State space model multiple imputation for missing data in non-stationary multivariate time series

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joint work with Xinru Wang, Justin Baker, J.P. Onnela, Linda Valeri

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mHealth

"mHealth is the use of mobile and wireless devices (cell phones, tablets, etc.) to improve health outcomes, health care services, and health research." – NIH

- Education and management of health care information
- Epidemic outbreak tracking
- Real-time monitoring of symptoms, life habits, digital social interactions for health management and early detection of a disease
- ...

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Opportunities of causal inference in mHealth

mHealth hold significant promise to improve long-term management and treatment for patients. However, the integration and translation of these cutting-edge technologies into rigorously evaluated health research have lagged behind.

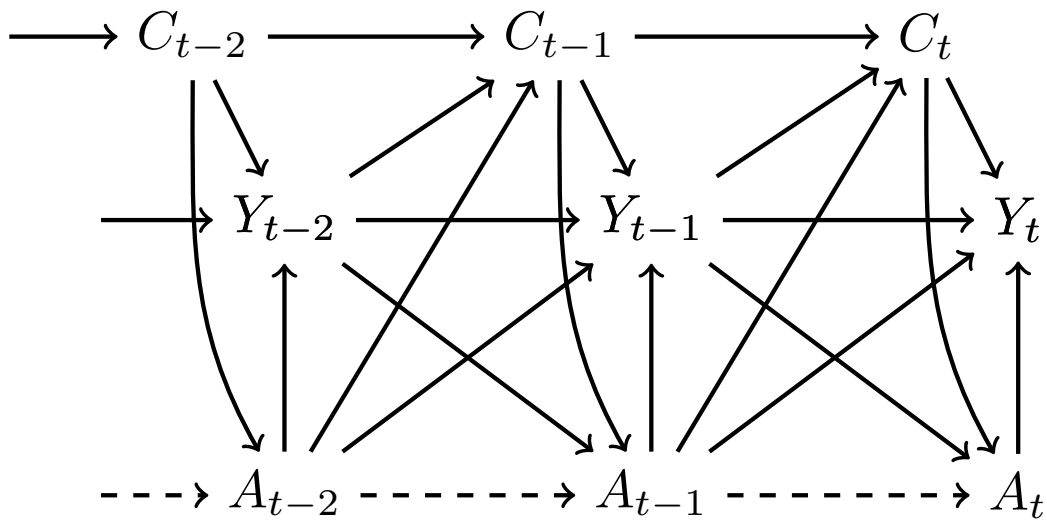
- Effective evaluation of dynamic exposure of intervention, mediation analysis, personalized treatment optimization, prediction, adaptive trial design, ...

Our research of interest

Evaluate the causal effect of social support on the improvement of mood in patients with serious mental illness in an observational n-of-1 trial.

Causal structure

- Outcome (Y_t): self-reported negative mood of the patient
- Exposure (A_t): social support (e.g., degree of calls and texts)
- Confounders (C_t): physical activity, medication, temperature, ...

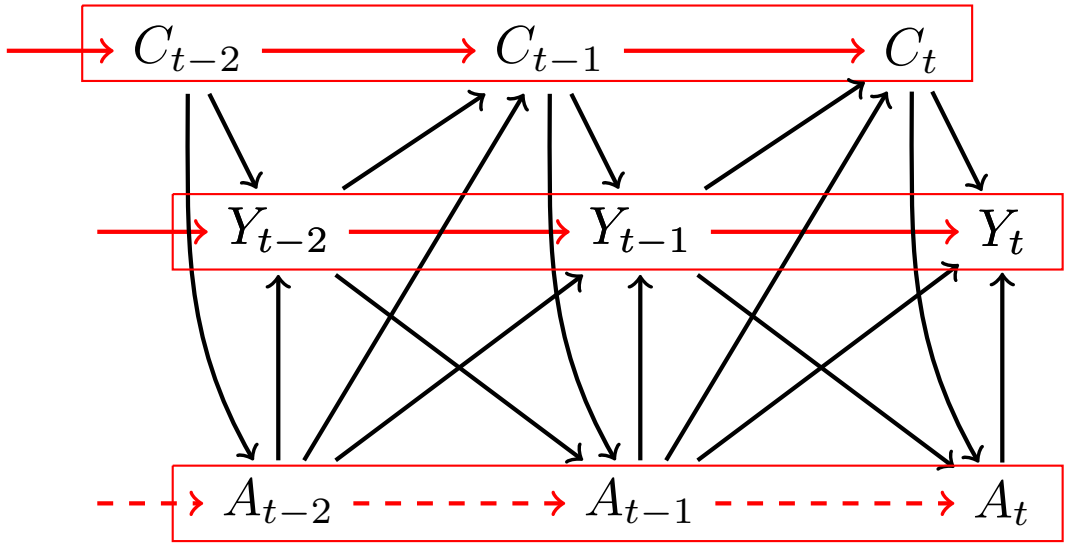


Causal effect: $\mathbb{E}[Y_t(A_t = 1)] - \mathbb{E}[Y_t(A_t = 0)]$

How to handle missing data for non-stationary time series?

Problem due to missing data in mHealth

Denote outcome as Y_t, exposure as A_t, and other confounders as C_t. Assume true data generation process as



1. High-autocorrelation with lagged values of the variables (Y_t, X_t, C_t) for $t = 1, \ldots, T$ constitute multivariate time series of outcome, exposure and covariates.
2. Elevated missing rate due to including previous values of variables

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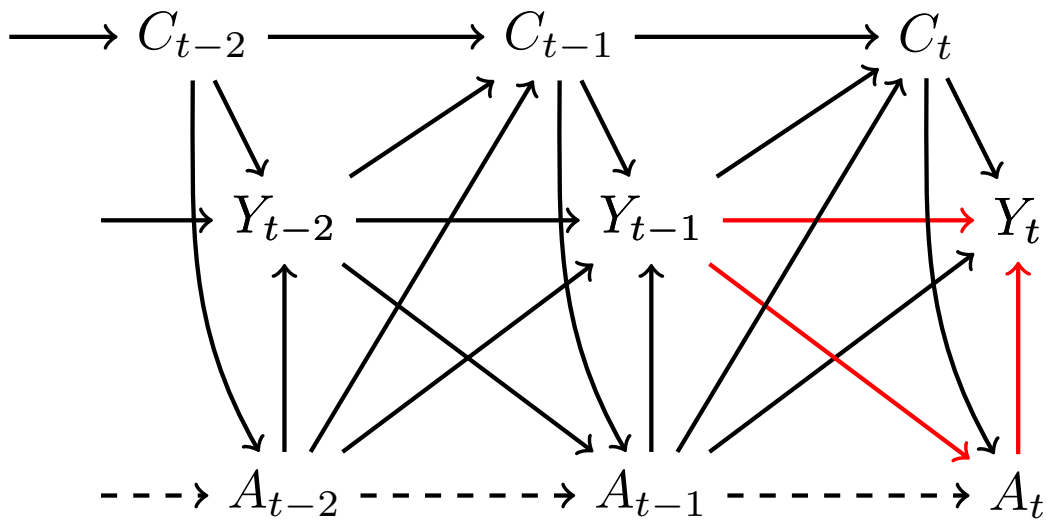
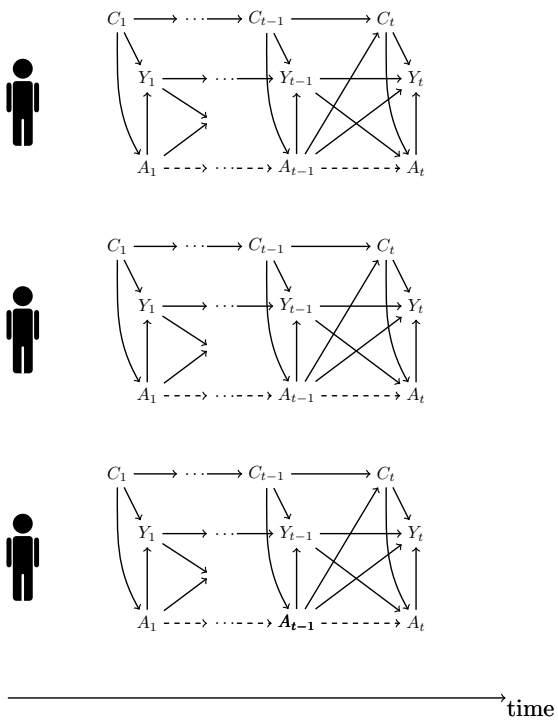


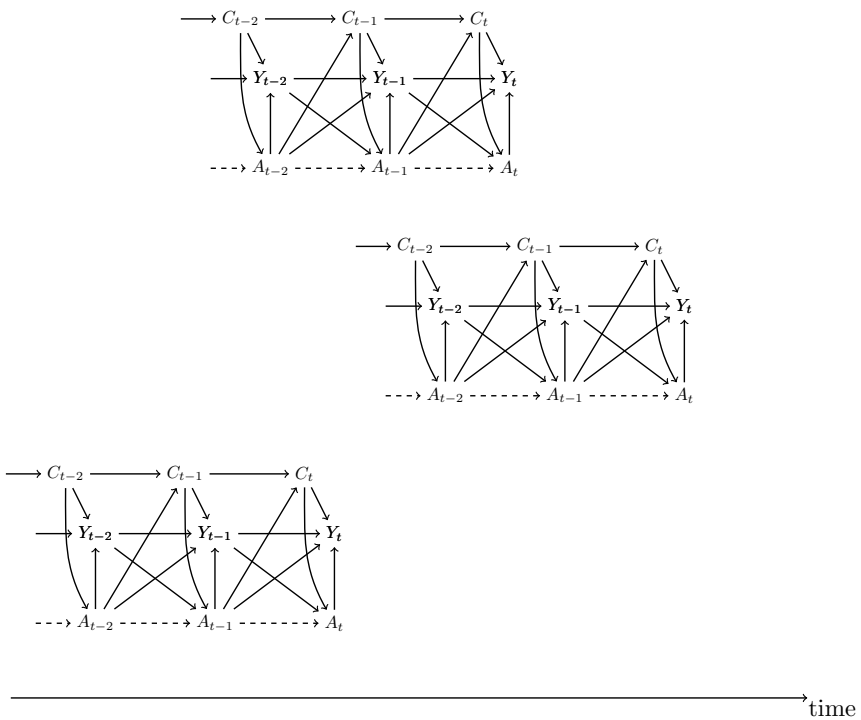
1. High-autocorrelation with lagged values of the variables
2. Elevated missing rate due to including previous values of variables
   study the effect of X_t on $Y_t \rightarrow Y_{t-1}$ is included
   $\rightarrow$ increase missing rate 50.1% $\rightarrow$ 74.1%

Observational N-of-1 study data

Mental health research studies heterogeneous patients, which follows up with a particular patient throughout the entire observation as in a N-of-1 study.



longitudinal data



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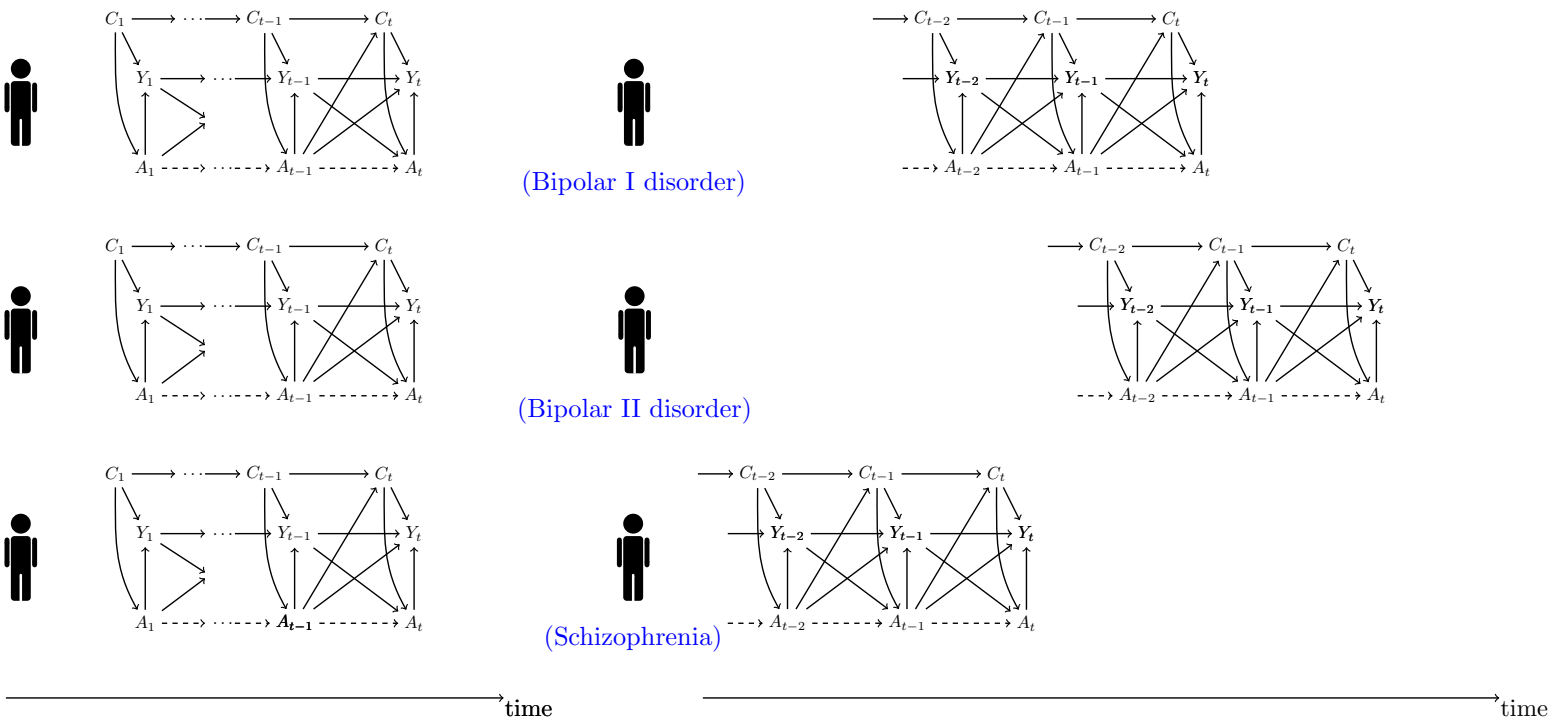

longitudinal data

mHealth data

Existing methods in handling missing data

A variety of statistical methods have been developed to tackle missing data problem in various settings.

