# What is a good imputation under MAR missingness

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"**Pre**cision **Me**dicine by **D**ata **I**ntegration & **Ca**usal **L**earning"

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Näf et al. (2024)
(https://arxiv.org/abs/2403.19196)

Jeffrey Näf

# Traumabase project: decision support for trauma patients

- ▷ 30 000 French trauma patients[1]
- ▷ 250 features from the accident site to the hospital discharge
- ▷ 30 hospitals
- ▷ 4000 new patients/ year

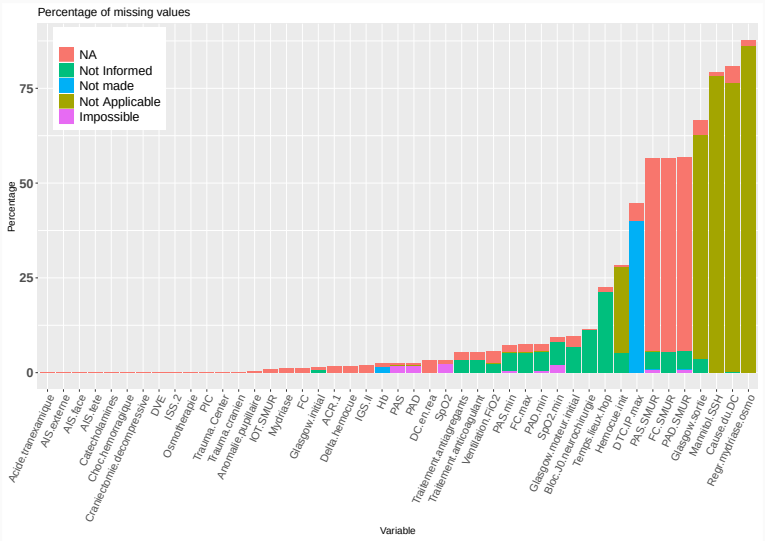
| Center | Accident | Age | Sex | Weight | Lactactes | BP | **TXA.** | $Y$ |
|---|---|---|---|---|---|---|---|---|
| Beaujon | fall | 54 | m | 85 | NM | 180 | treated | 0 |
| Pitie | gun | 26 | m | NR | NA | 131 | untreated | 1 |
| Beaujon | moto | 63 | m | 80 | 3.9 | 145 | treated | 1 |
| Pitie | moto | 30 | w | NR | Imp | 107 | untreated | 0 |
| HEGP | knife | 16 | m | 98 | 2.5 | 118 | treated | 1 |
| ⋮ | | | | | | | | ⋱ |

⇒ **Estimate causal effect**: Administration of the **treatment** *tranexamic acid (TXA)*, given within 3 hours of the accident, on the **outcome** $Y$ *28 days intra hospital mortality* for trauma brain patients

TXA decreases mortality for extra-cranial bleeding. Effect for intra-cranial bleeding? (detected by CT scan). TXA is one of the first treatments given

[1] `www.traumabase.eu - https://www.traumatrix.fr/`

# Missing data: important bottleneck in statistical practice



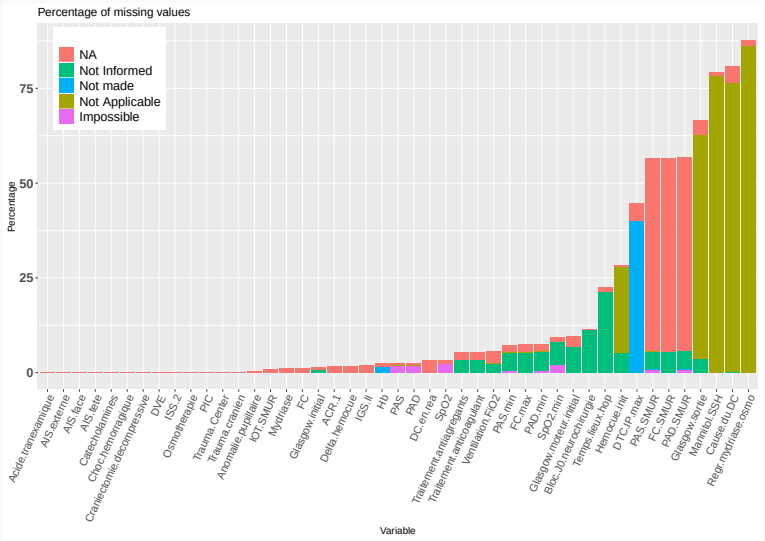

*"One of the ironies of Big Data is that missing data play an ever more significant role"*[2]

[2] Zhu, Wang, Samworth. High-dimensional PCA with heterogeneous missingness. *JRSSB*. 2022.

[3] J., et al. `https://rmisstastic.netlify.com/` - Tutorial JJ diableret.

[4] R Taskview https://cran.r-project.org/web/views/MissingData.html

# Missing data: important bottleneck in statistical practice




*"One of the ironies of Big Data is that missing data play an ever more significant role"*[2]

Complete-case analysis, often not a good idea! What are the alternatives?

Inferential aim: **Estimate parameters & their variance, i.e.** $\hat{\beta}$, $\hat{V}(\hat{\beta})$
Matrix completion aim: **Predict the missing values** - low rank approx.
Predictive aim: **Predict an outcome** with missing values in covariates
Rmistatic $>$ 150 packages,[3][4]

[2] Zhu, Wang, Samworth. High-dimensional PCA with heterogeneous missingness. *JRSSB*. 2022.
[3] J., et al. `https://rmisstastic.netlify.com/` - Tutorial JJ diableret.
[4] R Taskview https://cran.r-project.org/web/views/MissingData.html

# Missing values alter causal analyses

| Covariates | | | Treatment | Outcome(s) | |
|---|---|---|---|---|---|
| $X_1$ | $X_2$ | $X_3$ | W | Y(0) | Y(1) |
| NA | 20 | F | 1 | ? | 200 |
| -6 | 45 | NA | 0 | 10 | ? |
| 0 | NA | M | 1 | ? | 150 |
| NA | 32 | F | 1 | ? | 100 |
| 1 | 63 | M | 1 | 15 | ? |
| -2 | NA | M | 0 | 20 | ? |

## Both causal and missing assumptions

1. Classical unconfoundedness + classical missing values mechanisms[5]
2. Unconfoundedness with missing + (no) missing values mechanisms[6]
3. Latent unconfoundedness + MCAR[7]

[5] Seaman and White. IPW with missing predictors of treatment assignment, *Communications in Statistics, Theory & Methods*. 2014.

