How black-box use of imputation can cause bias

Nicole Erler

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Handling Missing Values is Easy!

Functions automatically exclude missing values:

```
## [...]
## Residual standard error:  2.305 on 69 degrees of freedom
##   (25 observations deleted due to missingness)
## Multiple R-squared:  0.09255, Adjusted R-squared:  0.02679
## F-statistic:  1.407 on 5 and 69 DF, p-value:  0.2325
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Imputation is super easy:

```
library("mice")
imp <- mice(mydata)
```

However ...

Handling Missing Values Correctly is Not So Easy!

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violation ➡ bias

Literature: mis-specification in Multiple Imputation

Several authors have

- investigated robustness to mis-specification (of distribution)
  - in MI using FCS / MICE
  - in joint model MI
- and/or proposed to use
  - Tukey's gh distribution
  - Fleishman polynomials
  - GAMs (in FCS)
  - Doubly-robust weighted estimating equations (instead of MI)

Fully Bayesian Analysis & Imputation

Joint distribution

$$\underbrace{p(y \mid X, b, \theta)}_{\substack{\text{analysis}\\\text{model}}} \; \underbrace{p(X \mid \theta)}_{\substack{\text{imputation}\\\text{part}}} \; \underbrace{p(b \mid \theta)}_{\substack{\text{random}\\\text{effects}}} \; \underbrace{p(\theta)}_{\text{priors}}$$

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Imputation part

$$p(\overbrace{x_1, \ldots, x_p, X_{compl.}}^{X} \mid \theta) = \begin{array}{l} p(x_1 \mid X_{compl.}, \theta) \\ p(x_2 \mid X_{compl.}, x_1, \theta) \\ p(x_3 \mid X_{compl.}, x_1, x_2, \theta) \\ \ldots \end{array}$$