Longitudinal studies

mean imputation
LOCF imputation
linear interpolation
spline interpolation
multiple imputation
Propensity score weighting
...

Univariate time series

simple moving average
exponential weighted
moving average
ARIMA model
...

Multivariate time series

recurrent neural network
Generative adversarial network
...

Complete case analysis

linear regression
ARIMA regression
State space model
...

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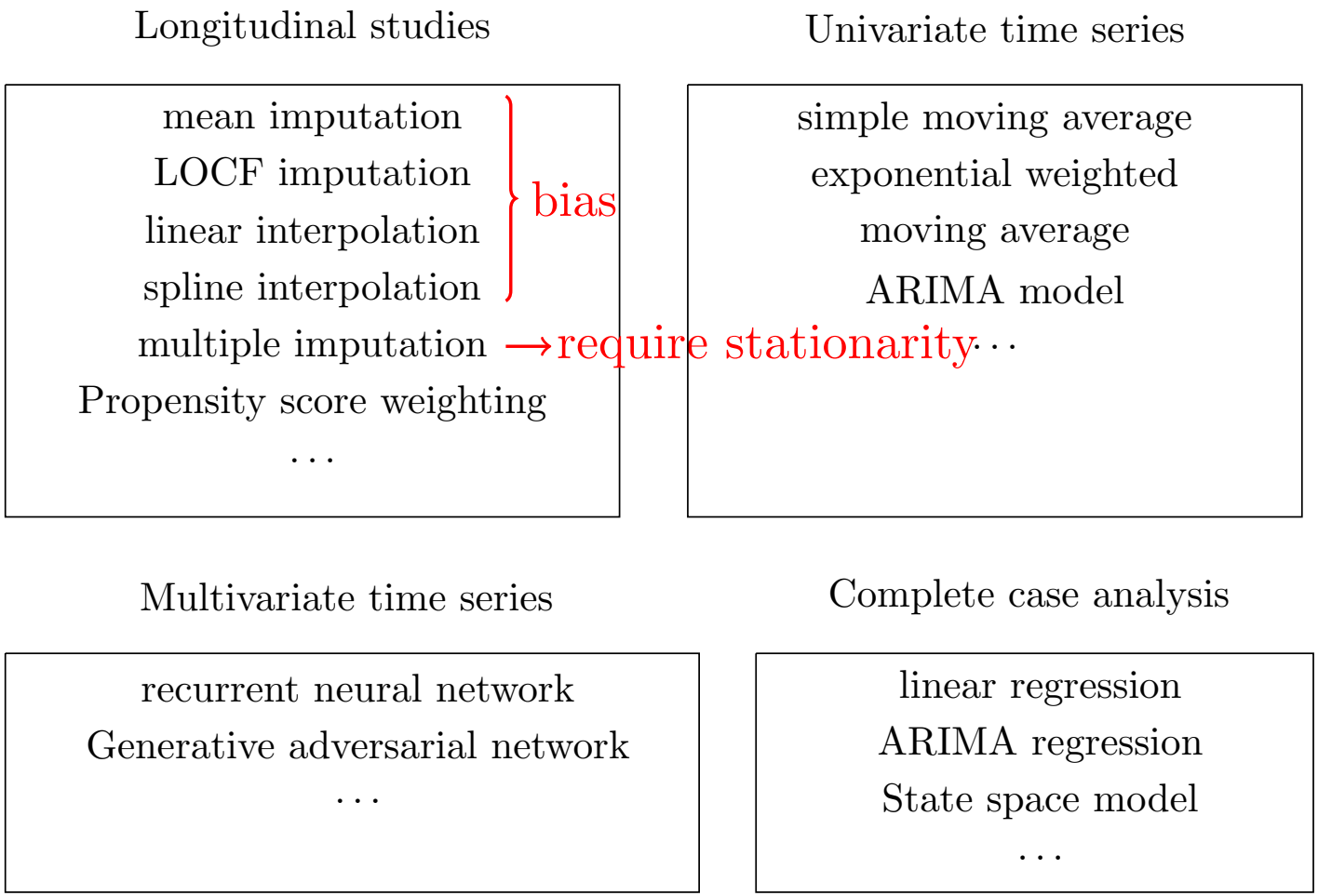

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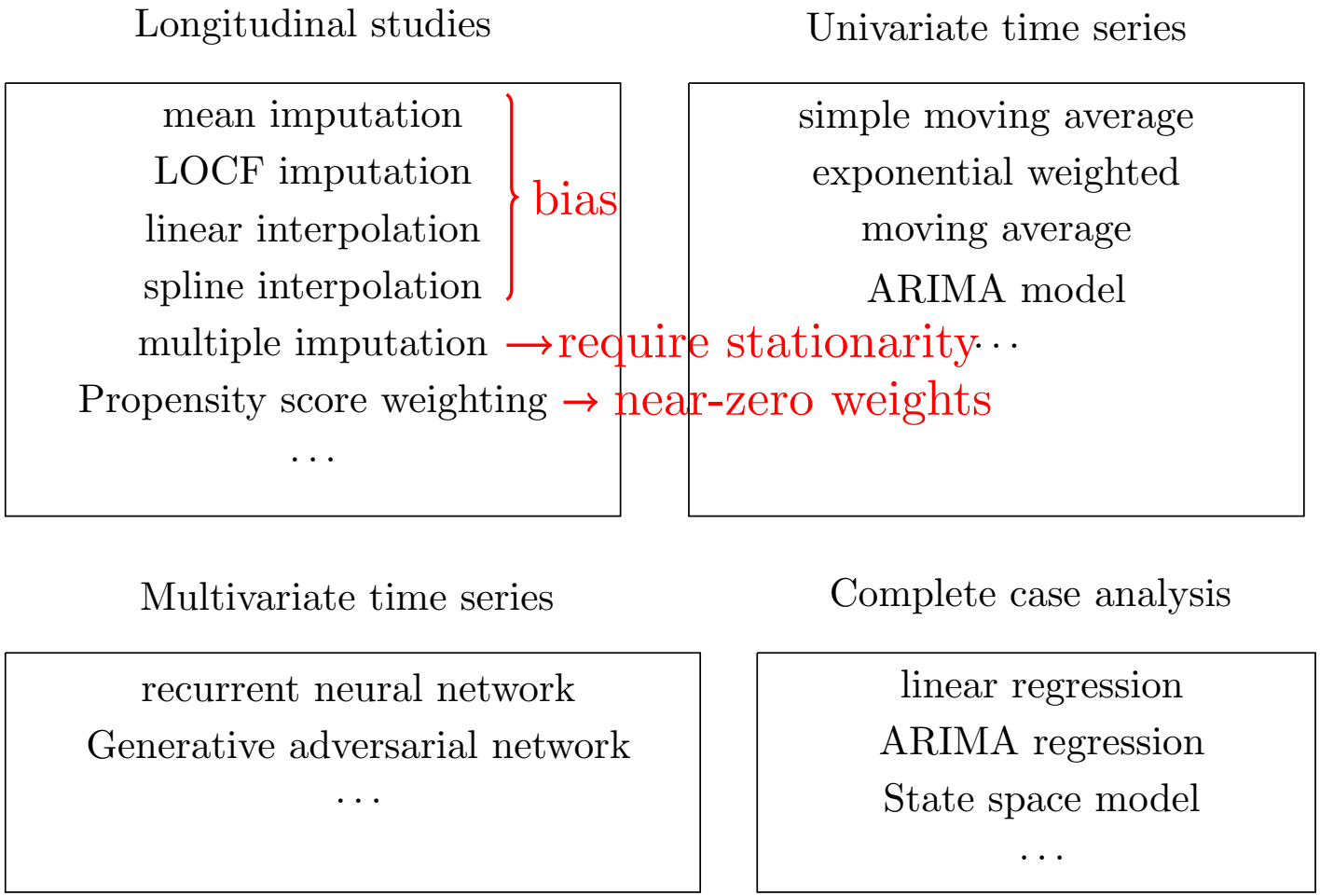

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spline interpolation
multiple imputation
Propensity score weighting
...

Univariate time series

simple moving average
exponential weighted
moving average
ARIMA model
...
(not for multivariate time series)

Multivariate time series

recurrent neural network
Generative adversarial network
...

Complete case analysis

linear regression
ARIMA regression
State space model
...

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Multivariate time series

recurrent neural network
Generative adversarial network
...
(require multiple subjects)

Complete case analysis

linear regression
ARIMA regression
State space model
...

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Complete case analysis

stationarity {
linear regression
ARIMA regression
State space model
...

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mean imputation
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Propensity score weighting
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Univariate time series

simple moving average
exponential weighted
moving average
ARIMA model
...

Multivariate time series

recurrent neural network
Generative adversarial network
..improve efficiency?

Complete case analysis

stationarity { linear regression
ARIMA regression
⟵ State space model
...

Challenges

The missing data problem for mHealth data has several unique features.

- Highly-correlated, entangled multivariate time series of outcome, exposure and confounders
- Simultaneous missingness in both response variable and explanatory variables induced by missing values only in the outcome
- (Potential) non-stationarity due to systematic changes in variance and coefficient parameters
- Long follow-up time of heterogeneous subjects
- Prone to MAR or MNAR rather than MCAR

Goal

Propose a imputation method for missingness in the outcomes in a (potentially non-stationary) multi-variate time series of a single subject.

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State space model and Kalman Filter

State space model is widely used for navigation, location tracking, voice recognition, automotive control system, and parameter estimation for time series analysis in biostatistics, econometric, and many other areas.

State space model

$$Y_t = (1, Y_{t-1}, A_t, A_{t-1}, C_t)^T \beta_t + v_t \quad \text{(Observational equation)}$$

where Y_t is the observed outcome, (A_t, A_{t-1}, C_t) are observed exposure and covariates, and $v_t \sim N(0, V_t)$.

$$\beta_t = G_t \beta_{t-1} + w_t \qquad . \qquad \text{(State equation)}$$

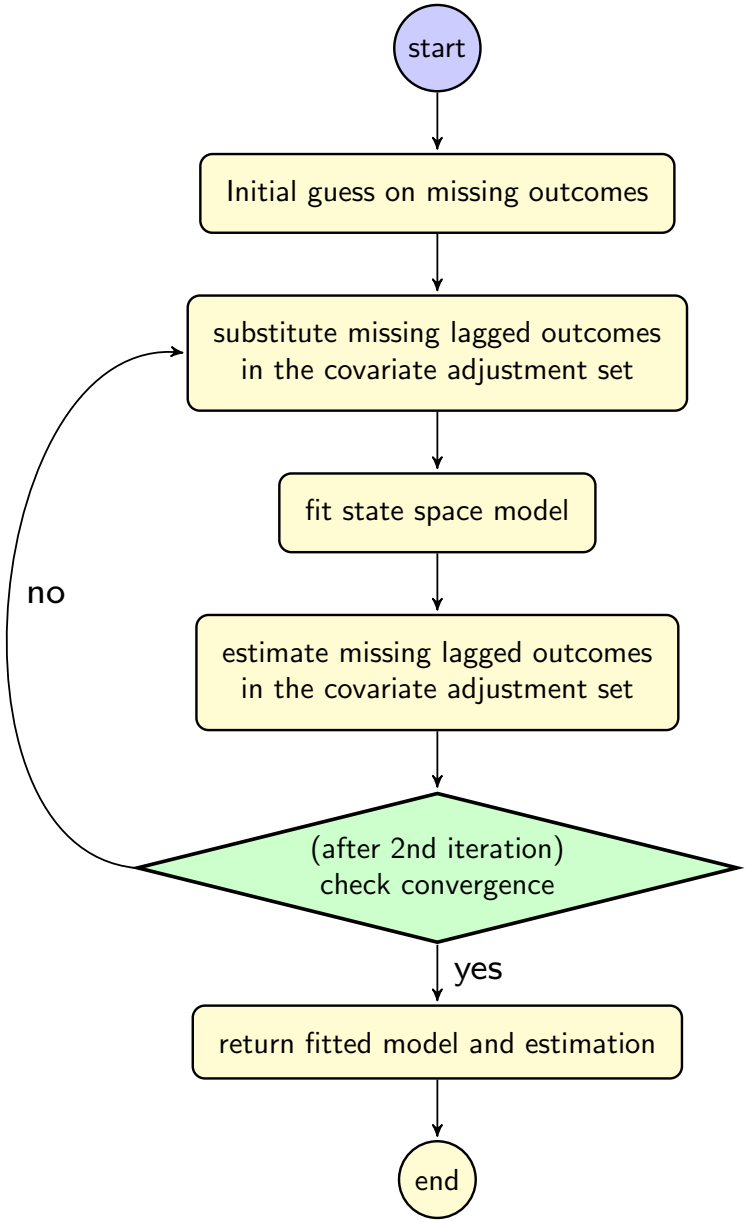
where β_t denotes unknown coefficients to be estimated, G_t is the transition matrix for how β_t evolves over time, and $w_t \sim N_p(0, W_t)$.