[6] Mayer, Wager, **J.** Doubly robust estimation with incomplete confounders. *AOAS*. 2020.

[7] Kallus et al. Causal inf. with noisy & missing covariates via matrix factorization. *Neurips*. 2018.

# 1. Popular multiple imputation for estimating treatment effect

| $X_1$ | $X_2$ | $X_3$ | ... | W | Y(0) | Y(1) |
|---|---|---|---|---|---|---|
| NA | 20 | 10 | ... | 1 | ? | 200 |
| -6 | 45 | NA | ... | 1 | 10 | ? |
| 0 | NA | 30 | ... | 0 | ? | 150 |
| NA | 32 | 35 | ... | 0 | ? | 100 |
| -2 | NA | 12 | ... | 0 | 20 | ? |

1) Generate $M$ plausible values for each missing value

| $X_1$ | $X_2$ | $X_3$ | ... | W | Y | $X_1$ | $X_2$ | $X_3$ | ... | W | Y | $X_1$ | $X_2$ | $X_3$ | ... | W | Y |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | 20 | 10 | ... | 1 | 200 | -7 | 20 | 10 | ... | 1 | 200 | 7 | 20 | 10 | ... | 1 | 200 |
| -6 | 45 | 6 | ... | 1 | 10 | -6 | 45 | 9 | ... | 1 | 10 | -6 | 45 | 12 | ... | 1 | 10 |
| 0 | 4 | 30 | ... | 0 | 150 | 0 | 12 | 30 | ... | 0 | 150 | 0 | -5 | 30 | ... | 0 | 150 |
| -4 | 32 | 35 | ... | 0 | 100 | 13 | 32 | 35 | ... | 0 | 100 | 2 | 32 | 35 | ... | 0 | 100 |
| -2 | 15 | 12 | ... | 0 | 20 | -2 | 10 | 12 | ... | 0 | 20 | -2 | 20 | 12 | ... | 0 | 20 |

2) Estimate Average Treatment Effect on each imputed data set with IPW: $\hat{\tau}_m$

3) Combine the results (Rubin's rules): $\hat{\tau} = \frac{1}{M} \sum_{m=1}^{M} \hat{\tau}_m$

## Consistency of multiple imputation with IPW[8]

Assume: **MAR** Proba to have missing depends on observed values

Classical **unconfoundedness** $\{Y_i(0), Y_i(1)\} \perp\!\!\!\perp W_i \mid X_i$,

Propensity Score and model for $(X \mid Y, W)$ correctly specified,

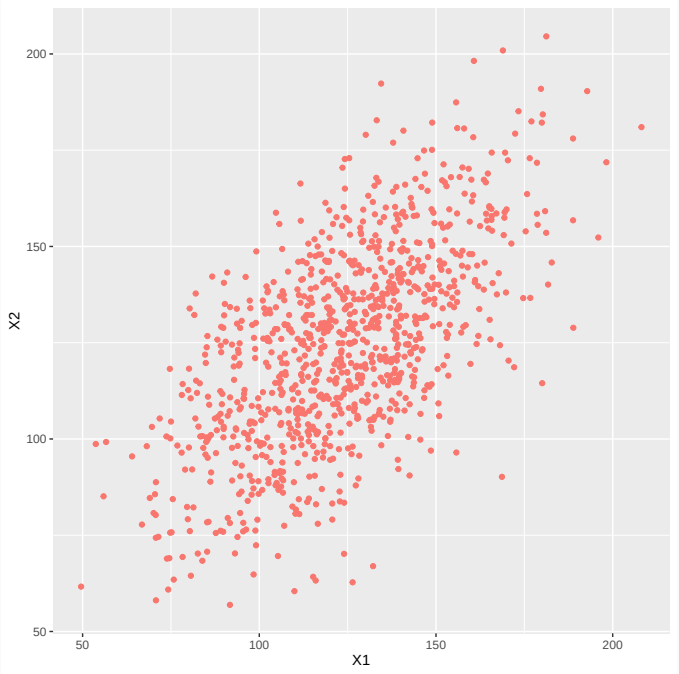
$\Rightarrow$ Multiple imputation (using $(X, W, Y)$) with IPW is consistent

[8] Seaman and White. 2014. IPW with missing predictors of treatment assignment, *Communications in Statistics, Theory & Methods*.

# Single imputation by the mean

▷ $(x_{i1}, x_{i2}) \underset{\text{i.i.d.}}{\sim} \mathcal{N}_2((\mu_{x_1}, \mu_{x_2}), \Sigma_{x_1 x_2})$

| $\mathbf{X}_1$ | $\mathbf{X}_2$ |
|---|---|
| -0.56 | -1.93 |
| -0.86 | -1.50 |
| ..... | ... |
| 2.16 | 0.7 |
| 0.16 | 0.74 |




$\mu_{x_2} = 0$

$\sigma_{x_2} = 1$

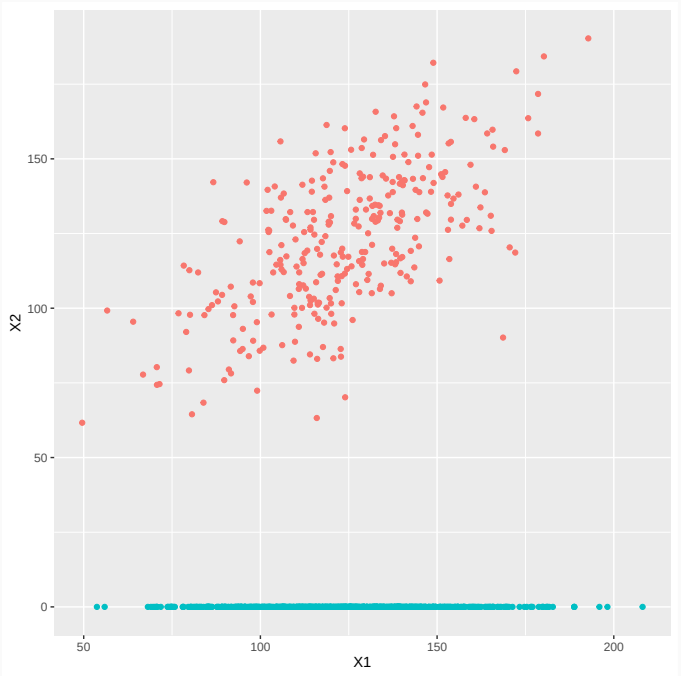
$\rho = 0.6$

| |
|---|
| $\hat{\mu}_{x_2} = -0.01$ |
| $\hat{\sigma}_{x_2} = 1.01$ |
| $\hat{\rho} = 0.66$ |