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Software

Implemented in the **R** package **JointAI**

MICE vs JointAI

Imputation in MICE

$$p(x_1 \mid y, X_{compl.}, x_2, x_3, x_4, \ldots, \theta)$$
$$p(x_2 \mid y, X_{compl.}, x_1, x_3, x_4, \ldots, \theta)$$
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Imputation in JointAI

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No issues with

- complex outcomes, e.g.:
  - multi-level
  - survival
- congeniality
- compatibility

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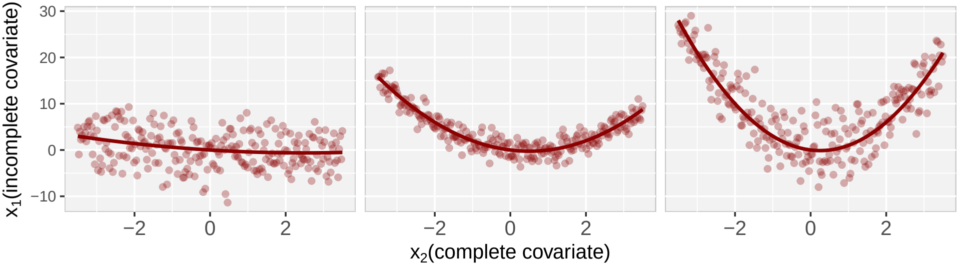
Potential mis-specification of

- association structure
- conditional distribution
- M(C)AR

Simulation Study: Quadratic Effect

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots$

Quadratic association between covariates: $x_1 \sim \alpha_0 + \alpha_1 x_2 + \cancel{\alpha_2 x_2^2} + \ldots$



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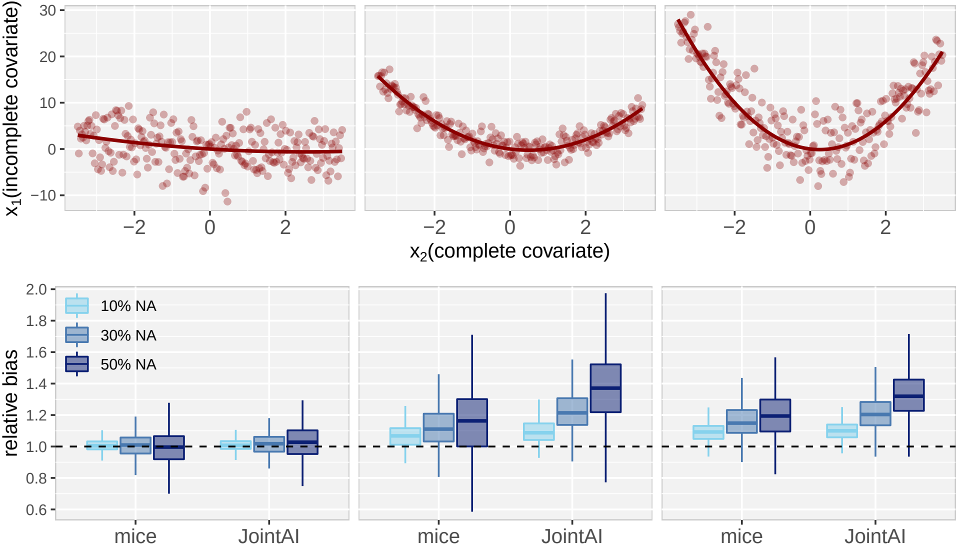
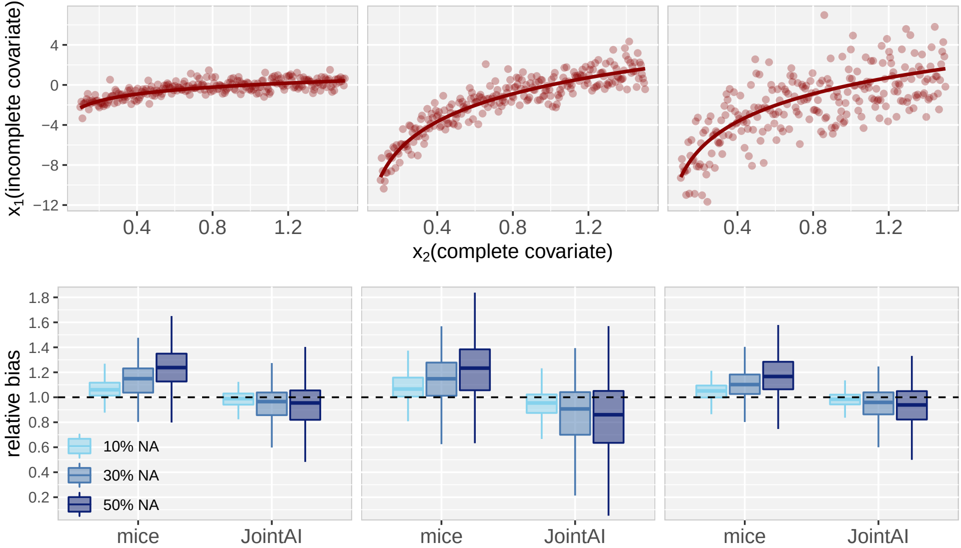


Simulation Study: Logarithmic Effect

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots$

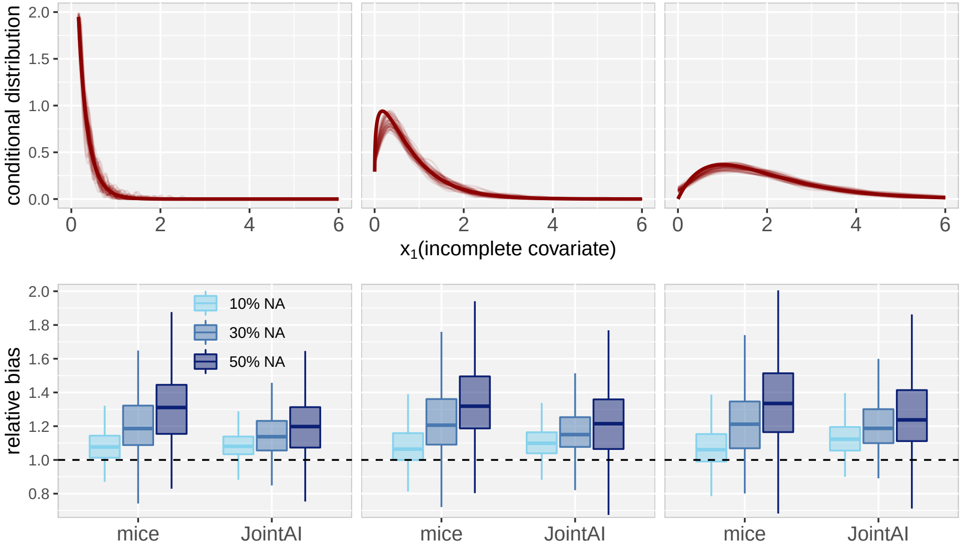
Log-association between covariates: $x_1 \sim \alpha_0 + \alpha_1 \bcancel{\log}(x_2) + \dots$



Simulation Study: Gamma distribution

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots$

Gamma-distributed covariate: $x_1 \mid x_2, x_3, \dots \sim Ga()$



Flexible Bayesian Models

We need more flexible imputation models!

Ideally: models that fit (almost) any distribution / association structure.