Kalman Filter provides the optimal estimate for the latest (possibly time-varying) unknown parameters, given observations by time t, $\hat{\beta}_t | y_{1:t}$.

State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$

y_1	a_1	a_0	c_0	y_0
y_2	a_2	a_1	c_1	y_1
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}
y_t	a_t	a_{t-1}	c_{t-1}	NA
NA	a_{t+1}	a_t	c_t	y_t
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	NA
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}



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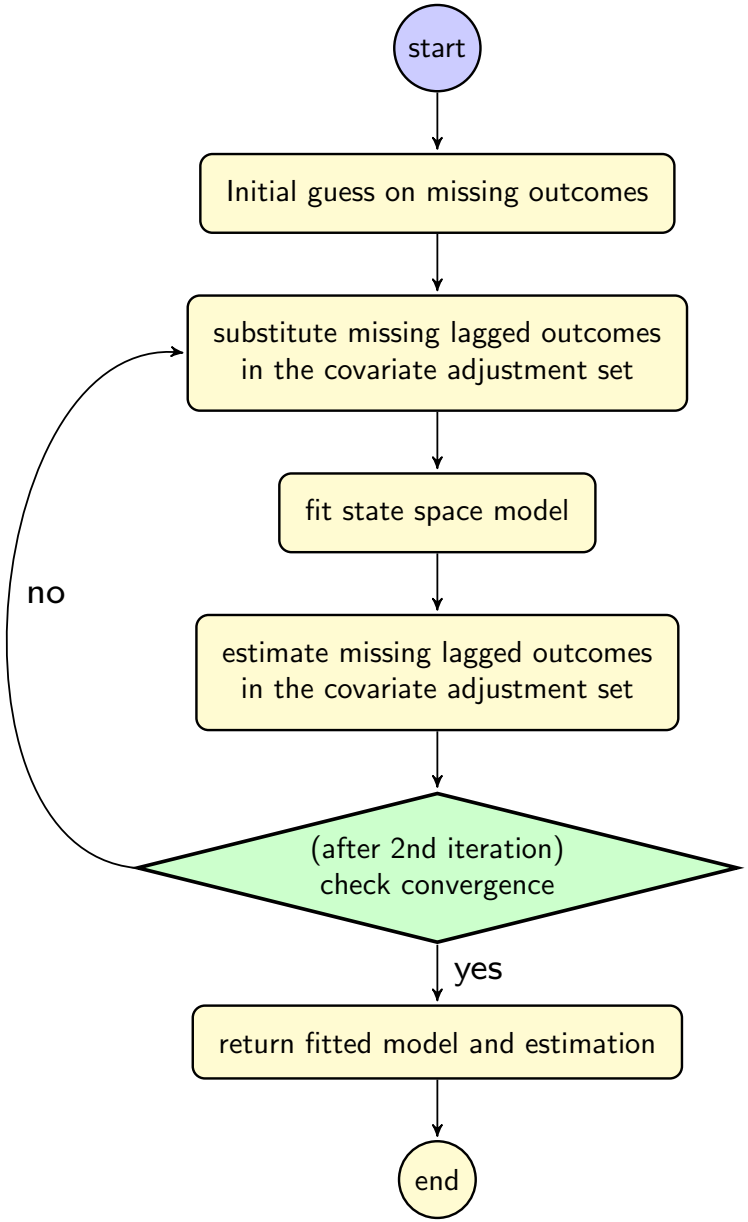
Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$

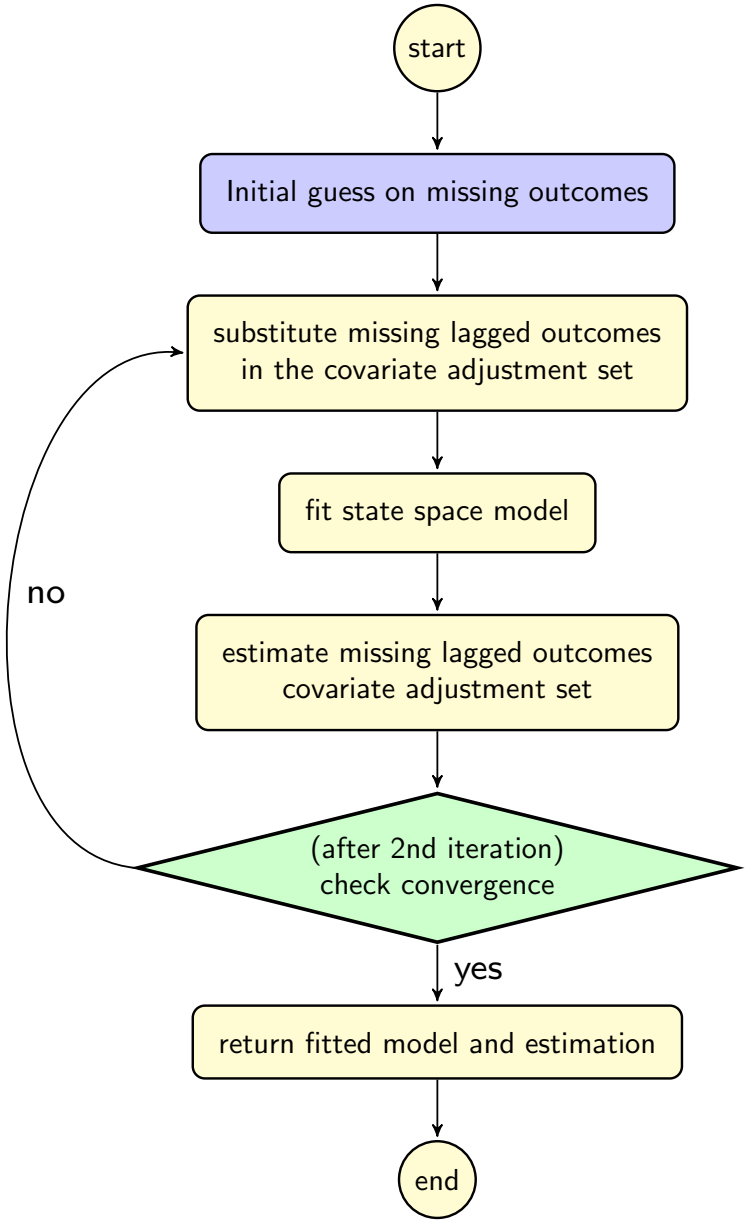
y_1	a_1	a_0	c_0	y_0
y_2	a_2	a_1	c_1	y_1
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}
y_t	a_t	a_{t-1}	c_{t-1}	NA
NA	a_{t+1}	a_t	c_t	y_t
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	NA
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}



State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ initial guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(0)}$
y_t	a_t	a_{t-1}	c_{t-1}	NA	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(0)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	NA	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T



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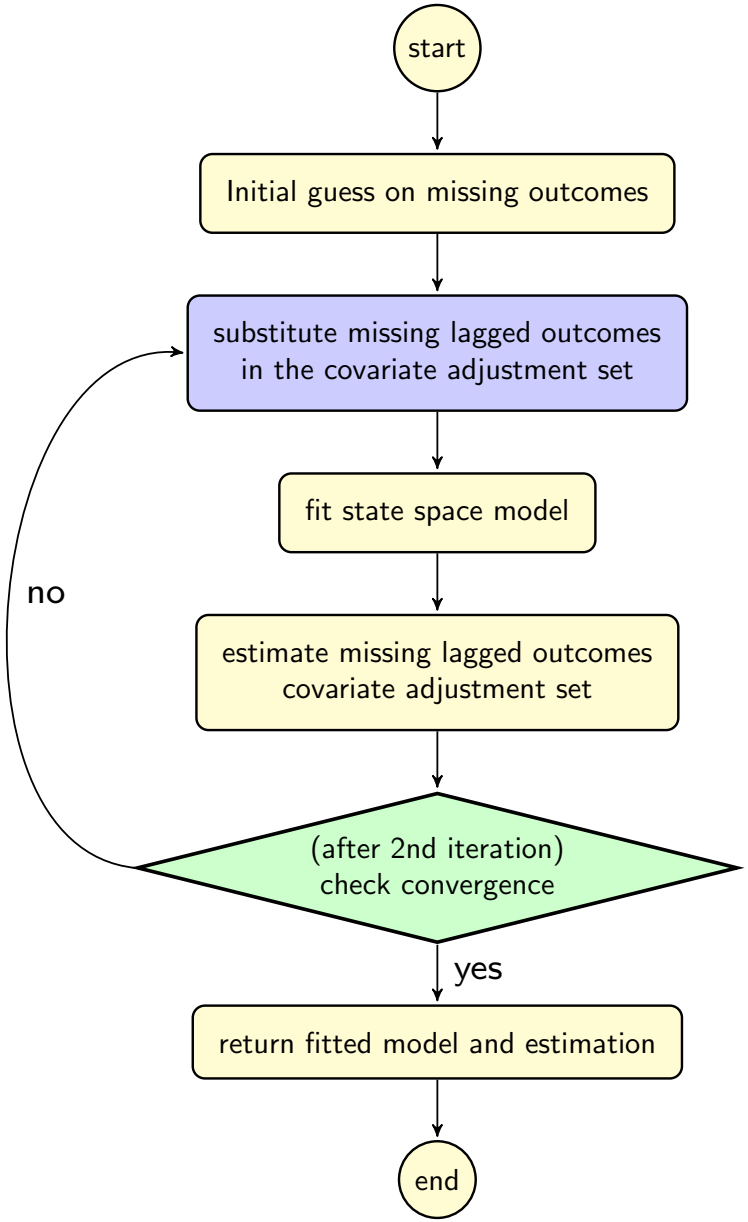
Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ initial guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}^{(0)}_{t-1}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}^{(0)}_{t-1}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}^{(0)}_{t+1}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}^{(0)}_{t+1}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

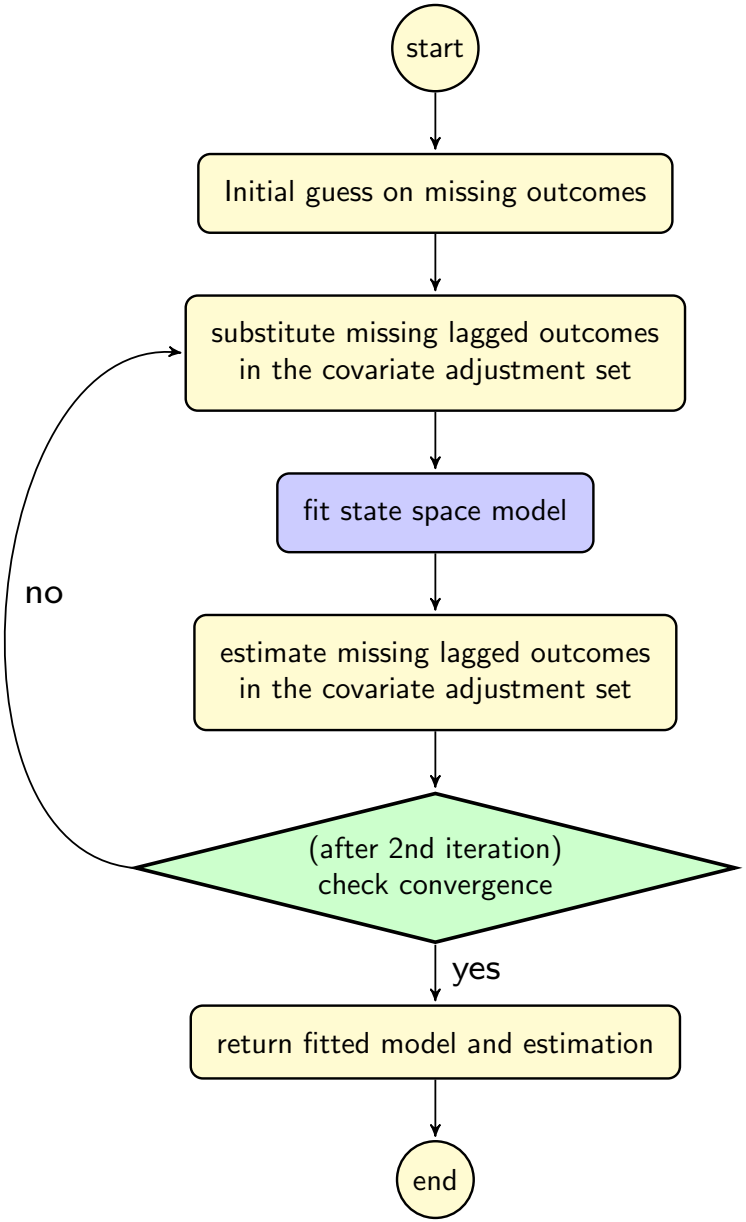


State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ initial guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(0)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(0)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(0)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(0)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$\hat{\beta}_{0,t}^{(1)}$	$\hat{\beta}_{1,t}^{(1)}$	$\hat{\beta}_{2,t}^{(1)}$	$\hat{\beta}_{c,t}^{(1)}$	$\hat{\rho}_t^{(1)}$