# Single imputation by the mean

- $(x_{i1}, x_{i2}) \underset{\text{i.i.d.}}{\sim} \mathcal{N}_2((\mu_{x_1}, \mu_{x_2}), \Sigma_{x_1 x_2})$
- 70 % of missing entries completely at random on $X_2$

| $\mathbf{X}_1$ | $\mathbf{X}_2$ |
|---|---|
| -0.56 | NA |
| -0.86 | NA |
| ..... | ... |
| 2.16 | 0.7 |
| 0.16 | NA |



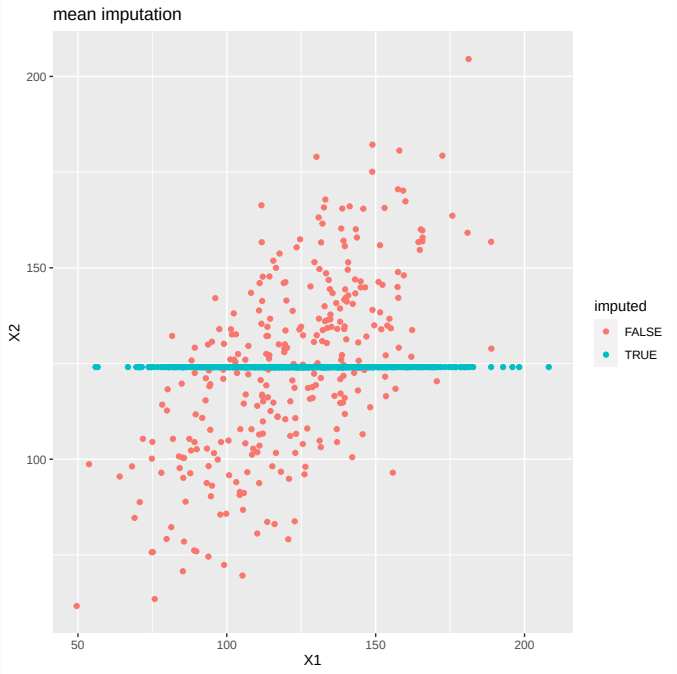

$\mu_{x_2} = 0$
$\sigma_{x_2} = 1$
$\rho = 0.6$

| |
|---|
| $\hat{\mu}_{x_2} = 0.18$ |
| $\hat{\sigma}_{x_2} = 0.9$ |
| $\hat{\rho} = 0.6$ |

# Single imputation by the mean

- $(x_{i1}, x_{i2}) \underset{\text{i.i.d.}}{\sim} \mathcal{N}_2((\mu_{x_1}, \mu_{x_2}), \Sigma_{x_1 x_2})$
- 70 % of missing entries completely at random on $X_2$
- Estimate parameters on the mean imputed data

| $\mathbf{X}_1$ | $\mathbf{X}_2$ |
|---|---|
| -0.56 | **0.01** |
| -0.86 | **0.01** |
| ..... | ... |
| 2.16 | 0.7 |
| 0.16 | **0.01** |




$\mu_{x_2} = 0$

$\sigma_{x_2} = 1$

$\rho = 0.6$

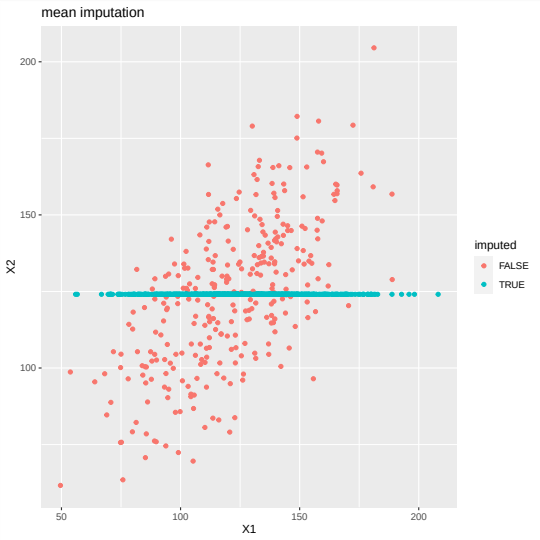
| |
|---|
| $\hat{\mu}_{x_2} = 0.01$ |
| $\hat{\sigma}_{x_2} = 0.5$ |
| $\hat{\rho} = 0.30$ |

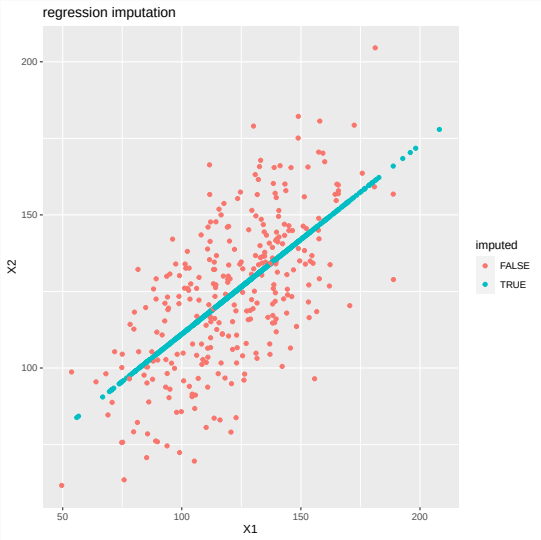
Mean imputation deforms joint and marginal distributions

