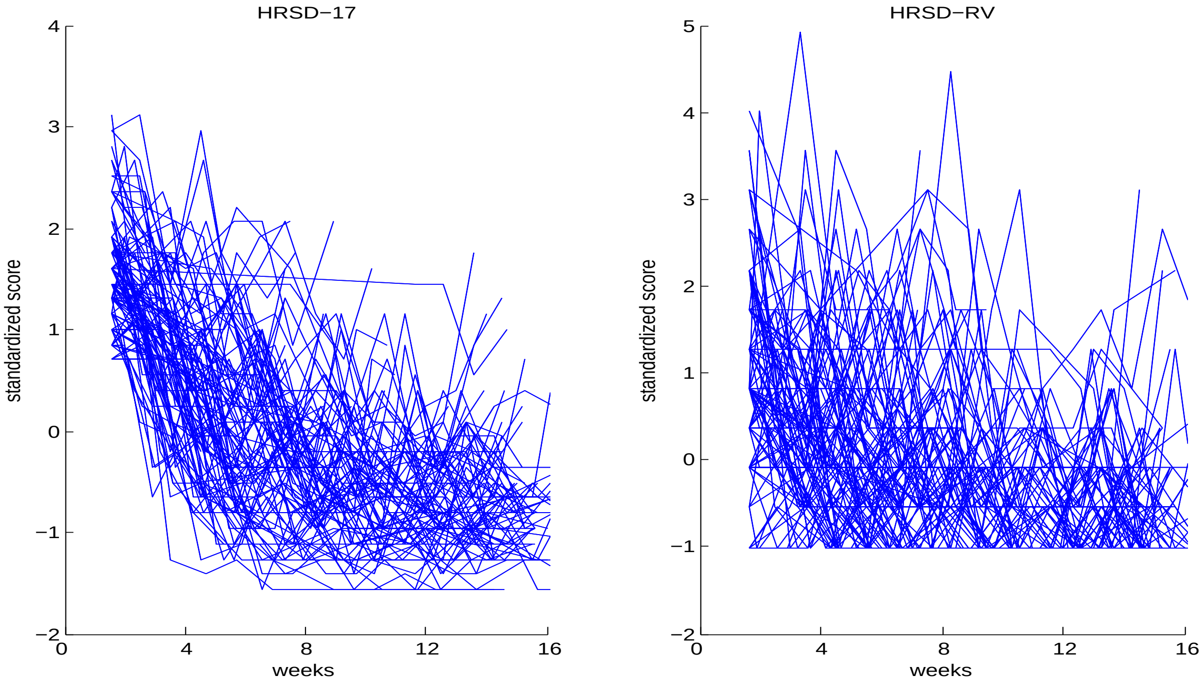
Prior on $C = BB'$:

- Let $C = LDL'$ (modified Cholesky factorization), where

$$L = \begin{pmatrix} 1 & 0 & 0 & \dots & 0 \\ l_{21} & 1 & 0 & \dots & 0 \\ l_{31} & l_{32} & 1 & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ l_{p1} & l_{p2} & l_{p3} & \dots & 1 \end{pmatrix}$$

  and $D = \text{diag}(d_1, \dots, d_p)$, $d_i > 0$, $i = 1, \dots, p$

- $l_{ij} \sim N(0, \sigma_L^2)$, $\log(d_i) \sim N(0, \sigma_D^2)$


HRSD−17
HRSD−RV
standardized score
standardized score
weeks
weeks
4
3
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1
0
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5
4
3
2
1
0
−1
−2
0
4
8
12
16
0
4
8
12
16

Example

- Psychiatric study to compare psychotherapy to pharmacotherapy at the University of Pisa, Italy. Total of 103 acutely depressed subjects.

- Response variables: 2 subscales of the clinician-administered Hamilton Depression rating Scale (measured at baseline and weekly):

  HRSD-17 (0–31)
  HRSD-RV (0–13).

  Higher values indicate more depressive symptoms.