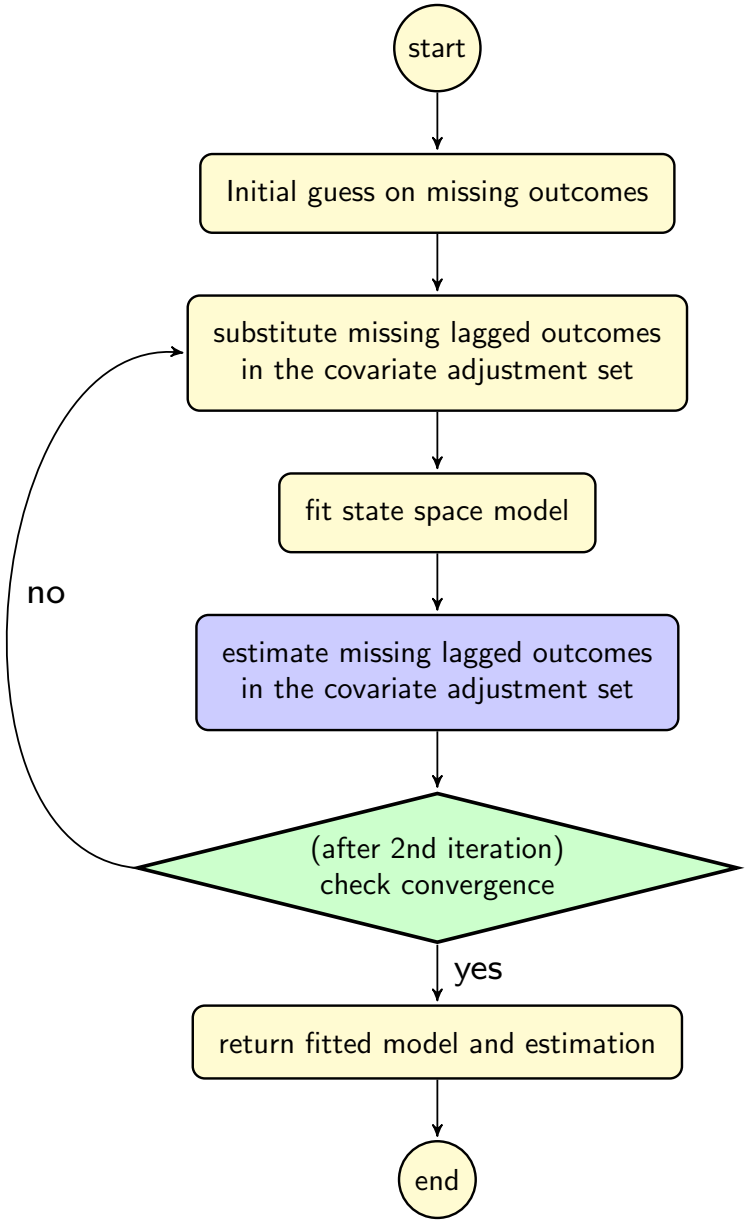
State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ $\quad 1^{st}$ guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(1)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(0)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(1)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(0)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$+$

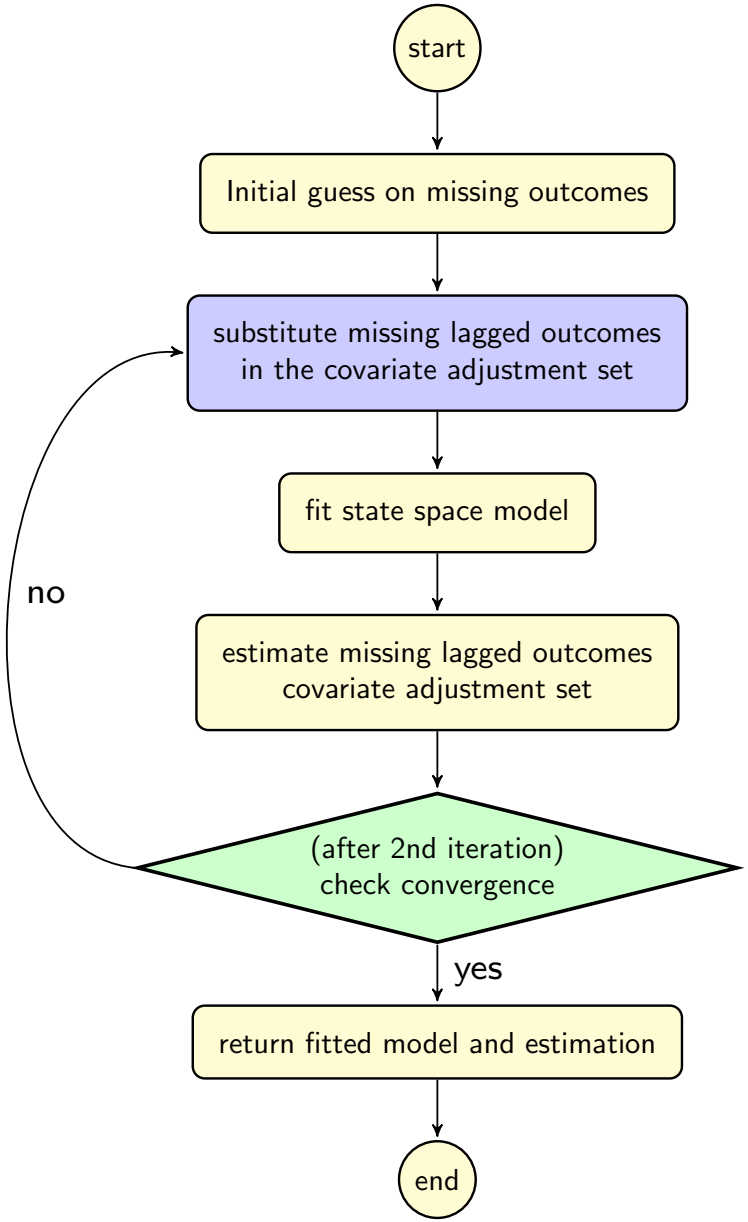
$\hat{\beta}_{0,t}^{(1)}$	$\hat{\beta}_{1,t}^{(1)}$	$\hat{\beta}_{2,t}^{(1)}$	$\hat{\beta}_{c,t}^{(1)}$	$\hat{\rho}_t^{(1)}$



State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 1^{st} guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}^{(1)}_{t-1}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}^{(1)}_{t-1}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}^{(1)}_{t+1}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}^{(1)}_{t+1}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

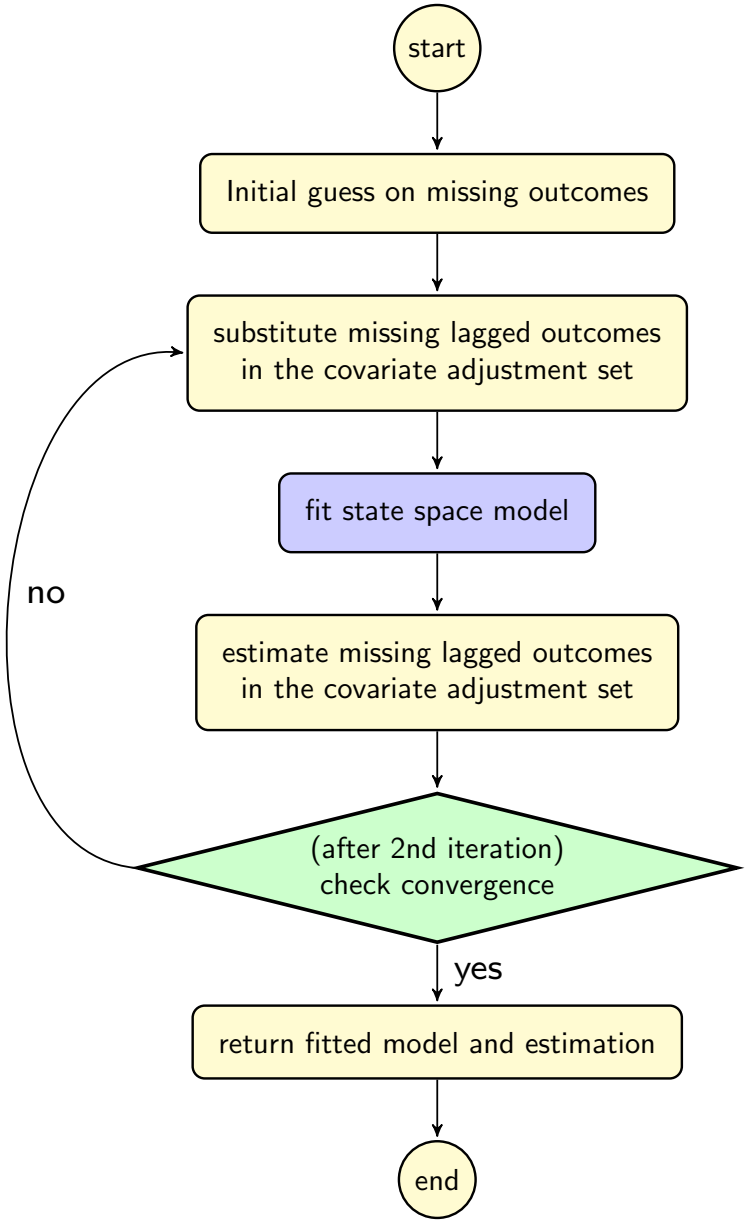


State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 1^{st} guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(1)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(1)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(1)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(1)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$\hat{\beta}_{0,t}^{(2)}$	$\hat{\beta}_{1,t}^{(2)}$	$\hat{\beta}_{2,t}^{(2)}$	$\hat{\beta}_{c,t}^{(2)}$	$\hat{\rho}_t^{(2)}$



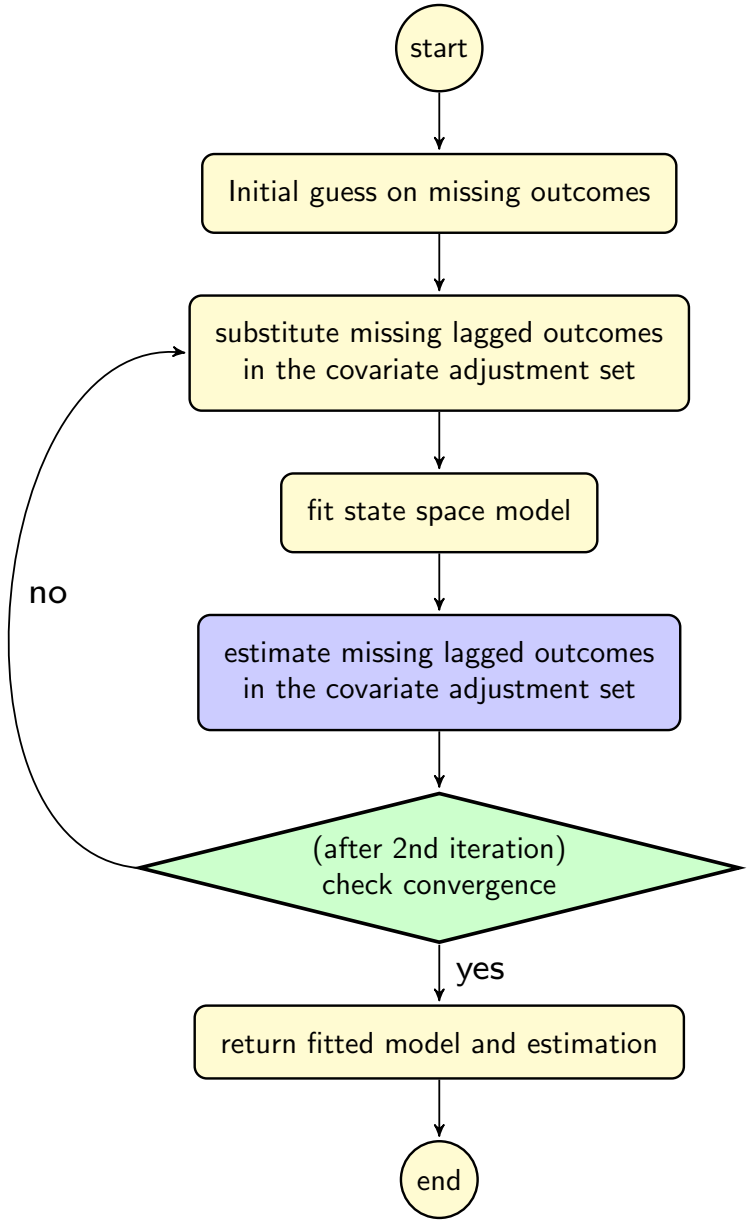
State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 2^{nd} guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}^{(2)}_{t-1}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}^{(1)}_{t-1}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}^{(2)}_{t+1}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}^{(1)}_{t+1}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$+$

$\hat{\beta}^{(2)}_{0,t}$	$\hat{\beta}^{(2)}_{1,t}$	$\hat{\beta}^{(2)}_{2,t}$	$\hat{\beta}^{(2)}_{c,t}$	$\hat{\rho}^{(2)}_t$