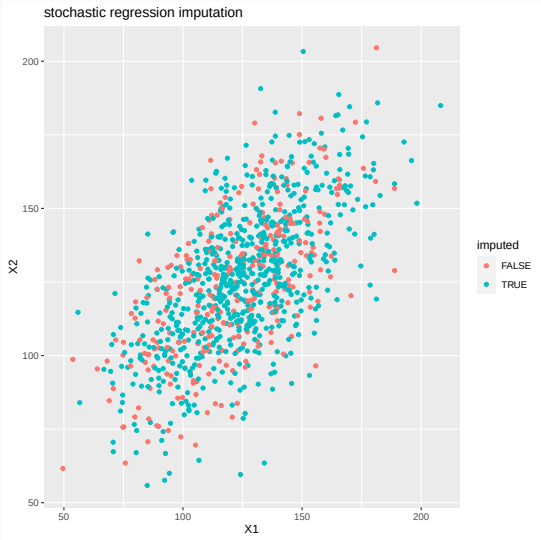
# Objective: to impute while preserving distribution

Assuming a bivariate gaussian distribution $x_{i2} = \beta_0 + \beta_1 x_{i1} + \varepsilon_i,\ \varepsilon_i \sim \mathcal{N}(0, \sigma^2)$

- ▷ Regression imputation: Estimate $\beta$ (here with complete data) and impute $\hat{x}_{i2} = \hat{\beta}_0 + \hat{\beta}_1 x_{i1} \Rightarrow$ variance underestimated and correlation overestimated
- ▷ Stochastic reg. imputation: Estimate $\beta$ and $\sigma$ - impute from the predictive $\hat{x}_{i2} \sim \mathcal{N}\left(\beta_0 + \hat{\beta}_1 x_{i1}, \hat{\sigma}^2\right) \Rightarrow$ preserve distributions




$\mu_{x_2} = 0$
$\sigma_{x_2} = 1$
$\rho = 0.6$

| |
|---|
| 0.01 |
| 0.5 |
| 0.30 |

| |
|---|
| 0.01 |
| 0.72 |
| 0.78 |

| |
|---|
| 0.01 |
| 0.99 |
| 0.59 |

# Impute while preserving distribution. Multivariate case

## Assuming a joint distribution

- Gaussian model $x_i \sim \mathcal{N}(\mu, \Sigma)$
- Low rank : $X_{n\times d} = \mu_{n\times d} + \varepsilon\ \varepsilon_{ij} \overset{\text{iid}}{\sim} \mathcal{N}\left(0,\ \sigma^2\right)$ with $\mu$ of low rank
  - $\Rightarrow$ Powerful in recommendation system: Netflix prize 90% of missing
  - $\Rightarrow$ Different regularization depending on noise regime[9]
  - $\Rightarrow$ Count data,[10] ordinal data, categorical data, blocks/multilevel data[11]
- Using optimal transport,[12] deep generative models (GAIN,[13] MIWAE,[14] etc.)

[9] **J.** & Wager. Stable autoencoding for regularized low-rank matrix estimation. *JMLR*. 2016.
[10] Robin, Klopp, **J.**, Moulines, Tibshirani. Main effects & interac. in mixed data. *JASA*. 2019.
[11] **J.** et al. Imputation of mixed data with multilevel SVD. *JCGS*. 2018.
[12] Muzelec, Cuturi, Boyer, **J.** Missing Data Imputation using Optimal Transport. *ICML*. 2020.
[13] Yoon et al. GAIN: Missing data imputation using generative adversarial nets. *ICML*. 2018.
[14] Mattei & Frellsen. Miwae: Deep generative model. & imput. of incomplete data. *ICML*. 2018.
[15] Stekhoven & Bühlmann. MissForest–non-parametric imputation for mixed data. *Bioinfo. 2012.*

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## Iterating conditional models (joint distribution implicitly defined)

- with multinomial, Poisson regression (ICE: Imputation by Chained Equations)
- iterative imputation of each variable by random forests[15]

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[9] **J.** & Wager. Stable autoencoding for regularized low-rank matrix estimation. *JMLR*. 2016.
[10] Robin, Klopp, **J.**, Moulines, Tibshirani. Main effects & interac. in mixed data. *JASA*. 2019.
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# Missing values mechanism: Rubin's taxonomy[16,17]

- Random Variables:
  - $X^\star \in \mathbb{R}^d$: complete unavailable data, $X \in \mathbb{R}^d$: observed data with NA
  - $M \in \{0,1\}^d$: missing pattern, or mask, $M_j = 1$ if and only if $X_j$ is missing

- Realizations: For a pattern $m$, $o(x,m) = (x_j)_{j \in \{1,\dots,d\}:m_j=0}$ the observed elements of $x$ and while $o^c(x,m) = (x_j)_{j \in \{1,\dots,d\}:m_j=1,}$ the missing elements.

$$x^\star = (1,2,3,8,5)$$
$$x = (1, \mathrm{NA}, -3, 8, \mathrm{NA})$$
$$m = (0,1,0,0,1)$$
$$o(x,m) = (1,3,8), \qquad o^c(x^\star, m) = (2,5)$$

[16] Rubin. Inference and missing data. *Biometrika.* 1976.
[17] What Is Meant by "Missing at Random"? Seaman, et al. Statistical Science. 2013.

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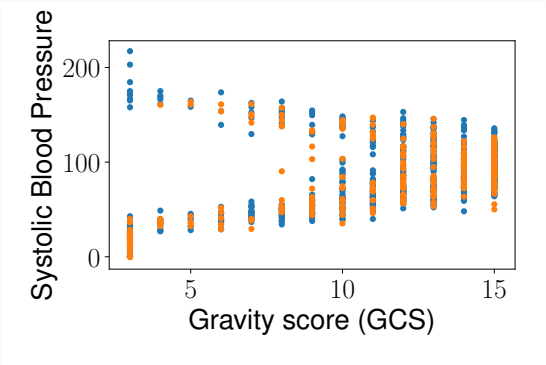
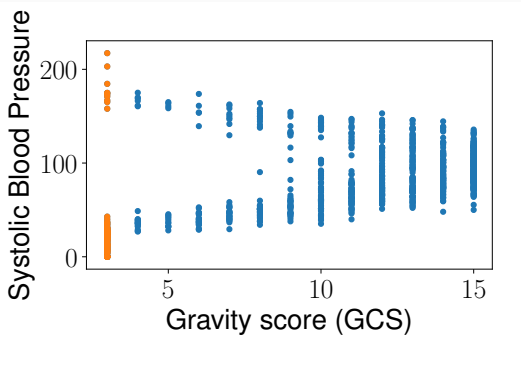
For a pattern $m$, $o(x,m) = (x_j)_{j \in \{1,\dots,d\}:m_j=0}$ the observed elements of $x$ and while $o^c(x,m) = (x_j)_{j \in \{1,\dots,d\}:m_j=1}$, the missing elements.