- Covariates:

  treatment group
  lifetime depression spectrum (LDS), assessed at baseline.

Example (Cont.)

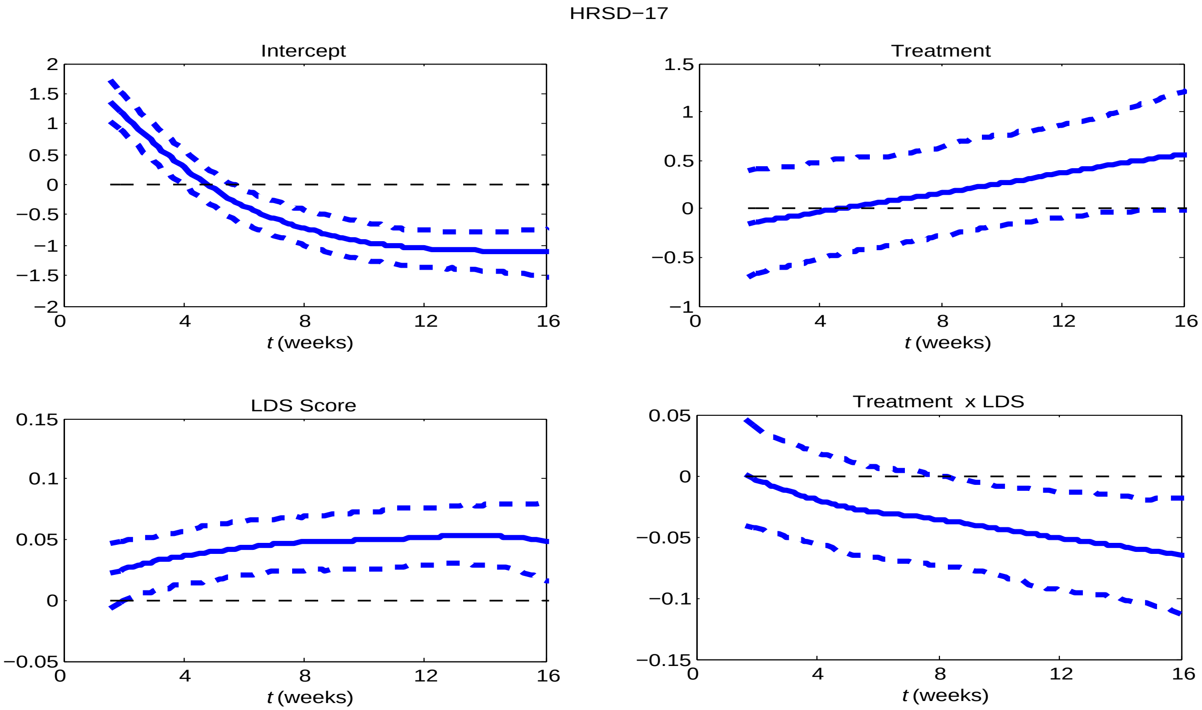
$$\boldsymbol{y}_i(t_{ij}) = X_{ij}\boldsymbol{\mu}(t_{ij}) + Z_{ij}\boldsymbol{g_i}(t_{ij}) + \boldsymbol{\delta}_i(t_{ij}) \ ,$$

where $X_{ij} = I_p \otimes \boldsymbol{x}'_{ij}$, $Z_{ij} = I_p \otimes \boldsymbol{z}'_{ij}$.

In the example $\boldsymbol{y}_i(t_{ij}) = (\text{HRSD-17}, \text{HRSD-RV})'$
$\boldsymbol{z}_{ij} = 1$
$\boldsymbol{x}_{ij} = (x_{ij1}, x_{ij2}, x_{ij3}, x_{ij4})'$
where $x_{ij1} = 1$

$$x_{ij2} = \begin{cases} 1 & \text{if subject } i \text{ received psychotherapy} \\ 0 & \text{if subject } i \text{ received pharmacotherapy,} \end{cases}$$

$x_{ij3} = \text{LDS score}$
$x_{ij4} = x_{ij2}x_{ij3}$.