State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 1^{st} guess of Y_t

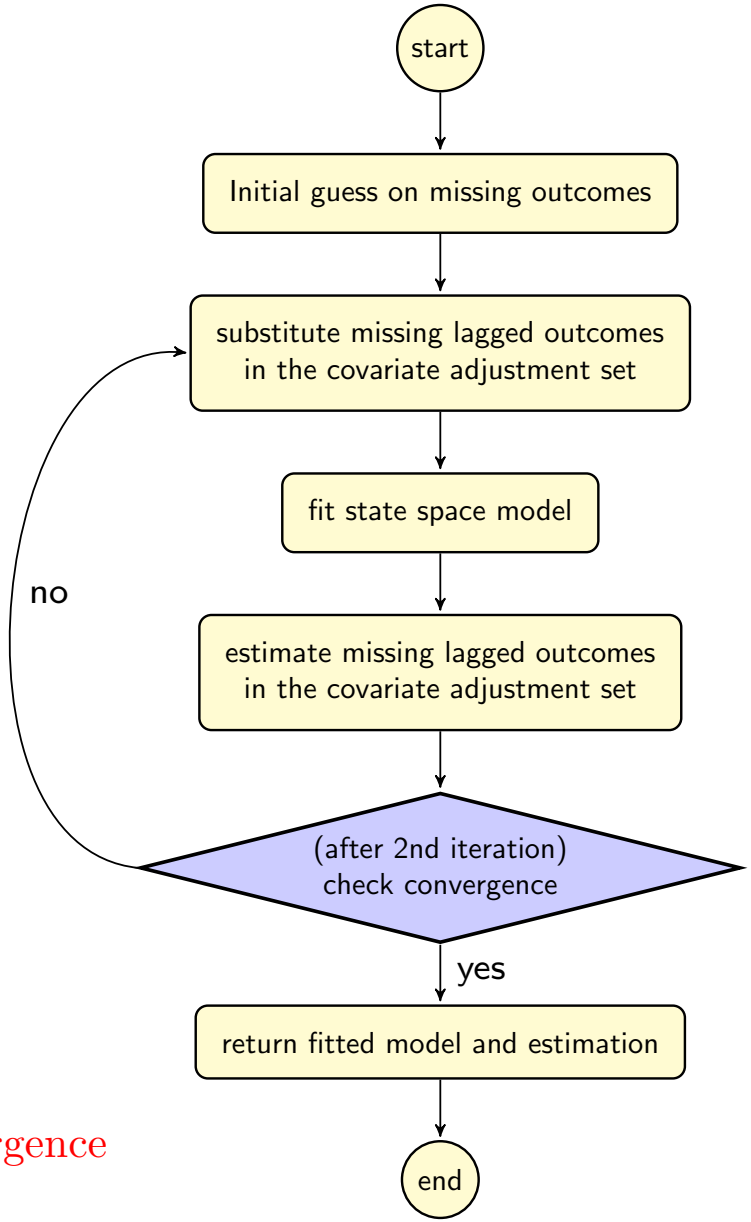
y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(2)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(1)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(1)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(1)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$\hat{\beta}_{0,t}^{(1)}$	$\hat{\beta}_{1,t}^{(2)}$	$\hat{\beta}_{2,t}^{(2)}$	$\hat{\beta}_{c,t}^{(2)}$	$\hat{\rho}_t^{(2)}$

+

likelihood and other unknown parameters

} check convergence

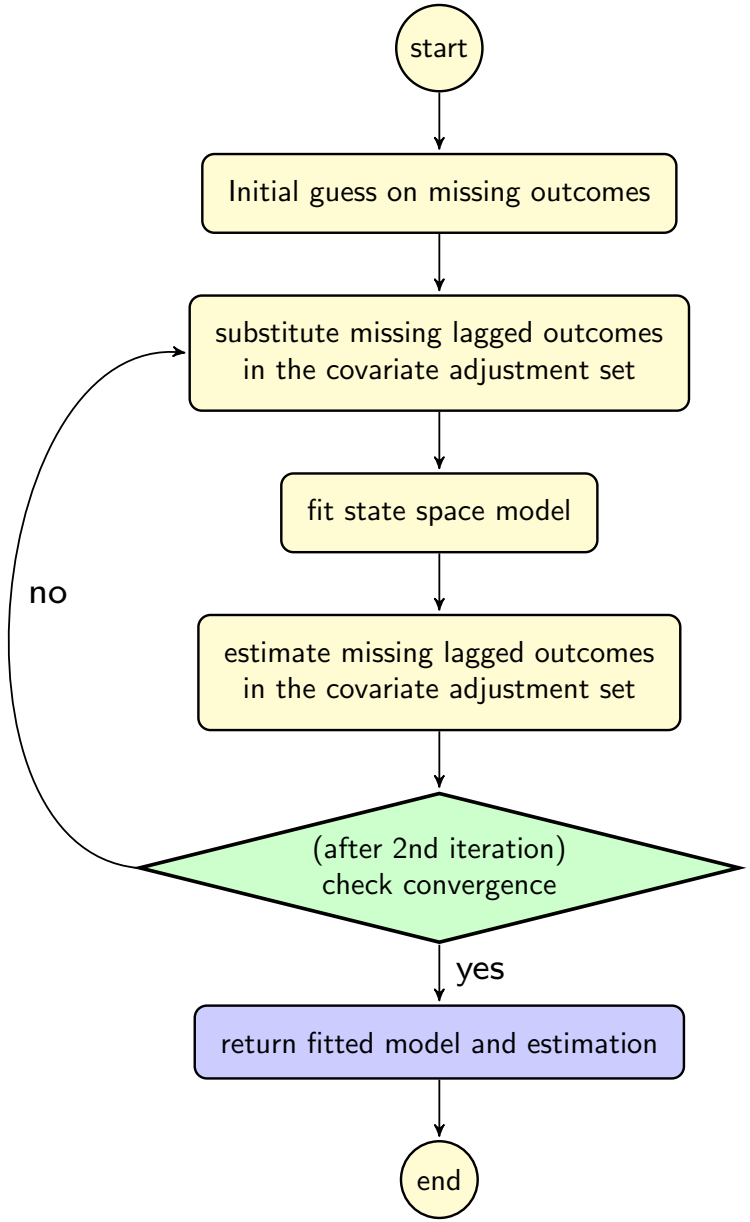


State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 3^{rd} guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(3)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(2)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(3)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(2)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$\hat{\beta}_{0,t}^{(3)}$	$\hat{\beta}_{1,t}^{(3)}$	$\hat{\beta}_{2,t}^{(3)}$	$\hat{\beta}_{c,t}^{(3)}$	$\hat{\rho}_t^{(3)}$

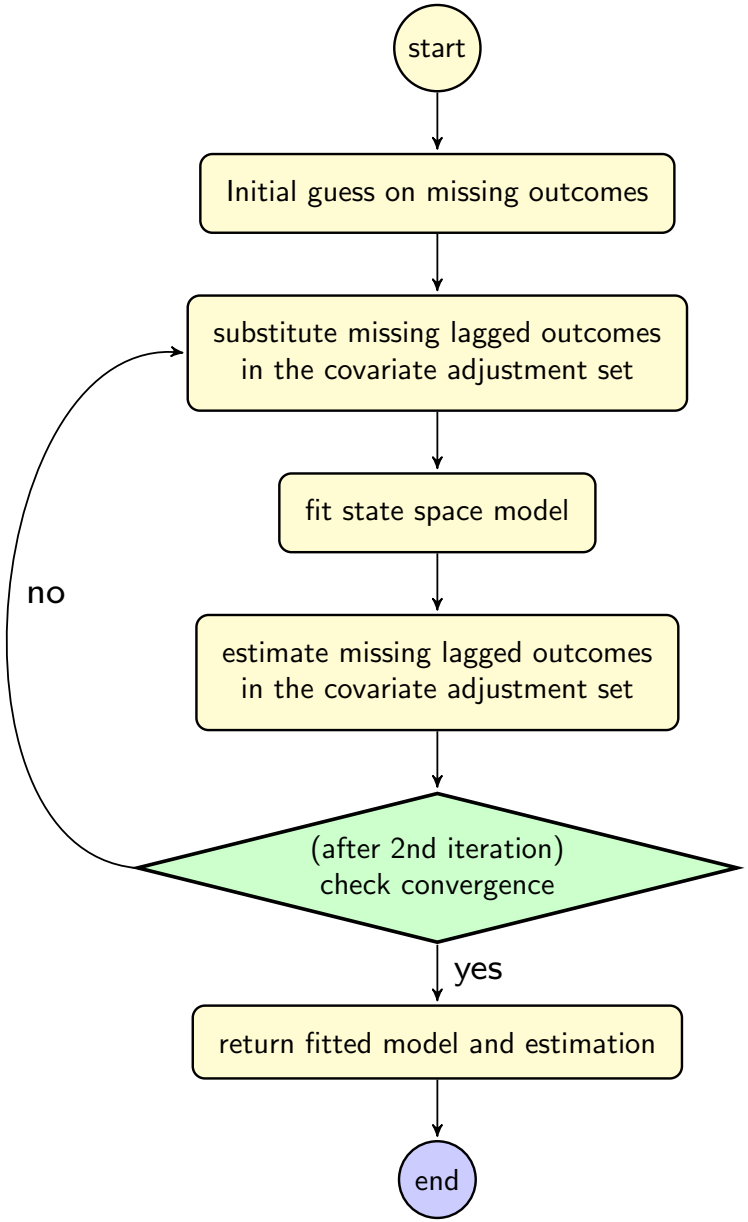


State space model imputation (SSMimpute)

Formula: $Y_t \sim A_t + A_{t-1} + C_t + Y_{t-1}$ 3^{rd} guess of Y_t

y_1	a_1	a_0	c_0	y_0	y_1
y_2	a_2	a_1	c_1	y_1	y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
NA	a_{t-1}	a_{t-2}	c_{t-2}	y_{t-2}	$\tilde{y}_{t-1}^{(3)}$
y_t	a_t	a_{t-1}	c_{t-1}	$\tilde{y}_{t-1}^{(2)}$	y_t
NA	a_{t+1}	a_t	c_t	y_t	$\tilde{y}_{t+1}^{(3)}$
y_{t+2}	a_{t+2}	a_{t+1}	c_{t+1}	$\tilde{y}_{t+1}^{(2)}$	y_{t+2}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
y_T	a_T	a_{T-1}	c_{T-1}	y_{T-1}	y_T

$\hat{\beta}_{0,t}^{(3)}$	$\hat{\beta}_{1,t}^{(3)}$	$\hat{\beta}_{2,t}^{(3)}$	$\hat{\beta}_{c,t}^{(3)}$	$\hat{\rho}_t^{(3)}$



State-space model imputation (SSMimpute)

Remark1

The state space model reveals its structure as well as its unknown parameters along with iterations until convergence.

Remark2

Missing values are only imputed for missing lagged outcomes in the confounder adjustment set, not for the missing outcome in the response variable.

Assumption

We require state space model to be correctly specified with no unmeasured confounders for unbiased estimation of the causal effect.

Simulation

- Stationary time series
- Non-stationary time series with varying variance
- Non-stationary time series with random-walk coefficients
- Non-stationary time series with coefficient having change points
- Non-stationary time series with multiple sources of non-stationarity

Methods to be compared:

- complete case analysis under both linear regression and state space model
- mean imputations, LOCF imputations, linear imputations, spline interpolation, multiple imputation under both linear regression and state space model
- Proposed state space model imputation (SSMimpute)

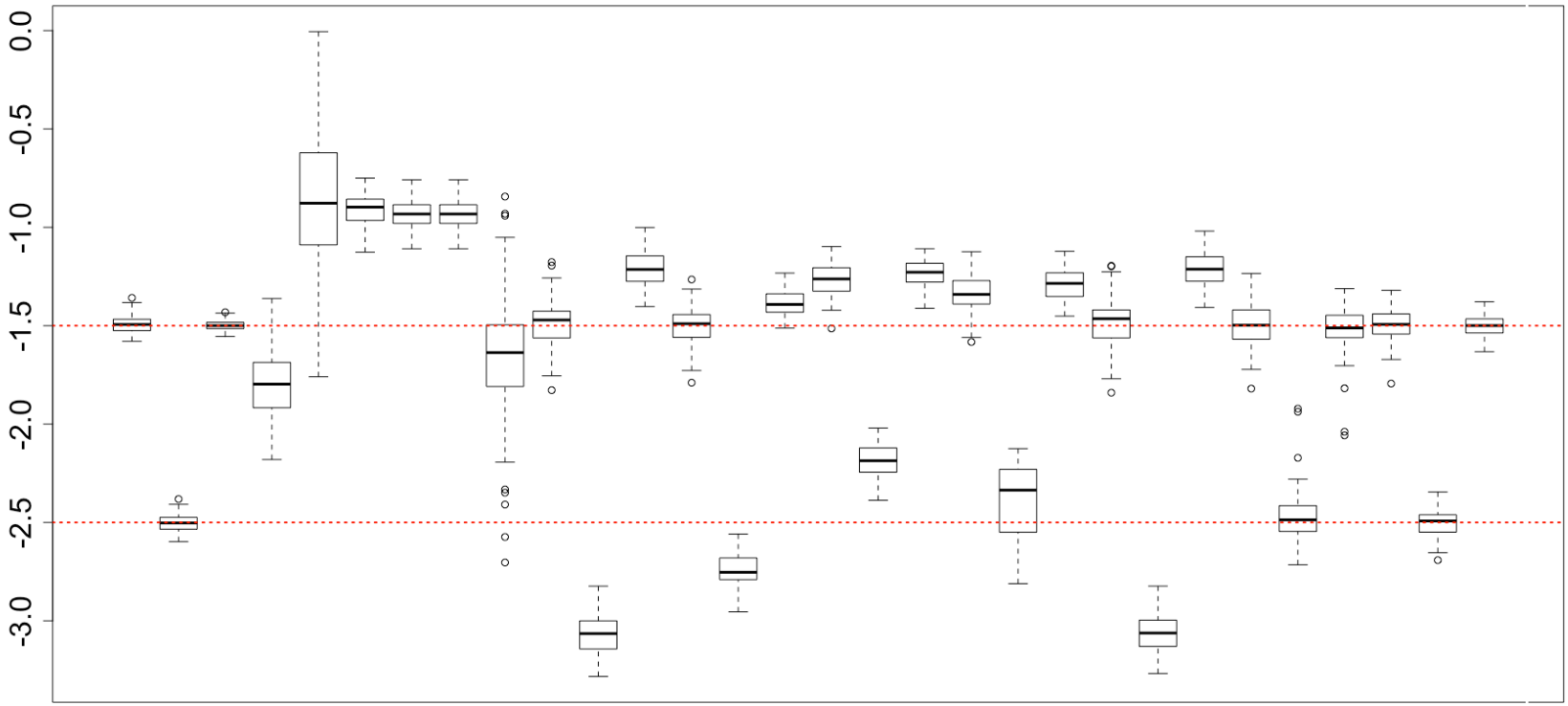
Missing mechanism:

- MCAR, MAR, MNAR

Simulation: non-stationary with sudden change points

$$Y_t = \beta_0 + \rho Y_{t-1} + \beta_{1,t} A_t + \beta_2 A_{t-1} + \beta_c C_t + v_t, \quad v_t \sim N(0, V)$$

where $\beta_{1,t} = -1.5$ for $t = 1, \ldots, 400, 701, \ldots, 1000$ and $\beta_{1,t} = -2.5$ for $t = 401, \ldots, 700$, and $t = 1, \ldots, 1000$. Missing rate is 50% under MCAR.