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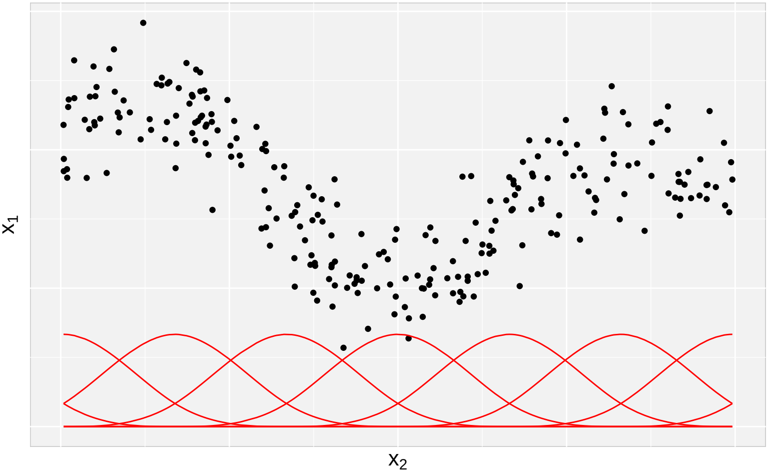
Ideas:

- flexible **association** structure: **penalized splines**
- flexible residual **distribution**: **mixture of Polya-Trees**

Bayesian P-Splines

Instead of $\beta_1 x_2$ we use $\sum_{\ell=1}^{d} \beta_\ell B_\ell(x_2)$:



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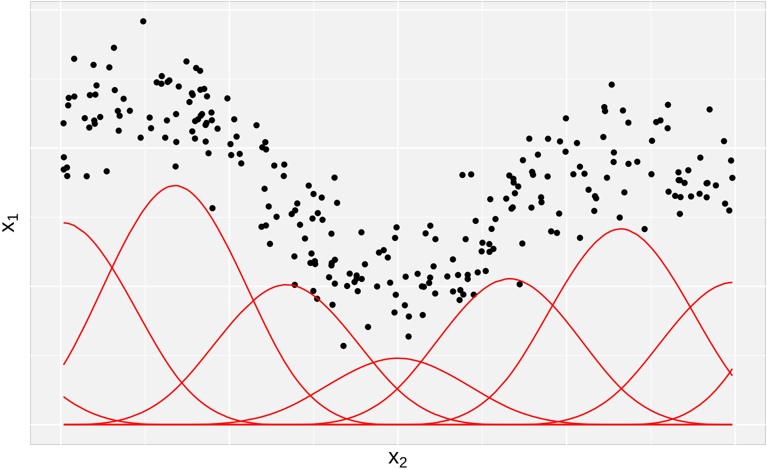

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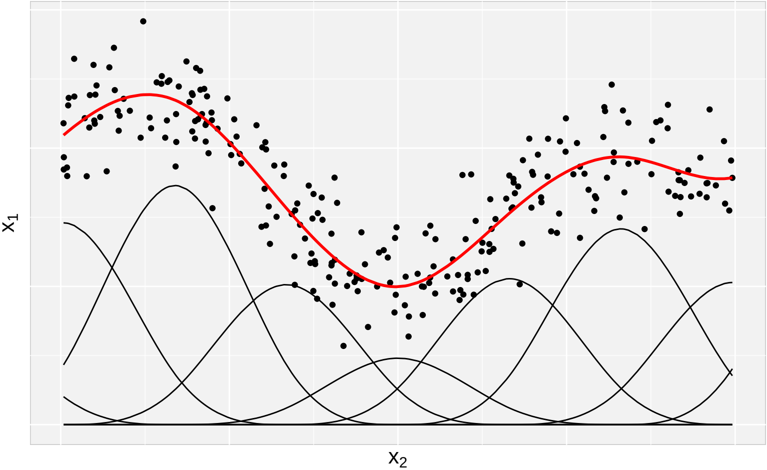

Simulation: Bayesian P-Splines

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots$