HRSD−17
Intercept
2
1.5
1
0.5
0
−0.5
−1
−1.5
−2
0
4
8
12
16
t (weeks)
Treatment
1.5
1
0.5
0
−0.5
−1
0
4
8
12
16
t (weeks)
LDS Score
0.15
0.1
0.05
0
−0.05
0
4
8
12
16
t (weeks)
Treatment x LDS
0.05
0
−0.05
−0.1
−0.15
0
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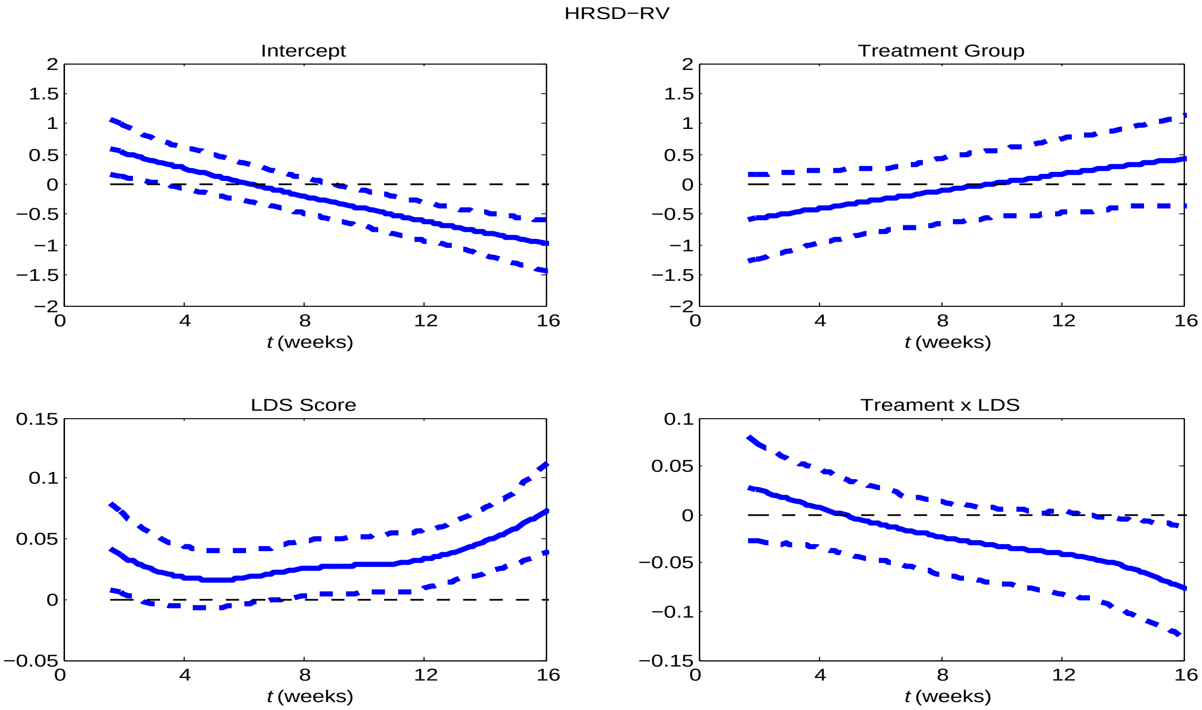
HRSD−RV

Intercept

Treatment Group

LDS Score

Treament x LDS

Conclusions from the Analysis

- Little evidence of a treatment effect
- Significant effect of LDS score – higher LDS predicts worse outcomes
- LDS effect is more pronounced in the middle period of HRSD-17, and towards the end of the 16 weeks for HRSD-RV.
- Interaction is significant in the last 8 weeks of HRSD-17, and marginally significant in the same time period for HRSD-RV.
- Interaction effect – LDS is less predictive of poor response in psychotherapy group than in pharmacotherapy group.
- Univariate fitting – interaction is not significant; wider pointwise credible intervals.