Simulation: non-stationary with sudden change points

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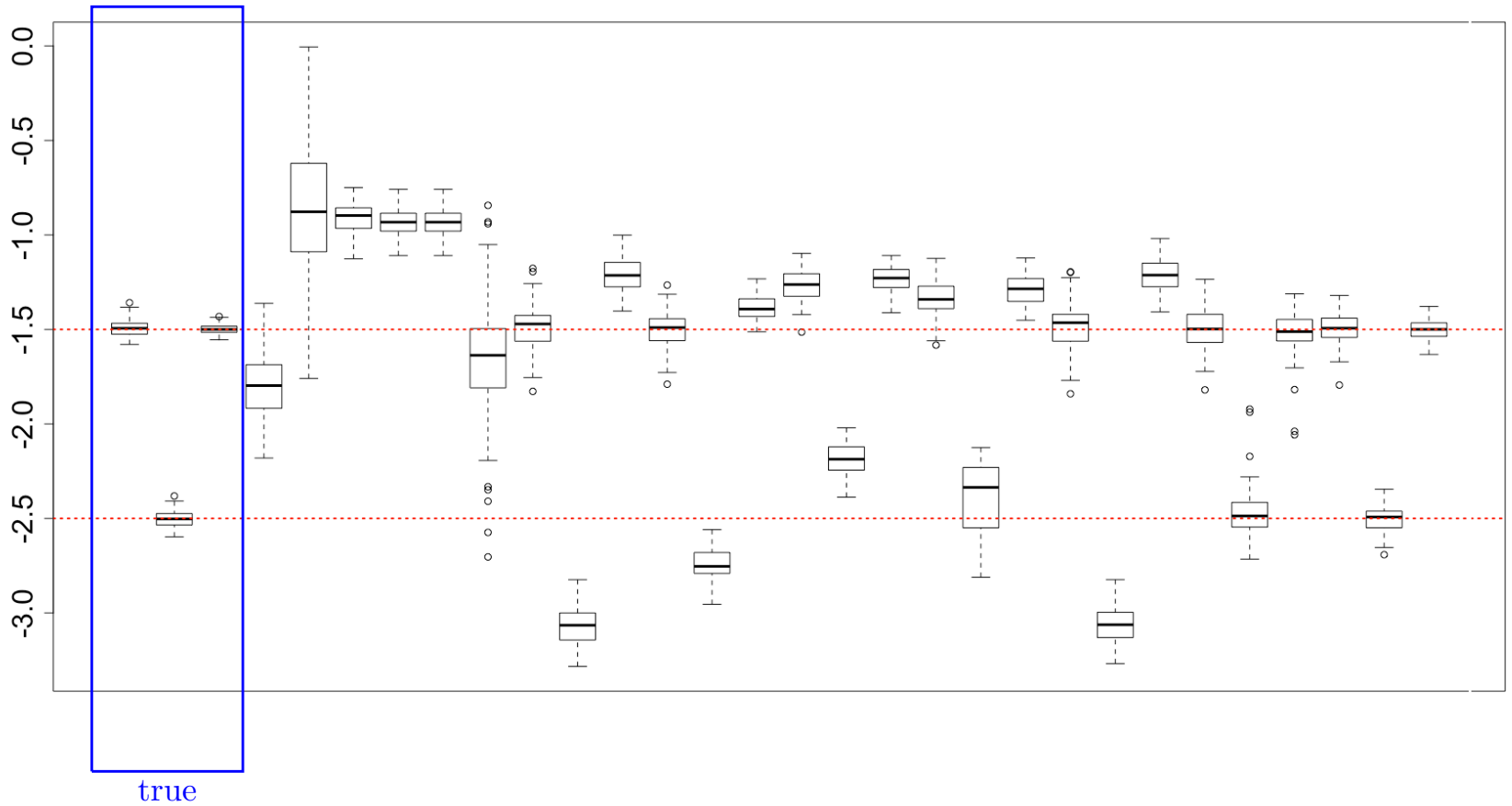

Simulation: non-stationary with sudden change points

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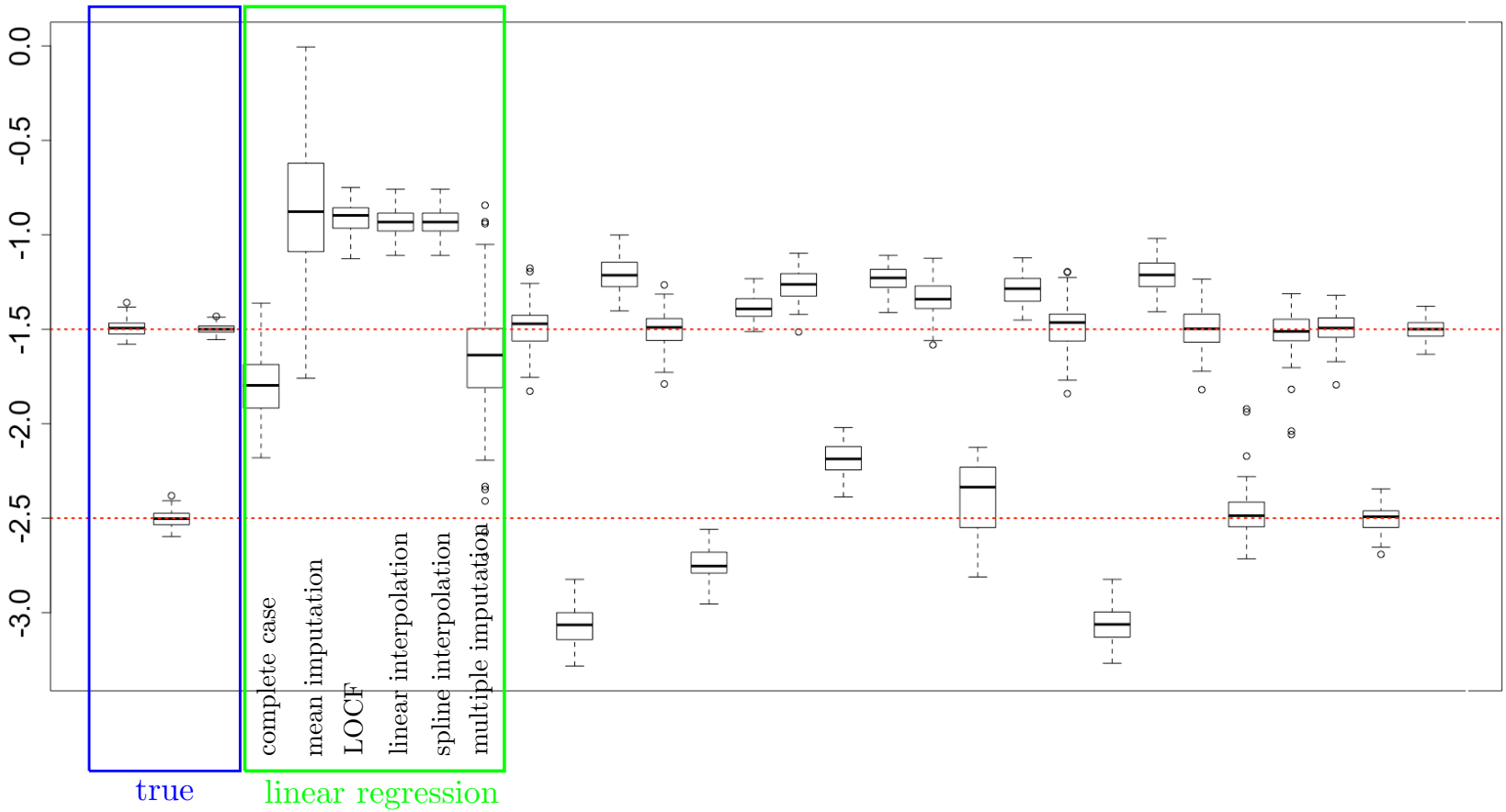

Simulation: non-stationary with sudden change points

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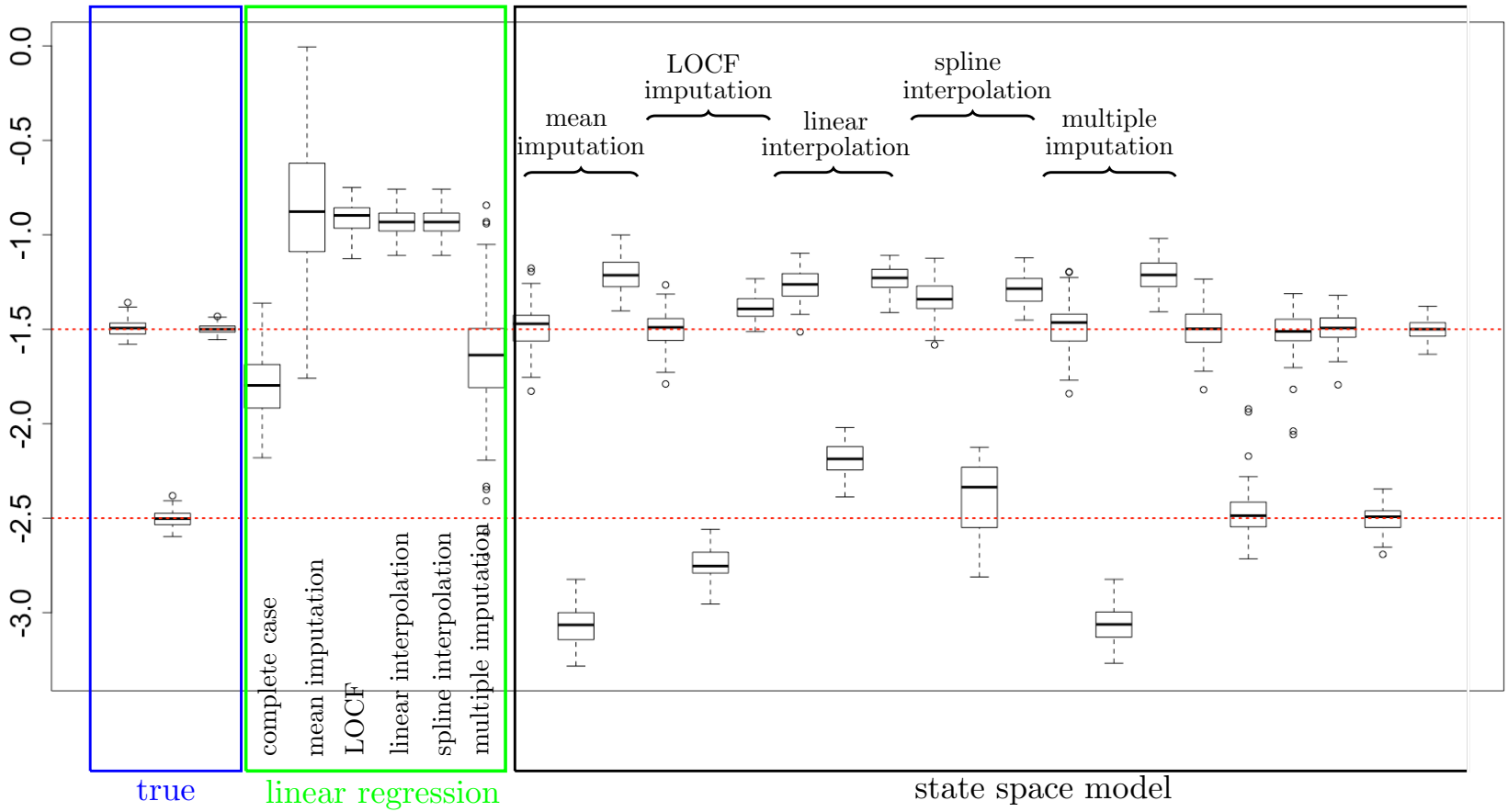