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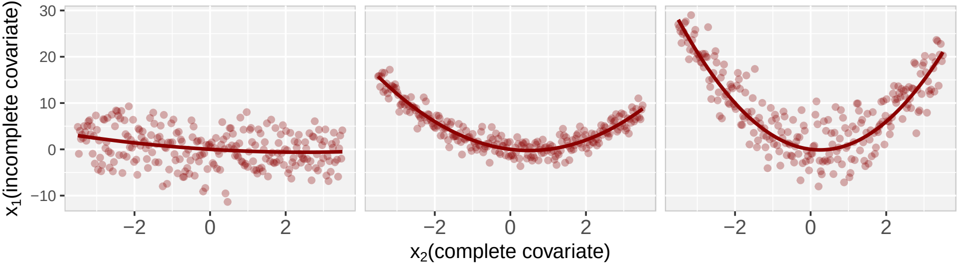

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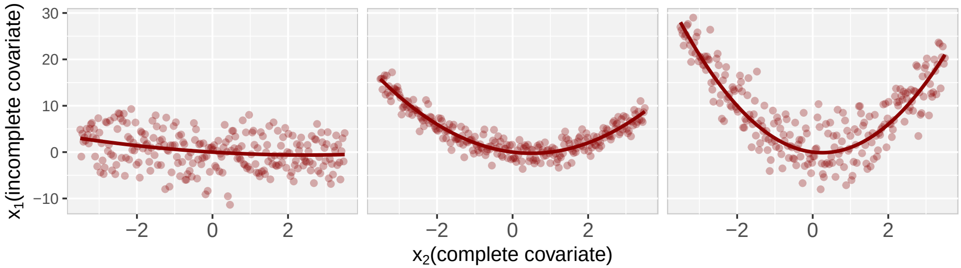
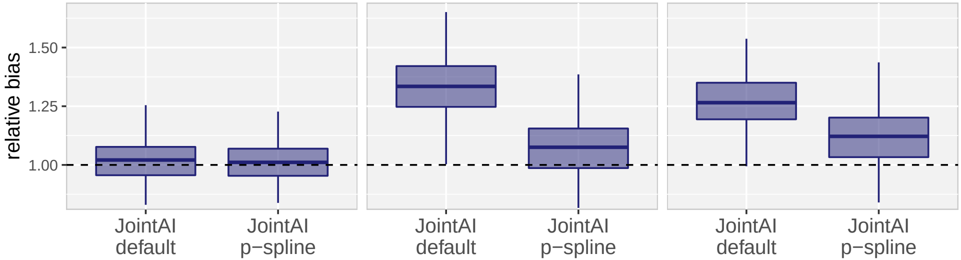
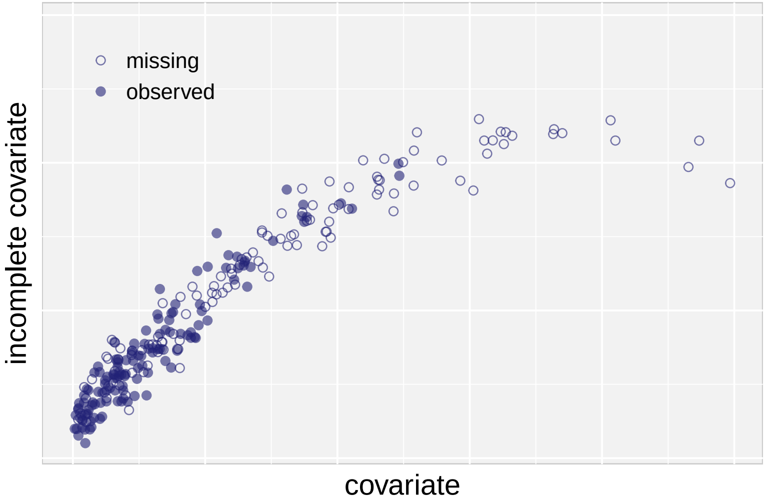




Simulation: Bayesian P-Splines

Potential Issue:



Simulation: Bayesian P-Splines

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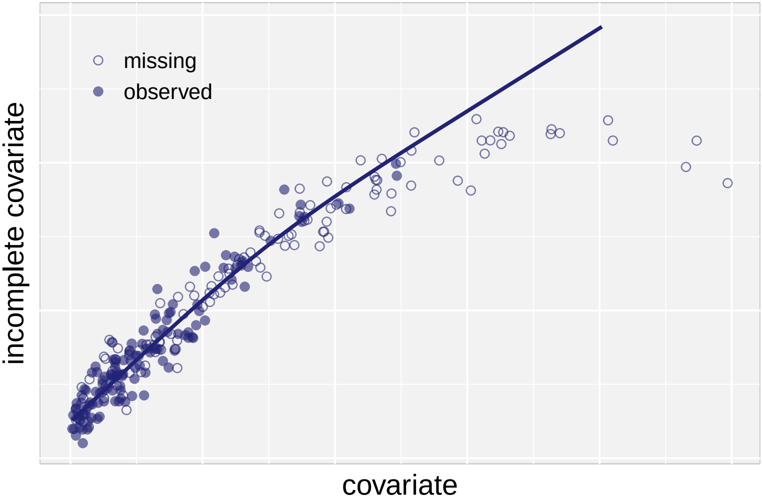
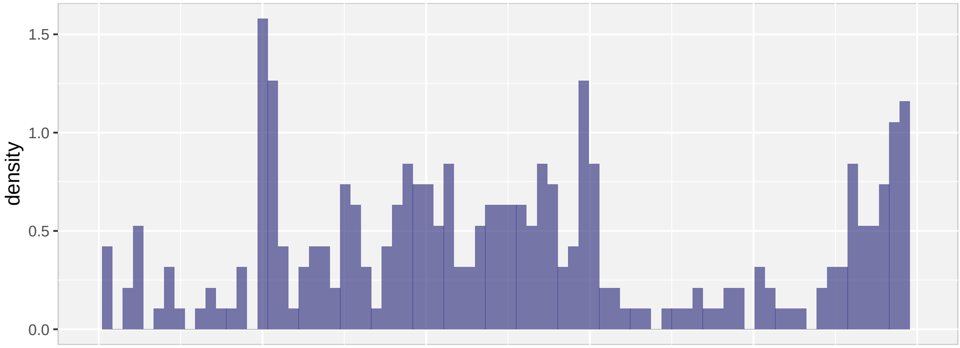


Mixture of Polya Trees



Beta(a_0, a_0)

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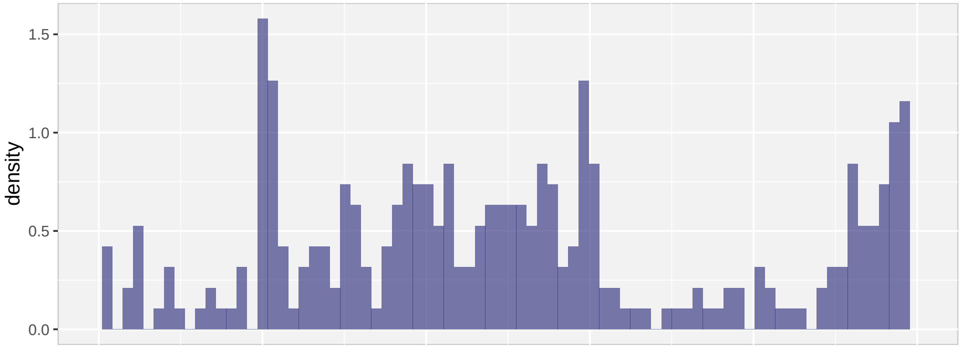

