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

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Modern Modeling Methods Conference 2024

June 25, 2024

Credit: Office of Chancellor, CU Boulder

Overview

1. Motivation
2. Methods
3. Results
   - Simulation studies
   - Wisconsin Smoker's Health Study
4. Conclusions

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

- 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,

$$Y_{ij} = \beta_{0Y}(t_{ij}) + X_i(t_{ij})\gamma_1(t_{ij}) + M_i(t_{ij})\beta_2(t_{ij}) + \epsilon_{iY}(t_{ij})$$

$$M_{ij} = \beta_{0M}(t_{ij}) + X_i(t_{ij})\alpha_1(t_{ij}) + \epsilon_{iM}(t_{ij})$$

- $\gamma_1(t_{ij})$ 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

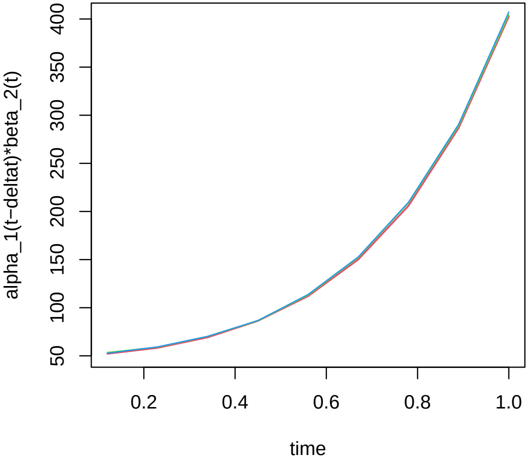
- Simulation studies
- Wisconsin smoker's health study

Simulation studies

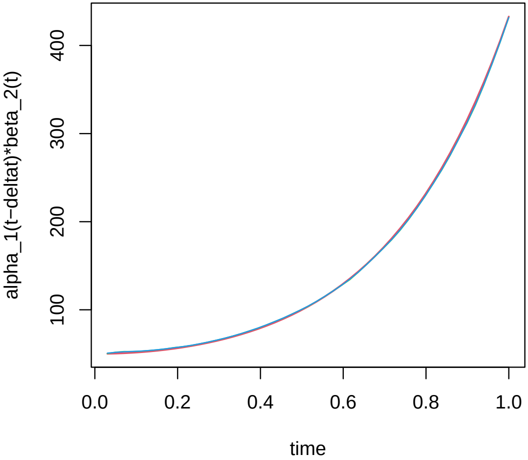
Models:

1. $\alpha_1(t) = 10 + 12t^3$, $\gamma_1(t) = -20 - 18t$, $\beta_2(t) = 50 + 150t^2$, $(s, t) = 15\exp(-0.3|s-t|)$
2. $\alpha_1(t) = 15 + 8.7\sin(2\pi t)$, $\gamma_1(t) = 4 - 17(t - 1/2)^2$, $\beta_2(t) = 1 + 2t^2 + 11.3(1-t)^3$, $\gamma(s, t) = 15\exp(-0.3|s-t|)$