Simulation: non-stationary with sudden change points

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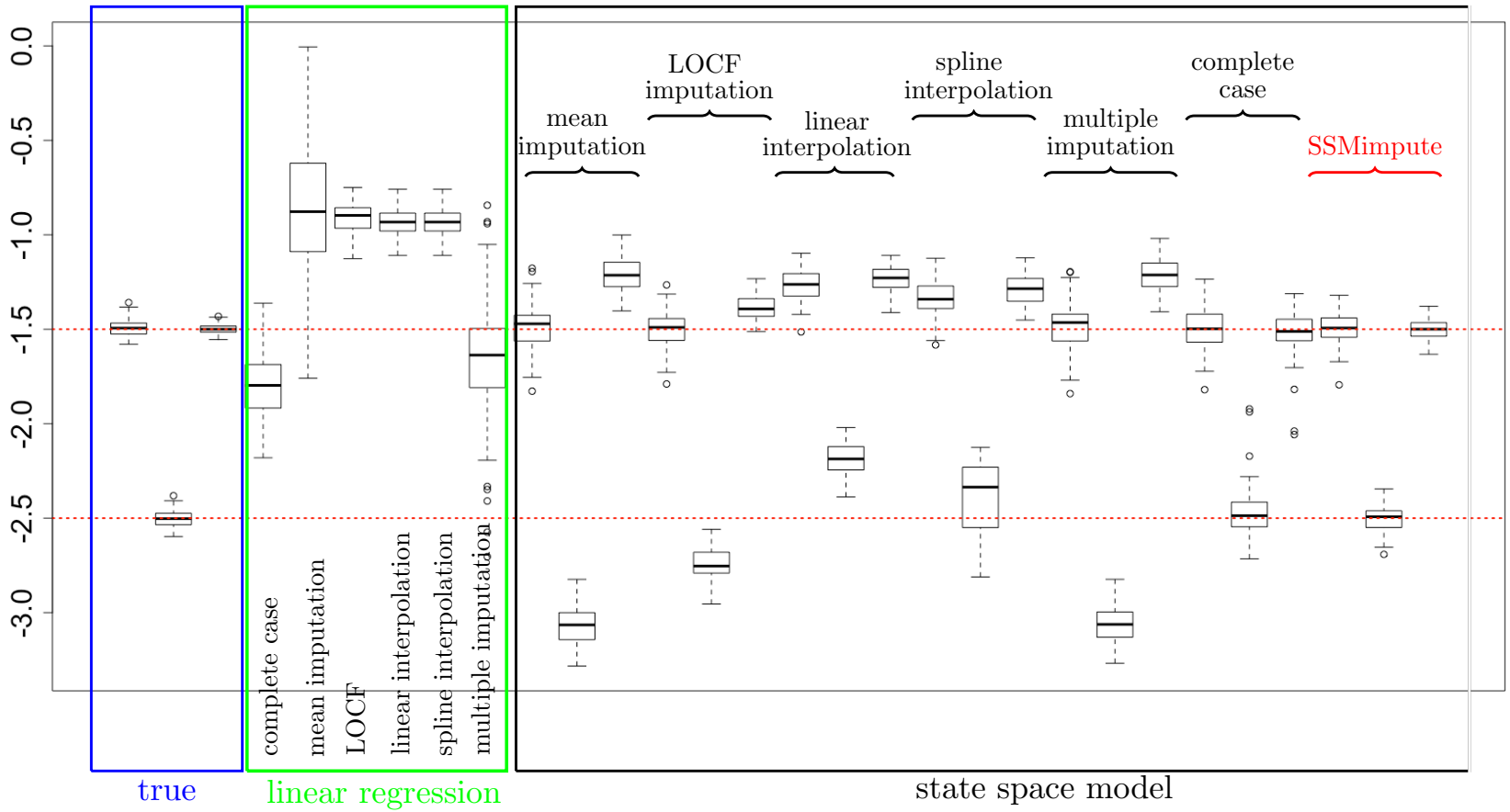
where $\beta_{1,t} = -1.5$ for $t = 1, \ldots, 400, 701, \ldots, 1000$ and $\beta_{1,t} = -2.5$ for $t = 401, \ldots, 700$, and $t = 1, \ldots, 1000$. Missing rate is 50% under MCAR.



Conclusions: (see more results in the paper)

For stationary time series,

- Complete case using linear regression and state space model are equivalent in theory and unbiased.
- Multiple imputation and SSMimpute are unbiased and more efficient than complete case analysis.
- Mean imputation, LOCF, linear and spline imputations are all biased.

For non-stationary time series,

- Linear model is unable to handle time-varying coefficients, and thus all imputation methods based on linear model are biased.
- State space model handles time-varying coefficients and variance, and provides unbiased estimation under complete case analysis and SSMimpute. SSMimpute is more efficient than complete case analysis.
- Mean imputation, LOCF, linear and spline interpolation, and multiple imputation are all biased even using state space model.

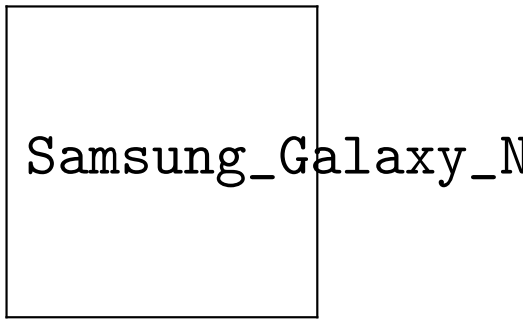
Bipolar Longitudinal Study (McLean Hospital)

The study explores how passive sensor data linked to moods and cognitive states in patients with Serious Mental Illness (SMI).
Following data is collected for 10 (out of 54) participants for up to 4 years.

- Self-reported survey data (moods, activities, life habits, in-person interactions, etc.)
- Passively collected telecommunication data (calls and texts)
- Passively collected accelerometer data
- ...

Bewei app

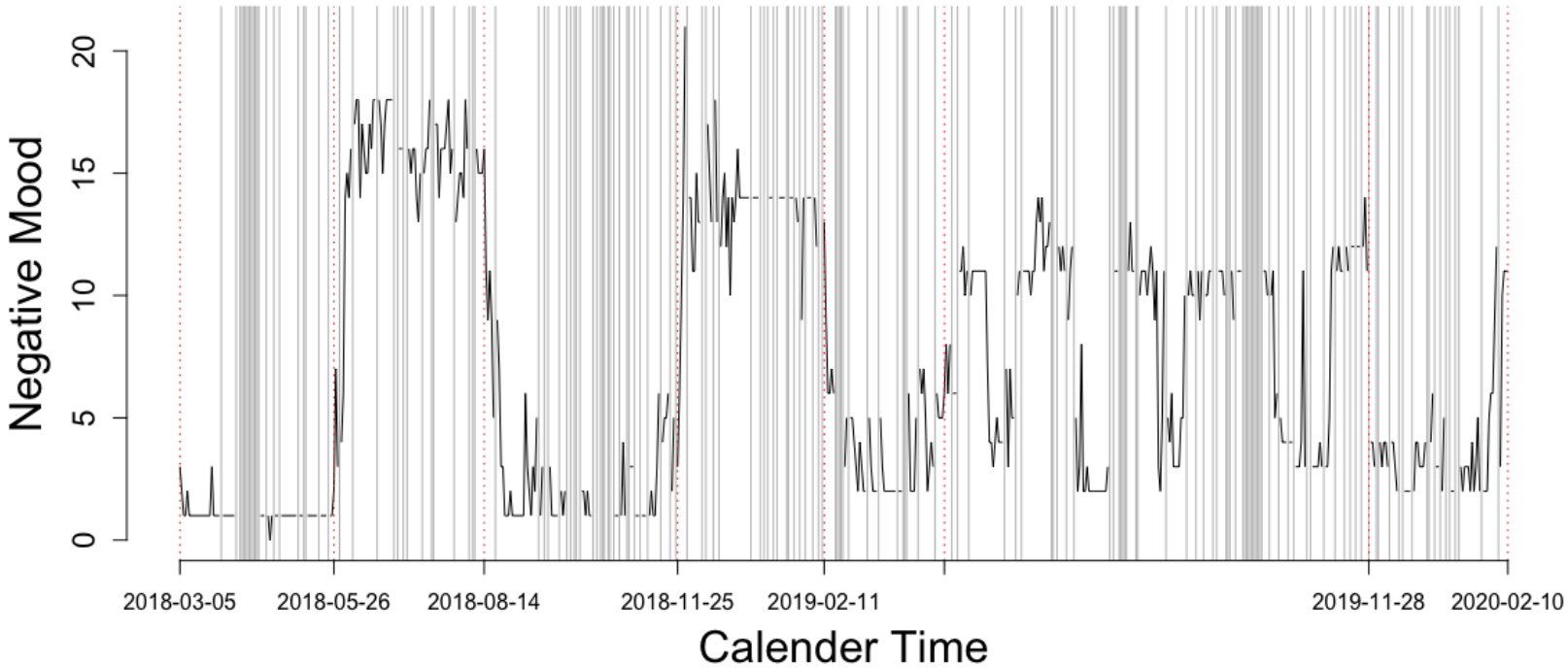
GEVEActiv watch



Samsung Galaxy Note 8

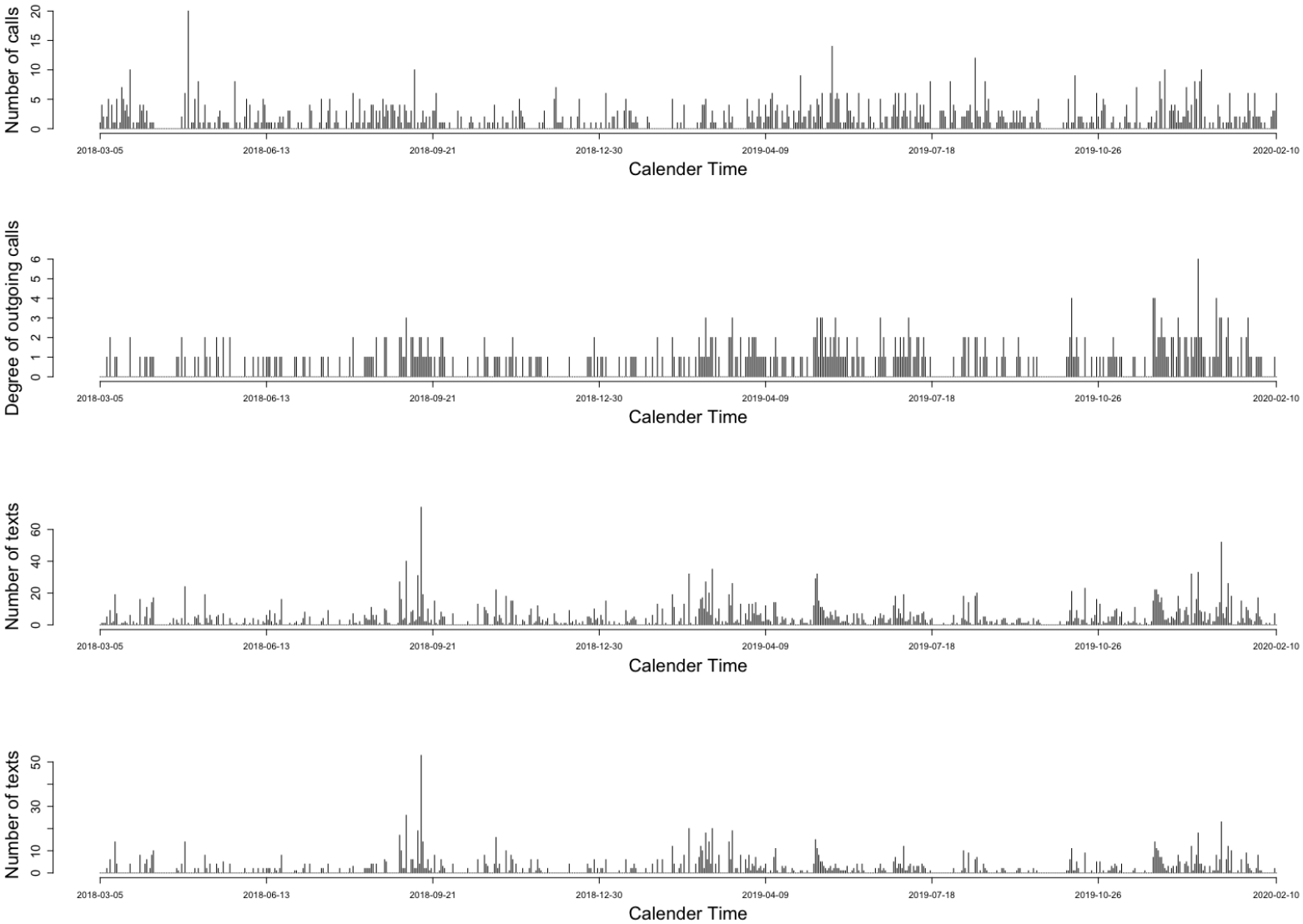
Bipolar Longitudinal Study (Outcome Y_t)

Focus on one female participant with Bipolar I disorder, who has been followed up from 03/05/2018 to 2020/20/10 (708 days).
Outcome is a composite index for negative mood of being afraid, anxious, ashamed, hostile, stressed, upset, irritable and lonely.

