An estimation approach for time-varying effect models using cubic splines

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Overview

1. Motivation

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   - Simulation studies
   - Wisconsin Smoker’s Health Study

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Motivation

- Traditional mediation analysis typically examines the relations among an intervention, a time-invariant mediator, and a time-invariant outcome variable.
- Obtain repeated assessments over time resulting in intensive longitudinal data.
- Extend the traditional mediation analysis to incorporate time-varying variables as well as time-varying effects.
Time-varying coefficient models have been used to model the time-varying effects of an independent variable on a dependent variable.

For each individual, $i$

The outcome variables are measured at multiple time points $\{t_{ij}, j = 1, 2, \ldots, T_i\}$

The data collected are $\{t_{ij}, X_i(t_{ij}), Y_i(t_{ij})\}$, for $i = 1, 2, \ldots, n, j = 1, 2, \ldots, T_i$
Time-varying coefficient models

• Example:

\[ Y_{ij} = \beta_0(t_{ij}) + X_i(t_{ij})\beta_1(t_{ij}) + \epsilon_i(t_{ij}) , \]

where \( \beta_0(t) \) and \( \beta_1(t) \) are time-varying coefficient functions and are assumed to be smooth functions of time.

• The error term \( \epsilon_i(t) \) is a zero-mean stochastic process with covariance function, \( \gamma(s, t) \), between time \( s > 0 \) and \( t > 0 \).
Time-varying mediation models

- The model can be extended to the mediation model, and given below,

\[ Y_{ij} = \beta_0 Y(t_{ij}) + X_i(t_{ij})\gamma_1(t_{ij}) + M_i(t_{ij})\beta_2(t_{ij}) + \epsilon_i Y(t_{ij}) \]

\[ M_{ij} = \beta_0 M(t_{ij}) + X_i(t_{ij})\alpha_1(t_{ij}) + \epsilon_i M(t_{ij}) \]

- \( \gamma_1(t_{ij}) \) is the time-varying effect of an intervention, \( X \), on the outcome, \( Y \), that is not due to the mediator, \( M \)
- \( \beta_2(t_{ij}) \) is the time-varying effect of \( M \) on \( Y \)
- \( \alpha_1(t_{ij}) \) is the time-varying effect of \( X \) on \( M \)
Time-varying mediation models

• Define the time-varying indirect or mediated effect as $\alpha_1(t_{ij})\beta_2(t_{ij})$, the product of the two functions

• $\beta_{0Y}(t_{ij})$ and $\beta_{0M}(t_{ij})$ are the time-varying intercepts and $\epsilon_{iY}(t_{ij})$ and $\epsilon_{iM}(t_{ij})$ are the error terms in the model for $Y_{ij}$ and $M_{ij}$, respectively

• The two models are estimated simultaneously
Time-varying mediation models

- There are essentially two estimation approaches for time-varying effect models: splines and local smoothing methods.
- Local smoothing methods, which locally approximate coefficient functions by linear or polynomial functions.
- We focus on spline methods, specifically cubic spline.
Time-varying mediation models

- **Local smoothing methods**
  - Pros: Easy to use, less computation, acceptable results
  - Cons: Runge’s phenomenon

- **Cubic Spline**
  - A special case for spline interpolation
  - Global fit
  - Avoid Runge’s phenomenon
Results

- Simulation studies
- Wisconsin smoker’s health study
Simulation studies

Models:

1. $\alpha_1(t) = 10 + 12t^3$, $\gamma_1(t) = -20 - 18t$, $\beta_2(t) = 50 + 150t^2$, $\gamma(s, t) = 15 \exp(-0.3|s - t|)$

2. $\alpha_1(t) = 15 + 8.7 \sin(2\pi t)$, $\gamma_1(t) = 4 - 17(t - 1/2)^2$, $\beta_2(t) = 1 + 2t^2 + 11.3(1 - t)^3$, $\gamma(s, t) = 15 \exp(-0.3|s - t|)$
Simulation Model 1

Figure: Local polynomial smoothing and cubic spline interpolation for Model (1) with 10 equally spaced time points.
Simulation Model 1

Figure: Local polynomial smoothing and cubic spline interpolation for Model (1) with 10 equally spaced time points.

\[ \alpha_1(t - \delta t) \beta_2(t) \]
Simulation Model 2

\[ \alpha_1(t - \delta t) \beta_2(t) \]

Figure: Local polynomial smoothing and cubic spline interpolation for Model (2) with 10 equally spaced time points.
Simulation Model 2

Figure: Local polynomial smoothing and cubic spline interpolation for Model (2) with 10 equally spaced time points.
Performance of Simulation Models

• The mean absolute deviation error (MADE)

\[ \text{MADE} = (4T)^{-1} \sum_{j=1}^{T} \frac{|\theta(t_j) - \hat{\theta}(t_j)|}{\text{range}(\theta)}, \]

• The weighted average squared error (WASE)

\[ \text{WASE} = (4T)^{-1} \sum_{j=1}^{T} \frac{|\theta(t_j) - \hat{\theta}(t_j)|}{\text{range}^2(\theta)}. \]
MADE of Model 2

Figure: Local polynomial smoothing and cubic spline interpolation for Model (2) with 10 equally spaced time points.
WASE of Model 2

Figure: Local polynomial smoothing and cubic spline interpolation for Model (2) with 10 equally spaced time points.
Figure: Mediation effect of varenicline on cessation fatigue via craving using local polynomial smoothing.
Figure: Mediation effect of varenicline on cessation fatigue via craving using cubic spline interpolation.
Figure: Mediation effect of cNRT on cessation fatigue via craving using local polynomial smoothing.
Figure: Mediation effect of cNRT on cessation fatigue via craving using cubic spline interpolation.
Conclusions

- Propose an estimation approach for time-varying effect models via cubic spline interpolation
- Validated the proposed model which can be extended to other applications in which intensive longitudinal data
Thank You!