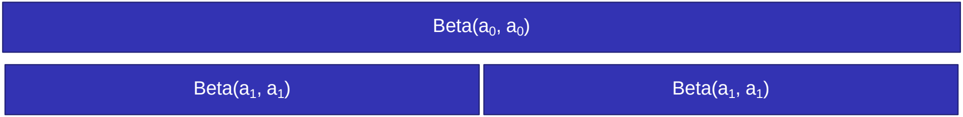

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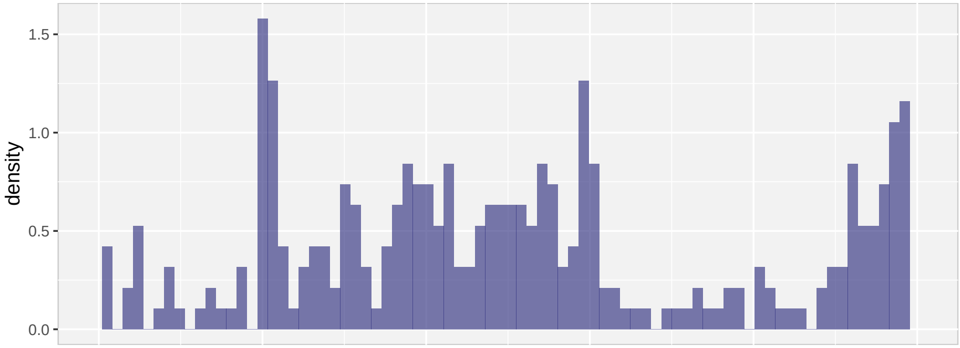

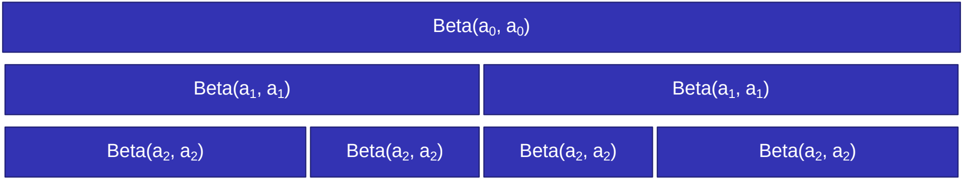

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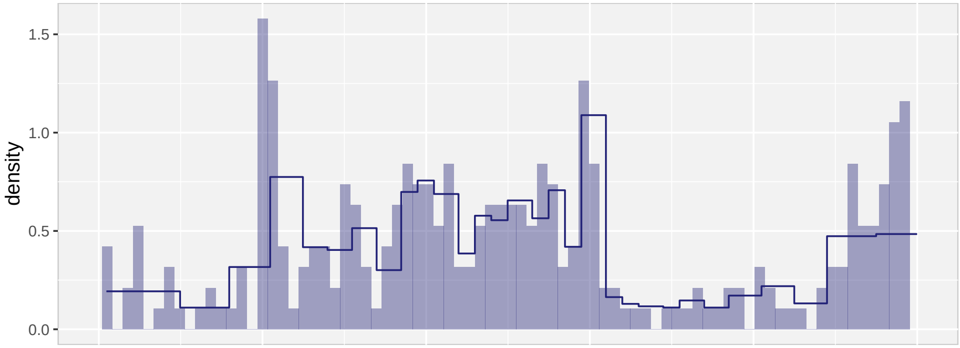

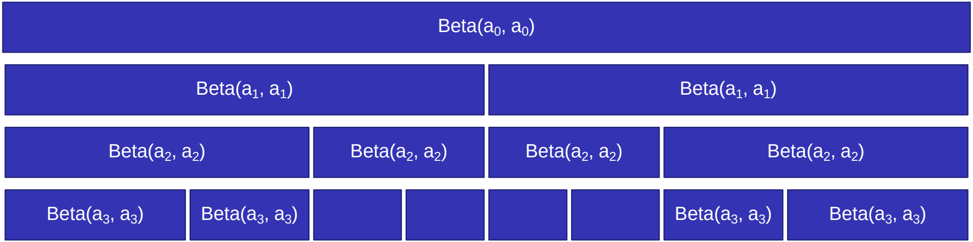
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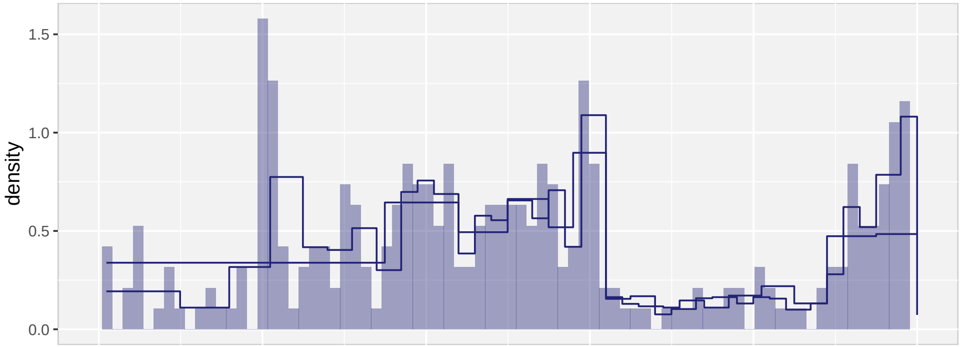

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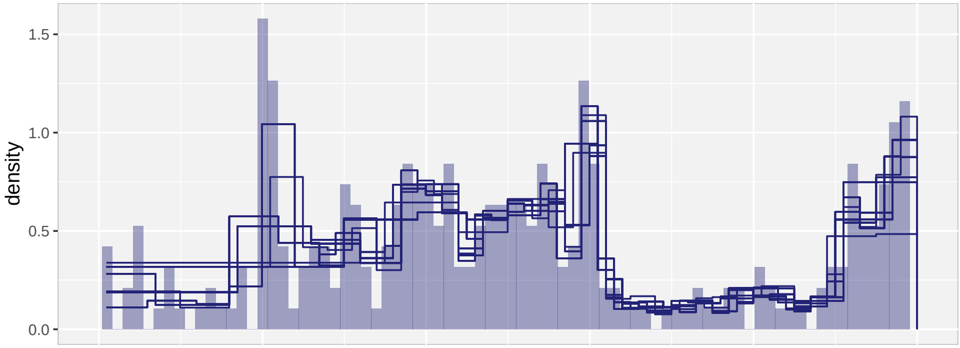

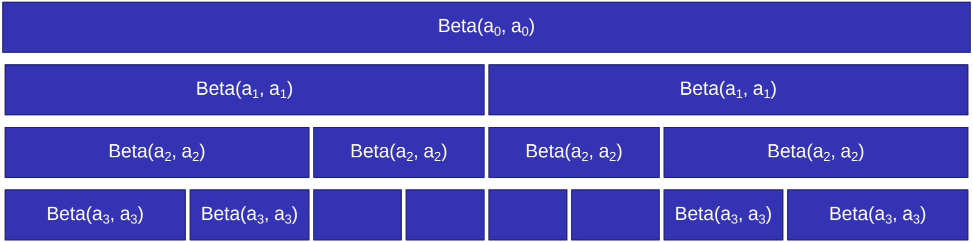

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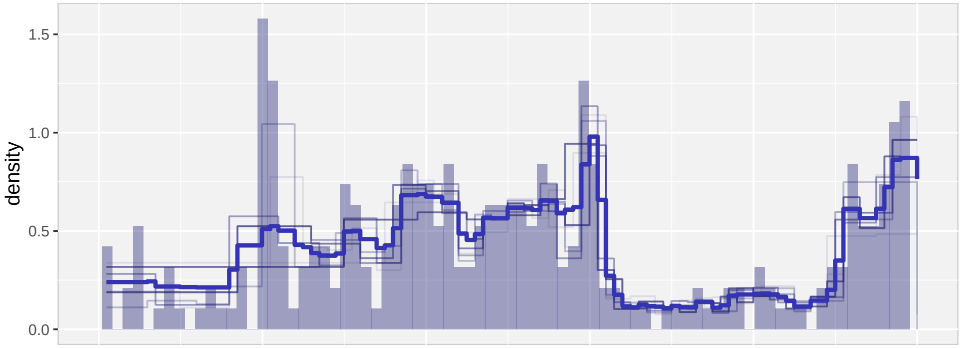