Ex: Simulated missing values according to the 3 mechanisms (Orange points will be missing) in Systolic Blood Pressure - GCS is always observed



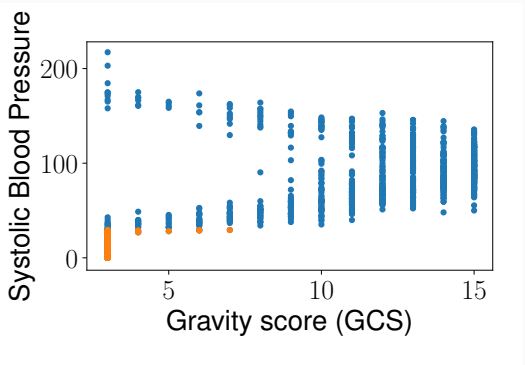

**Missing Completely at Random (MCAR)**

$m \in \mathcal{M}, x \in \mathcal{X}$,
$\mathbb{P}(M = m|x) = \mathbb{P}(M = m)$




**Missing at Random (MAR)**

$\forall m \in \mathcal{M}, x \in \mathcal{X}$
$\mathbb{P}(M = m|x) = \mathbb{P}(M = m|o(x,m))$




**Missing Not At Random (MNAR)**

If not MAR: it is MNAR

[16] Rubin. Inference and missing data. *Biometrika.* 1976.

[17] What Is Meant by "Missing at Random"? Seaman, et al. Statistical Science. 2013.

# Two views to model the joint distribution of $(X, M)$

**Selection Model**[18]**:** $p^*(M = m, x) = \mathbb{P}(M = m \mid x)p^*(x)$

**Definition (SM-MAR)**

$$\mathbb{P}(M = m|x) = \mathbb{P}(M = m|o(x, m)) \text{ for all } m \in \mathcal{M}, x \in \mathcal{X}.$$

The proba. of any $m$ occurring only depends on the obs part of $x$.

**Pattern Mixture Model**[19]**:** $p^*(M = m, x) = p^*(x \mid M = m)\mathbb{P}(M = m)$

**Definition (PMM-MAR)**

$$p^*(o^c(x, m) \mid o(x, m), M = m) = p^*(o^c(x, m) \mid o(x, m)).$$

for all $m \in \mathcal{M}, x \in \mathcal{X}$. The conditional distrib. of missing given obs. in each pattern is equal to the unconditional one.[20]

[18] Heckman. Sample selection bias as a specification error. *Econometrica*. 1979
[19] Little. Pattern-mixture models for multivariate incomplete data. *JASA*. 1993
[20] Molenberghs et al. Every MNAR model has a MAR counterpart with equal fit. *JRSSB*. 2008

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**Proposition (SM-MAR is equivalent to PMM-MAR)**

[18] Heckman. Sample selection bias as a specification error. *Econometrica*. 1979

[19] Little. Pattern-mixture models for multivariate incomplete data. *JASA*. 1993

[20] Molenberghs et al. Every MNAR model has a MAR counterpart with equal fit. *JRSSB*. 2008

# MAR with shift in marginal distribution between patterns

- Gaussian PMM: $X^* \mid M = m \sim N(\mu_m \mid \Sigma_m)$. Ex: for two patterns $m_1 = (0, 0)$ and $m_2 = (1, 0)$ and **a shift**:

$$\mathbf{X} = \begin{pmatrix} x_{1,1} & x_{1,2} \\ NA & x_{2,2} \end{pmatrix}, \mathbf{M} = \begin{pmatrix} 0 & 0 \\ 1 & 0 \end{pmatrix} = \begin{pmatrix} m_1 \\ m_2 \end{pmatrix}.$$

# MAR with shift in marginal distribution between patterns

- Gaussian PMM: $X^* \mid M = m \sim N(\mu_m \mid \Sigma_m)$. Ex: for two patterns $m_1 = (0, 0)$ and $m_2 = (1, 0)$ and **a shift**:

$$(X_1, X_2) \mid M = m_1 \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} 2 & 1 \\ 1 & 1 \end{pmatrix}\right) (X_1, X_2) \mid M = m_2 \sim N\left(\begin{pmatrix} 5 \\ 5 \end{pmatrix}, \begin{pmatrix} 2 & 1 \\ 1 & 1 \end{pmatrix}\right).$$

# MAR with shift in marginal distribution between patterns

• Gaussian PMM: $X^* \mid M = m \sim N(\mu_m \mid \Sigma_m)$. Ex: for two patterns $m_1 = (0, 0)$ and $m_2 = (1, 0)$ and **a shift**:

$$(X_1, X_2) \mid M = m_1 \sim N\left(\begin{pmatrix}0\\0\end{pmatrix}, \begin{pmatrix}2 & 1\\1 & 1\end{pmatrix}\right) (X_1, X_2) \mid M = m_2 \sim N\left(\begin{pmatrix}5\\5\end{pmatrix}, \begin{pmatrix}2 & 1\\1 & 1\end{pmatrix}\right).$$

• Not identifiable without constraints. PMM-MAR: the conditional distrib. of $X_1 \mid X_2$ in each pattern is equal to the unconditional one

$$\underbrace{p^*(x_1 \mid x_2, M = m_1)}_{p^*(o^c(x,m_2)|o(x,m_2),M=m_1)} = \underbrace{p^*(x_1 \mid x_2, M = m_2)}_{p^*(o^c(x,m_2)|o(x,m_2),M=m_2)} = N(x_2, 1)(x_1) = p^*(x_1 \mid x_2).$$

# MAR with shift in marginal distribution between patterns

• Gaussian PMM: $X^* \mid M = m \sim N(\mu_m \mid \Sigma_m)$. Ex: for two patterns $m_1 = (0, 0)$ and $m_2 = (1, 0)$ and **a shift**:

$$(X_1, X_2) \mid M = m_1 \sim N\left(\begin{pmatrix}0\\0\end{pmatrix}, \begin{pmatrix}2 & 1\\1 & 1\end{pmatrix}\right) (X_1, X_2) \mid M = m_2 \sim N\left(\begin{pmatrix}5\\5\end{pmatrix}, \begin{pmatrix}2 & 1\\1 & 1\end{pmatrix}\right).$$