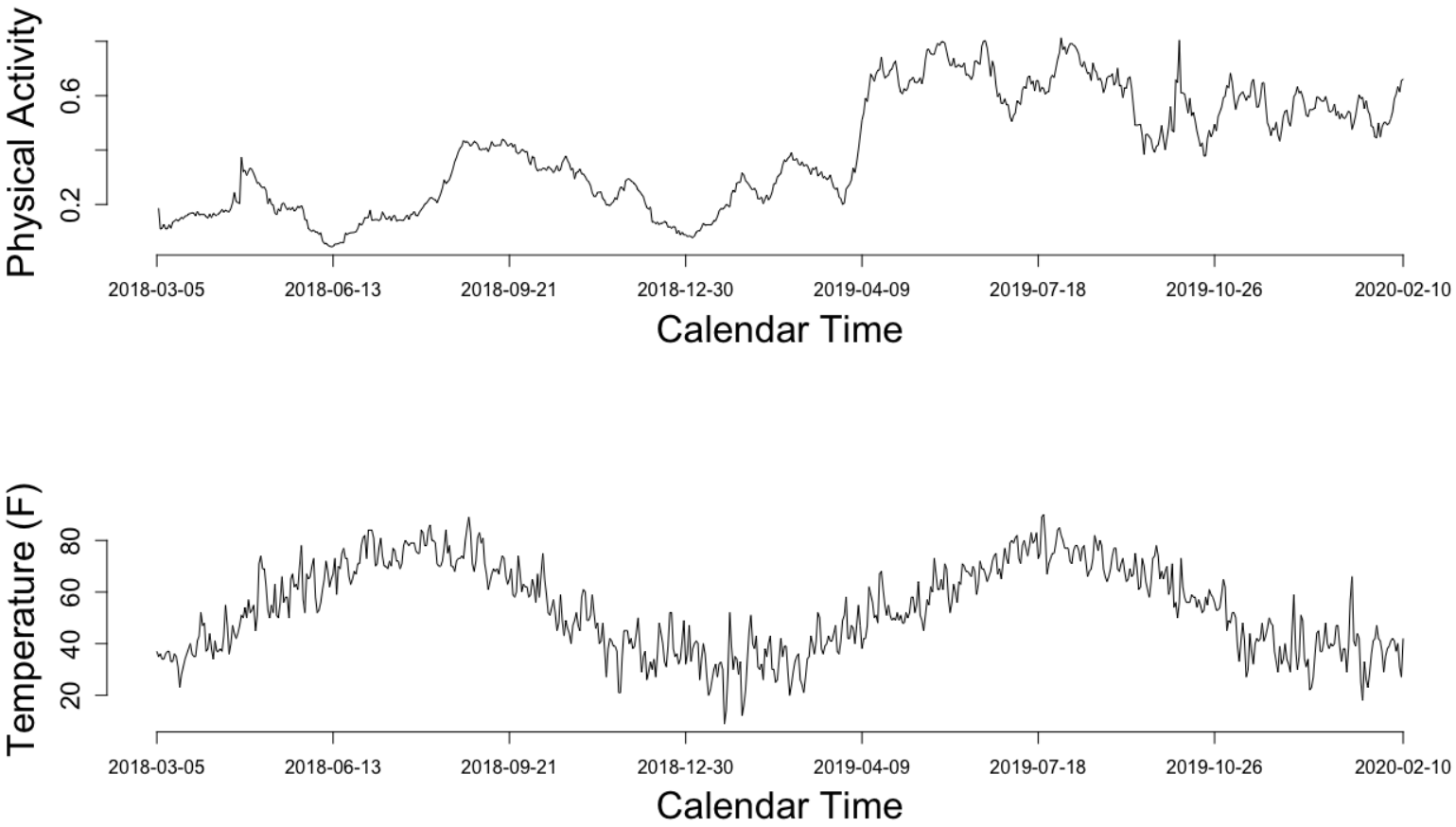


Longest consecutive missing days: 11
Missing rates: 23.31%

Bipolar Longitudinal Study (Telecommunication A_t)



Bipolar Longitudinal Study (Other covariates C_t)



Temperature is obtained from National Centers for Environmental Information (NOAA) Database. Physical activity is processed following Bai (2013,2014)

Estimation model

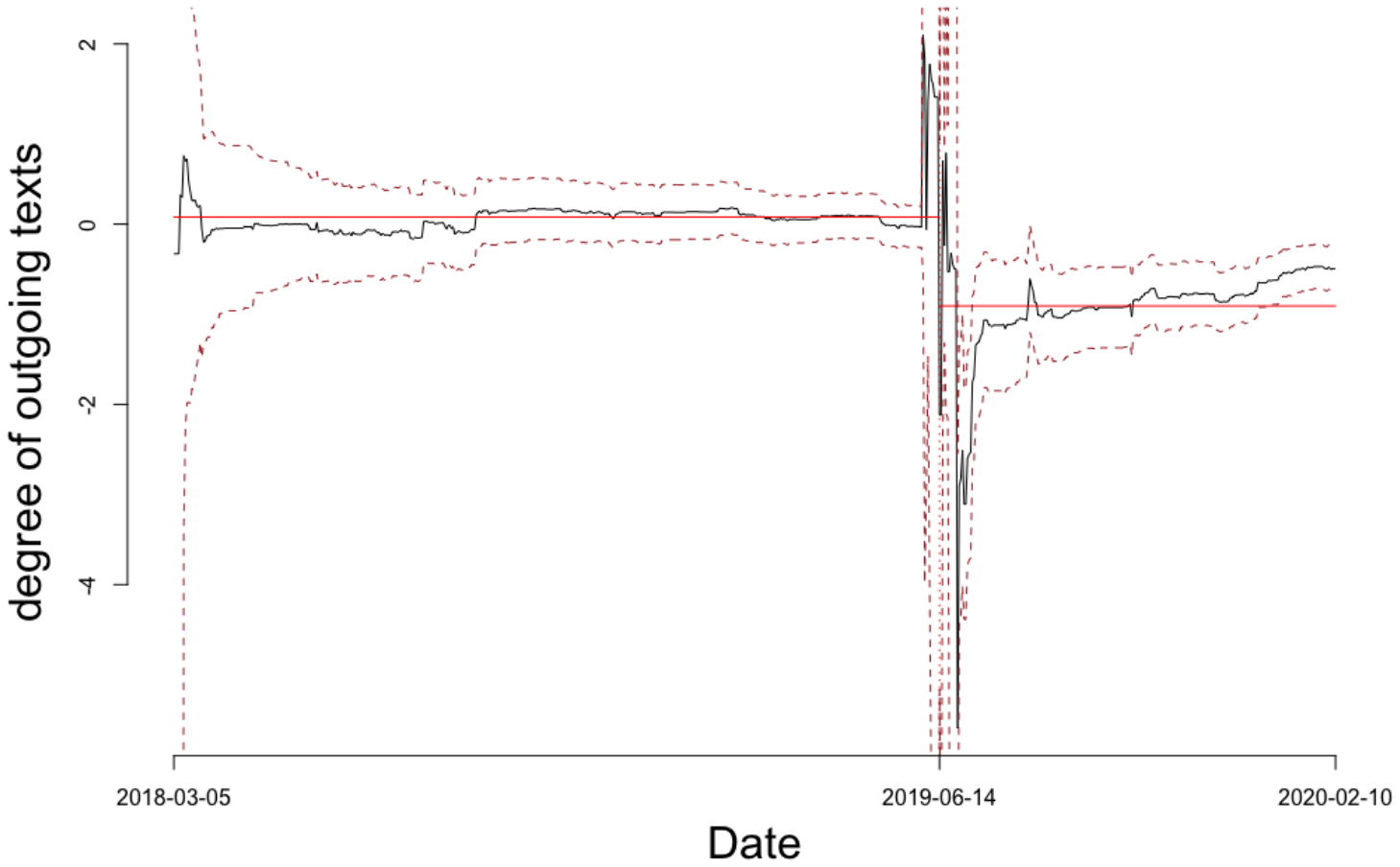
We estimate the association between the degree of outgoing calls and texts and the negative mood, controlling physical activity and temperature.

- Outcome: negative mood (Y_t)
- Exposures: degree of outgoing calls ($A_{1,t}$) and outgoing texts ($A_{2,t}$)
- Covariates: temperature (Temp_t), past physical activity (PA_t)

$$\begin{aligned} Y_t = {} & \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} \\ & + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t \end{aligned}$$

Missing rate before imputation $\rightarrow$ 40.4%
Missing rate after imputation $\rightarrow$ 23.3%

Estimation result: estimated coefficient for degree of outgoing texts



Estimation result: compared to complete case analysis

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

	SSMimpute (n=542)		complete case (n=423)	
	Estimate	90% CI	Estimate	90% CI
intercept_t	(random walk)		(random walk)	
ρ_t (for Y_{t-1})	0.64	(0.57,0.71)	0.72	(0.65,0.78)
$\beta_{11,t}$	-0.14	(-0.27,0.00)	-0.15	(-0.30,0.00)
$\beta_{12,t}$	0.00	(-0.12,0.12)	-0.09	(-0.23,0.05)
$\beta_{21,t}$ (period 1)	-0.03	(-0.30,0.24)	0.03	(-0.25,0.30)
$\beta_{21,t}$ (period 2)	-0.49	(-0.78,-0.21)	-0.5	(-0.81,-0.19)
$\beta_{22,t}$	-0.17	(-0.37,0.03)	-0.19	(-0.41,0.02)
$\beta_{\text{PA},t}$ (period 1)	-5.87	(-16.73,5.00)	-8.12	(-18.62,2.38)
$\beta_{\text{PA},t}$ (period 2)	-12.19	(-21.27,-3.11)	-12.66	(-21.06,-4.26)
$\beta_{\text{PA},t}$ (period 3)	2.31	(-1.00,5.62)	2.34	(-0.84,5.52)
$\beta_{\text{temp},t}$	-0.01	(-0.03,0.01)	-0.01	(-0.03,0.02)

Estimation result: compared to complete case analysis

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

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Estimation result: compared to complete case analysis

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Estimation result: compared to complete case analysis

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

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$\beta_{\text{temp},t}$	-0.01	(-0.03,0.01)	-0.01	(-0.03,0.02)

Estimation result: compared to multiple imputation

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

	SSMimpute (n=542)		multiple imputation (n=542)	
	Estimate	90% CI	Estimate	90% CI
intercept_t	(random walk)		(random walk)	
ρ_t (for Y_{t-1})	0.64	(0.57,0.71)	0.11	(-0.14,0.36)
$\beta_{11,t}$	-0.14	(-0.27,0.00)	-0.11	(-0.23,0.01)
$\beta_{12,t}$	0.00	(-0.12,0.12)	-0.05	(-0.16,0.07)
$\beta_{21,t}$ (period 1)	-0.03	(-0.30,0.24)	-0.02	(-0.27,0.23)
$\beta_{21,t}$ (period 2)	-0.49	(-0.78,-0.21)	-0.38	(-0.65,-0.1)
$\beta_{22,t}$	-0.17	(-0.37,0.03)	-0.23	(-0.42,-0.05)
$\beta_{\text{PA},t}$ (period 1)	-5.87	(-16.73,5.00)	-3.94	(-18.65,10.76)
$\beta_{\text{PA},t}$ (period 2)	-12.19	(-21.27,-3.11)	-16.96	(-32.94,-0.98)
$\beta_{\text{PA},t}$ (period 3)	2.31	(-1.00,5.62)	1.64	(-3.97,7.25)
$\beta_{\text{temp},t}$	-0.01	(-0.03,0.01)	-0.01	(-0.03,0.01)

Estimation result: compared to multiple imputation

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

	SSMimpute (n=542)		multiple imputation (n=542)	
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intercept_t	(random walk)		(random walk)	
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Estimation result: compared to multiple imputation

$$Y_t = \text{intercept}_t + \rho_t Y_{t-1} + \beta_{11,t} A_{\text{calls},t} + \beta_{12,t} A_{\text{calls},t-1} + \beta_{21,t} A_{\text{texts},t} + \beta_{22,t} A_{\text{texts},t-1} + \beta_{temp,t} \text{Temp}_t + \beta_{PA,t} \text{PA}_t + v_t$$

	SSMimpute (n=542)		multiple imputation (n=542)	
	Estimate	90% CI	Estimate	90% CI
intercept_t	(random walk)		(random walk)	
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$\beta_{\text{temp},t}$	-0.01	(-0.03,0.01)	-0.01	(-0.03,0.01)

Conclusions

- Estimated coefficient of the intercept is non-stationary and modeled as a random walk ($\rightarrow$ unknown systematic changes over time)
- "degree of outgoing calls" is significantly negatively associated with the negative mood.
- Estimated coefficient of "degree of outgoing texts" shows two periods: no significant association in stage I, and significant negative association in stage II.
- Estimated coefficient of "previous physical activity" shows three periods: no significant association in stage I and III, and significant negative association in stage II.

Summary

- Existing imputation methods mostly assume the time series to be stationary.
- We proposed a EM imputation algorithm based on state-space model, which applies to non-stationary multi-variate time series of a single subject.
- The proposed imputation method provides unbiased and more efficient estimation for non-stationary time series with missing outcomes.

Limitation and future work:

- Extend the SSMimpute method to missing values in exposures and covariates.
- Apply more flexible state space modeling than linear regression
- Evaluate lagged effect or long-term effect of exposure, combining g-methods for confounding adjustment
- The current model may suffer from unmeasured confounders.

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Thank you!