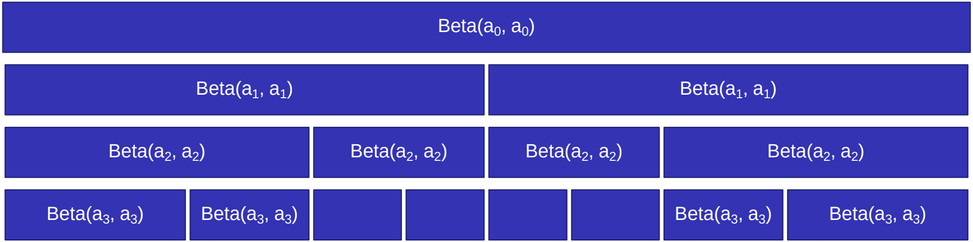

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Practical Issues & Ideas

Potential / probable issues for practice:

- flexible fit needs observed data everywhere
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- check first if simple model fits, e.g. posterior predictive checks
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  - discordance tests?

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  - χ^2 type of tests
  - Kolmogorov-Smirnoff test?
  - discordance tests?
- feasibility checks before running the complex model

Take home message

- **assumptions** of imputation models can easily be **violated** ➡ **bias**
- **more flexible** imputation models are **needed**
- semi- / **non-parametric (Bayesian) methods** can offer a **solution**
- more **flexibility** ➡ more **complexity** ➡ need for **guidance** tools

Thank you for your attention.

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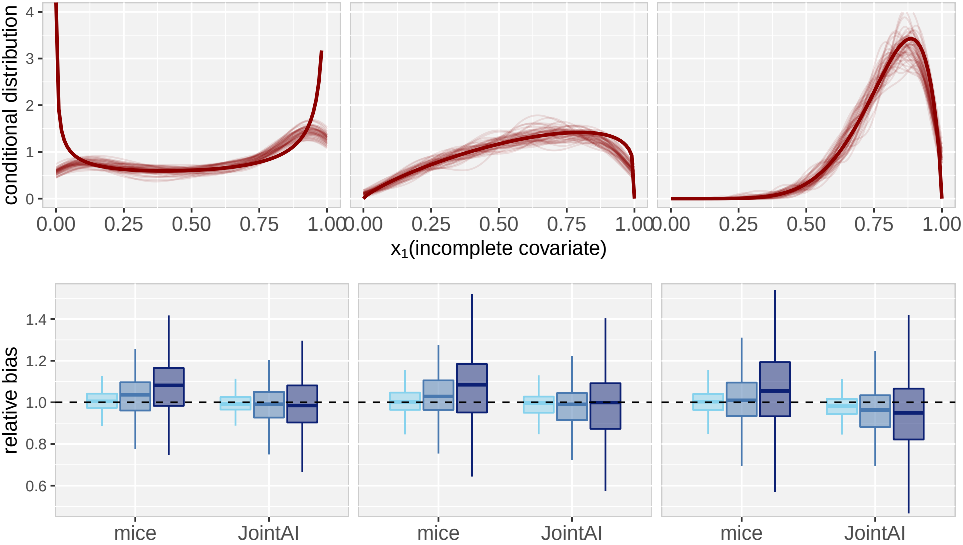
Simulation Study: Beta Distribution

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 + \dots$

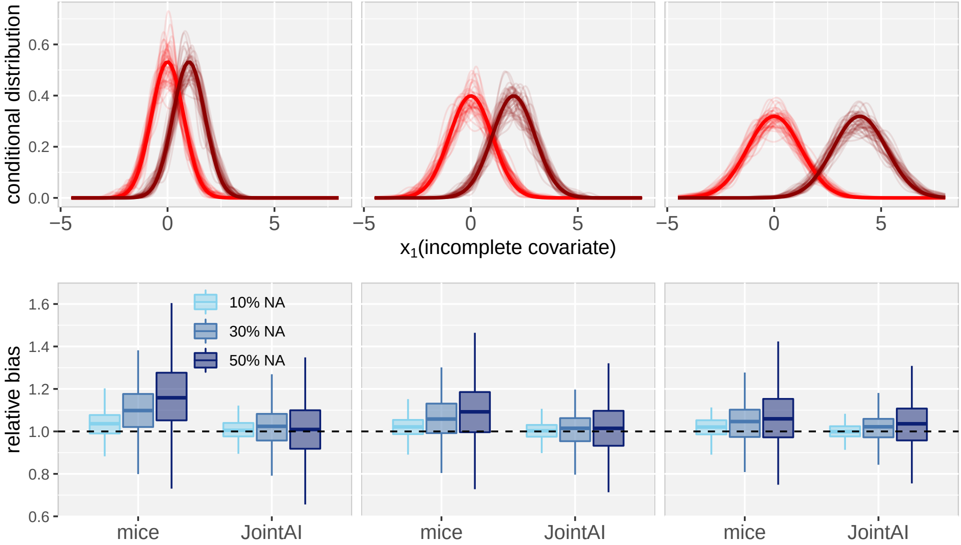
Beta-distributed covariate: $x_1 \mid x_2, x_3, \dots \sim Be()$



Simulation Study: Reverting the sequence