• Not identifiable without constraints. PMM-MAR: the conditional distrib. of $X_1 \mid X_2$ in each pattern is equal to the unconditional one

$$\underbrace{p^*(x_1 \mid x_2, M = m_1)}_{p^*(o^c(x,m_2)\mid o(x,m_2), M=m_1)} = \underbrace{p^*(x_1 \mid x_2, M = m_2)}_{p^*(o^c(x,m_2)\mid o(x,m_2), M=m_2)} = N(x_2, 1)(x_1) = p^*(x_1 \mid x_2).$$

**Definition (Conditional indep. MAR - CIMAR)**

$$p^*(o^c(x, m) \mid o(x, m), M = m') = p^*(o^c(x, m) \mid o(x, m), M = m'')$$

for all $m, m', m'' \in \mathcal{M}, x$.equivalent to $o^c(X, M) \mid o(X, M) \perp\!\!\!\perp M$

# MAR with shifts in conditional distribution between patterns

$$\mathbf{X} = \begin{pmatrix} x_{1,1} & x_{1,2} & x_{1,3} \\ NA & x_{2,2} & x_{2,3} \\ NA & NA & x_{3,3} \end{pmatrix}, \mathbf{M} = \begin{pmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 1 & 0 \end{pmatrix} = \begin{pmatrix} m_1 \\ m_2 \\ m_3 \end{pmatrix}$$

## CIMAR

$p^*(x_1, x_2 \mid x_3, M = m_1) = p^*(x_1, x_2 \mid x_3, M = m_2) = p^*(x_1, x_2 \mid x_3, M = m_3)$

Distrib. of $X_1, X_2 \mid X_3$ is not allowed to change from one pattern to another, though the marginal distrib. of $X_3$ can change. CIMAR allows to learn the conditional distrib. from any pattern.

## PMM-MAR

$p^*(x_1, x_2 \mid x_3, M = m_3) = p^*(x_1, x_2 \mid x_3)$

**Both distrib. of observed variables and conditional ones can change from pattern to pattern.**

## MCAR

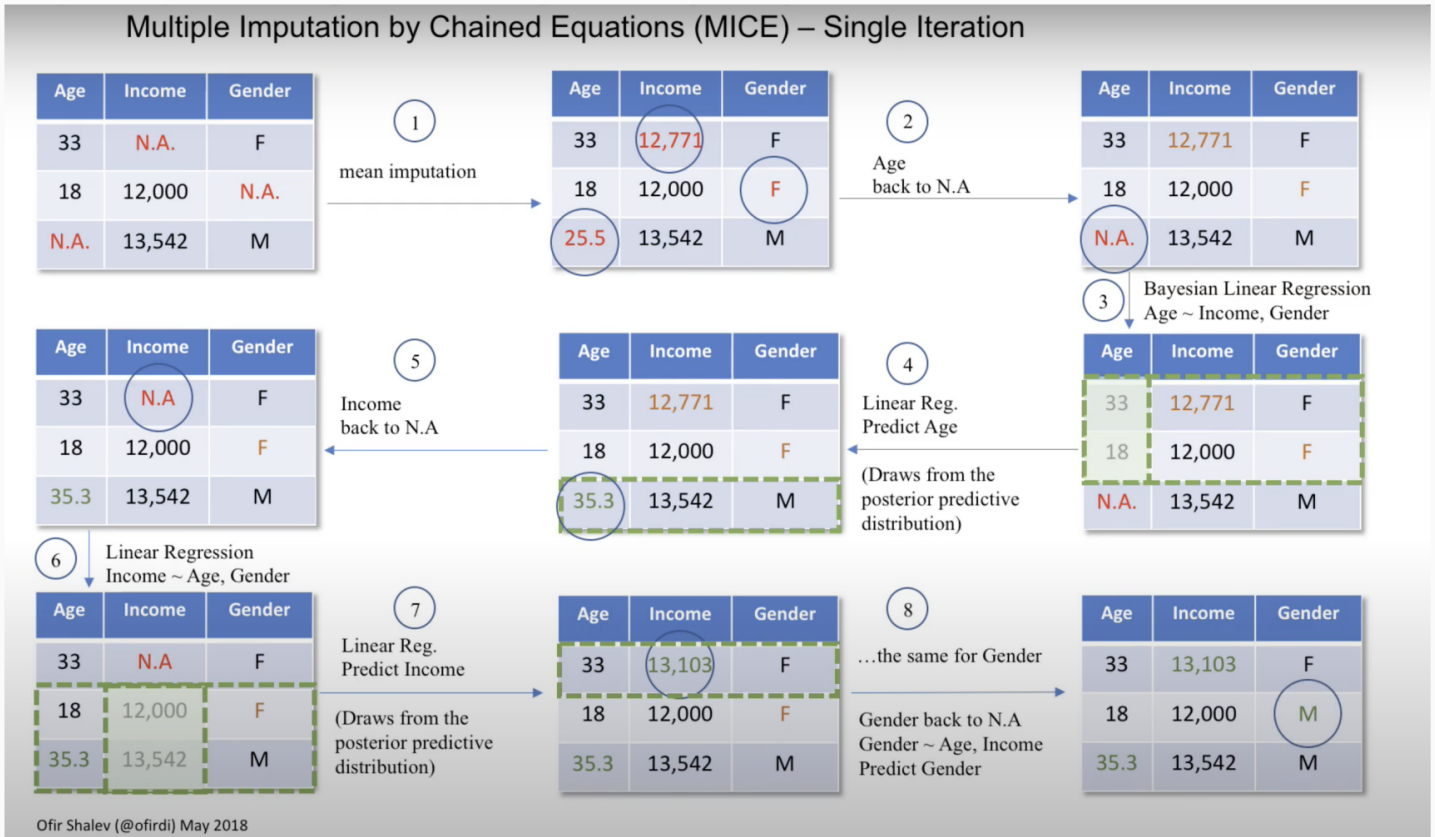
No change is allowed.

# Fully conditional specification - FCS, (M)ICE

1. Fill NA with plausible values to get an initial completed dataset

2. For $j \in \{1, \ldots, d\}$, $t \geq 1$ use a univariate imputation to sample new imputed values $x_j^{(t+1)} \sim p^*(x_j \mid x_{-j}^{(t)})$, where $x_{-j}^{(t)} = \{x_l^{(t)}\}_{l \neq j}$ the imputed & observed values of other variables except $j$ at the $t$th iteration.