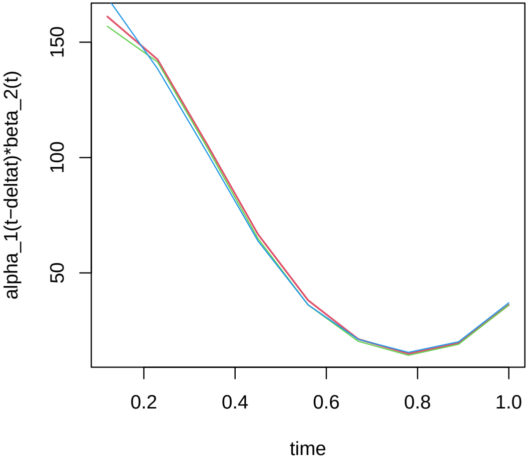
Simulation Model 1



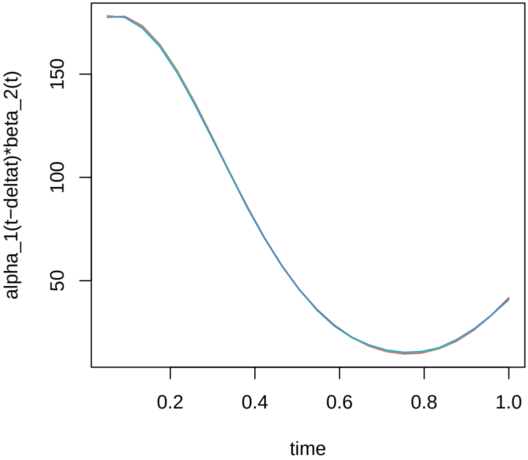
Simulation Model 1



Simulation Model 2



Simulation Model 2



Performance of Simulation Models

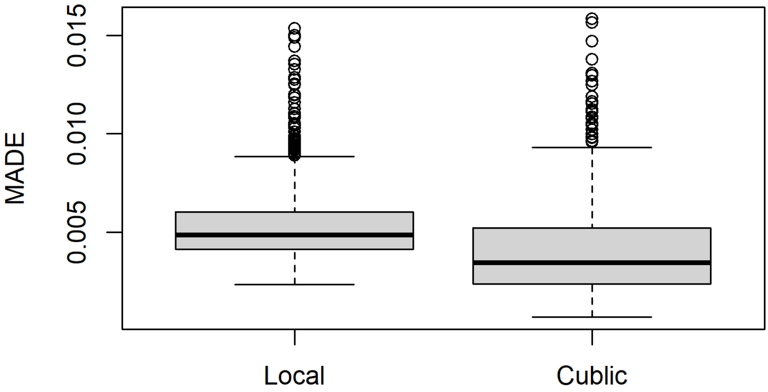
- The mean absolute deviation error (MADE)

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

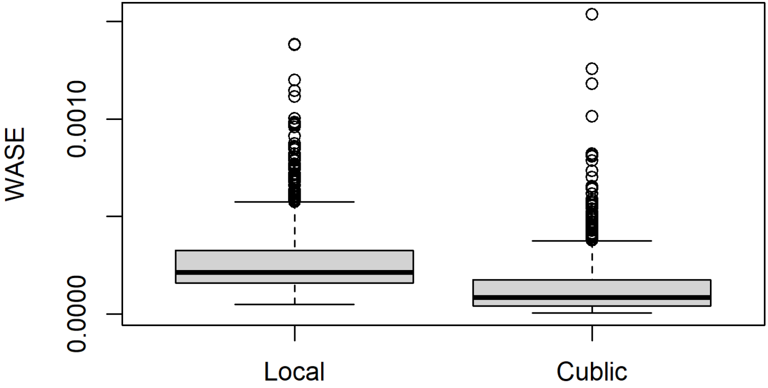
- The weighted average squared error (WASE)

$$WASE = (4T)^{-1} \sum_{j=1}^{T} \frac{|\theta(t_j) - \hat{\theta}(t_j)|}{\text{range}^2(\theta)}$$

MADE of Model 2



WASE of Model 2



Winsconsin Smoker's Health Study

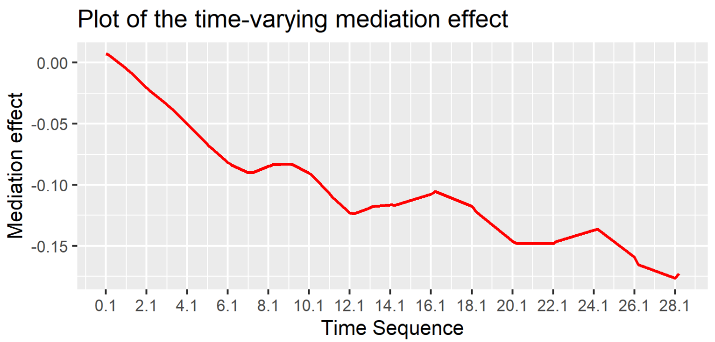


Figure: Mediation effect of varenicline on cessation fatigue via craving using local polynomial smoothing.