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots$

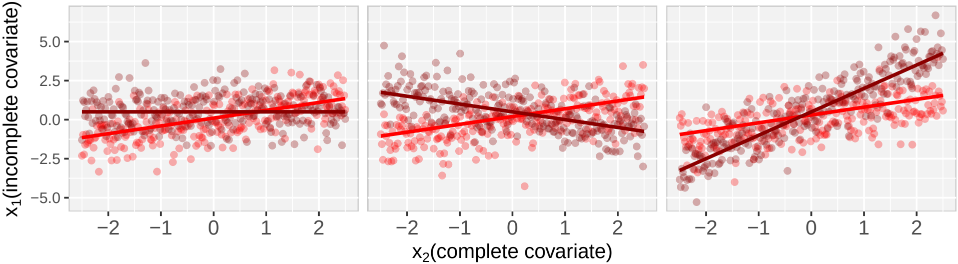
Exclusion of important predictor: $x_1 \sim \alpha_0 + \alpha_1 x_2 + \cancel{\alpha_2 x_3} + \dots$

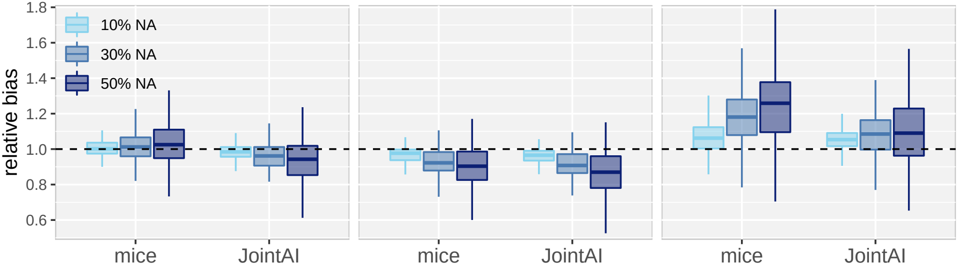


Simulation Study: Ignoring an Interaction

Analysis model: $y \sim \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots$

Interaction between covariates: $x_1 \sim \alpha_0 + \alpha_1 x_2 + \alpha_2 x_3 + \cancel{\alpha_3 x_2 x_3} + \ldots$


x₁(incomplete covariate)
x₂(complete covariate)


relative bias
10% NA
30% NA
50% NA
mice
JointAI
mice
JointAI
mice
JointAI