3. Iterate until convergence



# Fully conditional specification under MAR

- Assume $x_{-j}$ is well imputed: we have $p^*(x_{-j})$
- Impute by drawing from the conditional distrib. of $X_j \mid X_{-j}$ **learned from all patterns in which $x_j$ is observed**:

$$h^*(x_j \mid x_{-j}) = \sum_{m \in L_j} \frac{\mathbb{P}(M = m)}{\sum_{m \in L_j} p^*(x_{-j} \mid M = m)\mathbb{P}(M = m)} p^*(x \mid M = m),$$

with $L_j = \{m \in \mathcal{M} : x_j \in o(x, m)\}$ the patterns where $x_j$ is observed

**Theorem: Identifiability (Näf et al., 2024)**

Assume PMM-MAR holds,

$$h^*(x_j \mid x_{-j}) = p^*(x_j \mid x_{-j}), \text{ for all } x_{-j} \text{ with } p^*(x_{-j}) > 0$$

$\Rightarrow$ In a population setting (perfect estimation), **FCS identifies the right distributions** to impute missing values under MAR.

Remark: Different from learning the conditional distributions from the fully observed data and then impute the missing variables.

# What is a good imputation method?

- ▷ both conditional and marginal **distribution shifts** can occur for different patterns under MAR.
- ▷ conditional shifts are handled with FCS

**An ideal imputation method should**

- ▷ (1) be a distributional regression method,
- ▷ (2) be able to capture nonlinearities in the data,
- ▷ (3) be able to deal with distributional shifts in the observed variables,
- ▷ (4) be fast to fit,
- ▷ (5) the method is able to deal with multivariate responses.

1-3 are crucial for imputation under MAR

4-5 are only relevant to reduce the computational burden.

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| Method | (1) | (2) | (3) | (4) | (5) |
|---|---|---|---|---|---|
| missForest (Stekhoven & Bühlmann, 2011) | | ✓ | | ✓ | |
| mice-cart (Burgette & Reiter, 2010) | ✓ | ✓ | | ✓ | |
| mice-RF (Doove et al., 2014) | ✓ | ✓ | | ✓ | |
| mice-DRF (Näf et al., 2024) | ✓ | ✓ | | ✓ | ✓ |
| mice-norm.nob (Gaussian) | ✓ | | ✓ | ✓ | ✓ |
| mice-norm.predict (Regresssion) | | | ✓ | ✓ | ✓ |

[21] Cevid et al., Distributional Random Forests. *JMLR*. 2022

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- ▷ mice-cart/RF estimate a tree, a forest, on observed data and then draw imputations from the leaves (approx conditional distribution) whereas distributional forest[21] is a distributional method

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# Forests generalize poorly outside of the training set

Ex: Variables income & age with MAR missing values in income

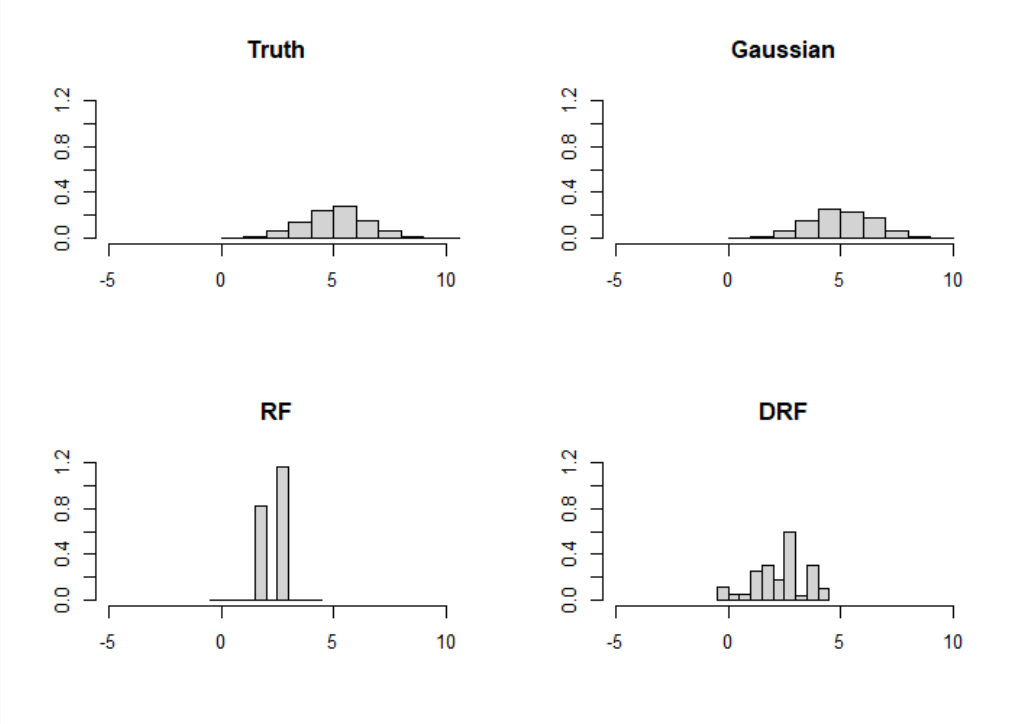
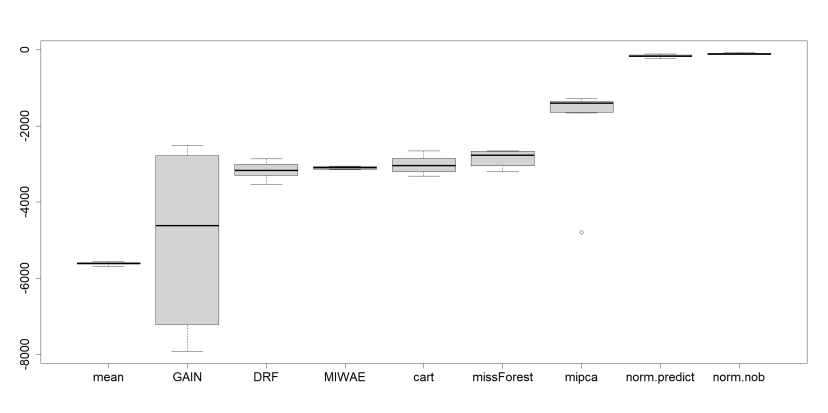