Winsconsin Smoker's Health Study

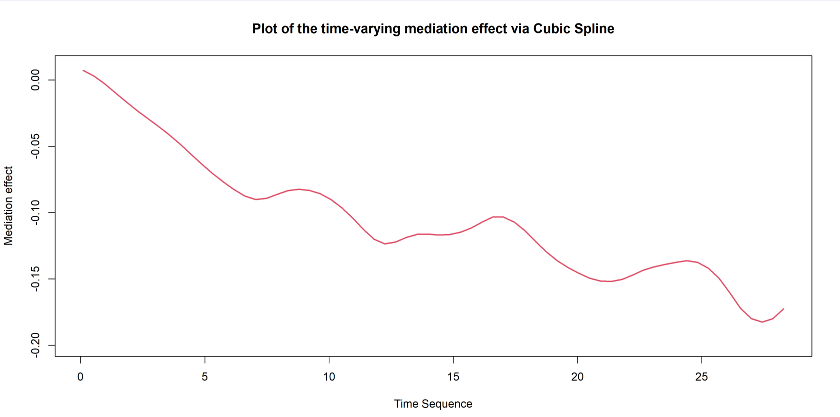


Figure: Mediation effect of varenicline on cessation fatigue via craving using cubic spline interpolation.

Winsconsin Smoker's Health Study

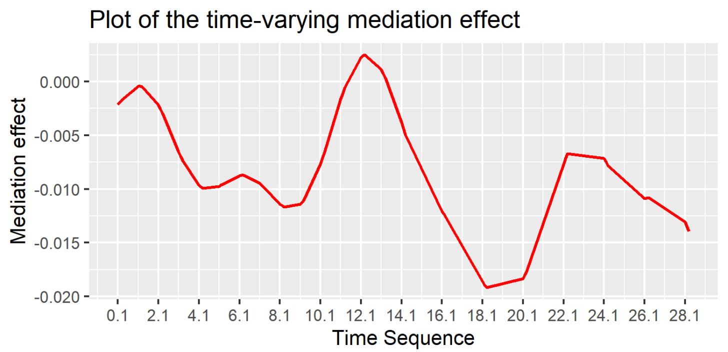


Figure: Mediation effect of cNRT on cessation fatigue via craving using local polynomial smoothing.

Winsconsin Smoker's Health Study

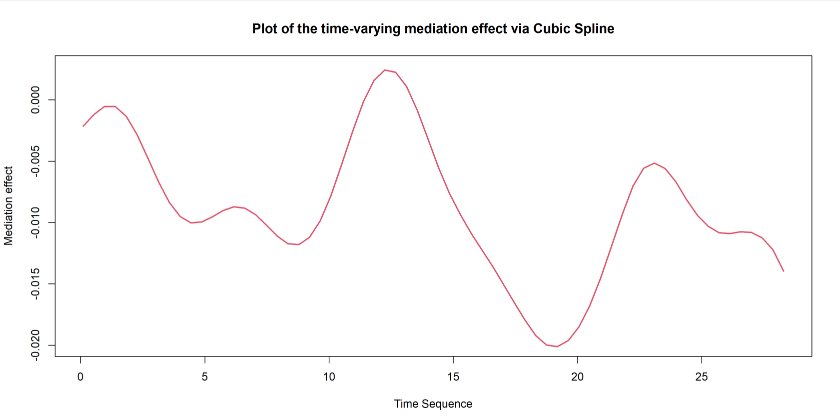


Figure: Mediation effect of cNRT on cessation fatigue via craving using cubic spline interpolation.

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!