**Figure 2:** True distribution against a draw from different imputation methods.

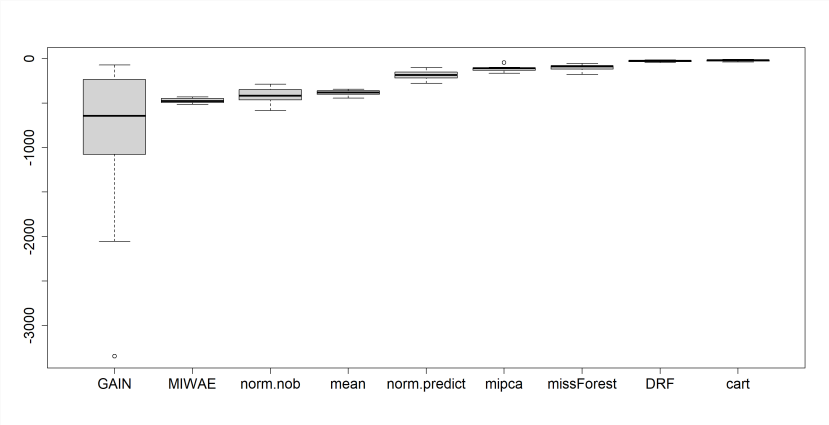
DRF, a distributional method $>$ mice-RF but fails to deal with the covariate shift (centering $\approx 2$ instead of 5).

Finding an imputation method that meets (1) - (5) is still an open problem!

# Empirical study: ranking with energy scores and not RMSE




Gaussian relation with shifts




Non linear relation with shifts

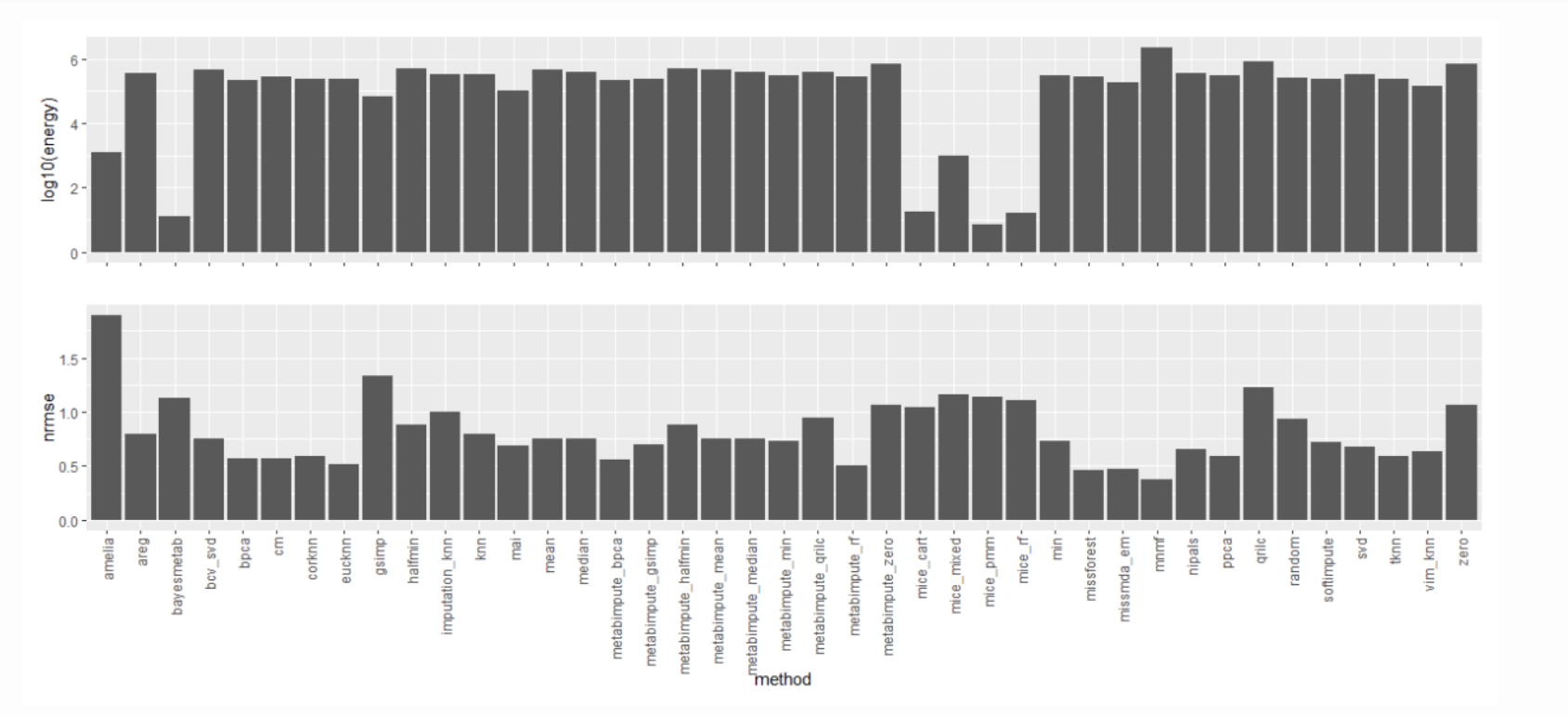
Ex with $d = 6$, $n = 1500$, 20% NA and CIMAR, $X_{O^c} = \mathbf{B}f(X_O) + \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \end{pmatrix}$,

## Energy distance between imputed & real data

$$d(H, P^*) = 2\mathbb{E}[\|X - Y\|_{\mathbb{R}^d}] - \mathbb{E}[\|X - X'\|_{\mathbb{R}^d}] - \mathbb{E}[\|Y - Y'\|_{\mathbb{R}^d}],$$

where $\|\cdot\|_{\mathbb{R}^d}$ is the Euclidean metric on $\mathbb{R}^d$, $X \sim H$, $Y \sim P^*$ and $X', Y'$ are independent copies of $X$ and $Y$.

# Empirical study: ranking with energy scores and not RMSE




credit: Krystyna Grzesiak, Michal Burdukiewicz[22] 230 scenarios (10 missing values patterns 23 different-sized datasets)

[22]imputomics: web server and R package for missing values imputation in metabolomics data. *Bioinformatics 2024*.

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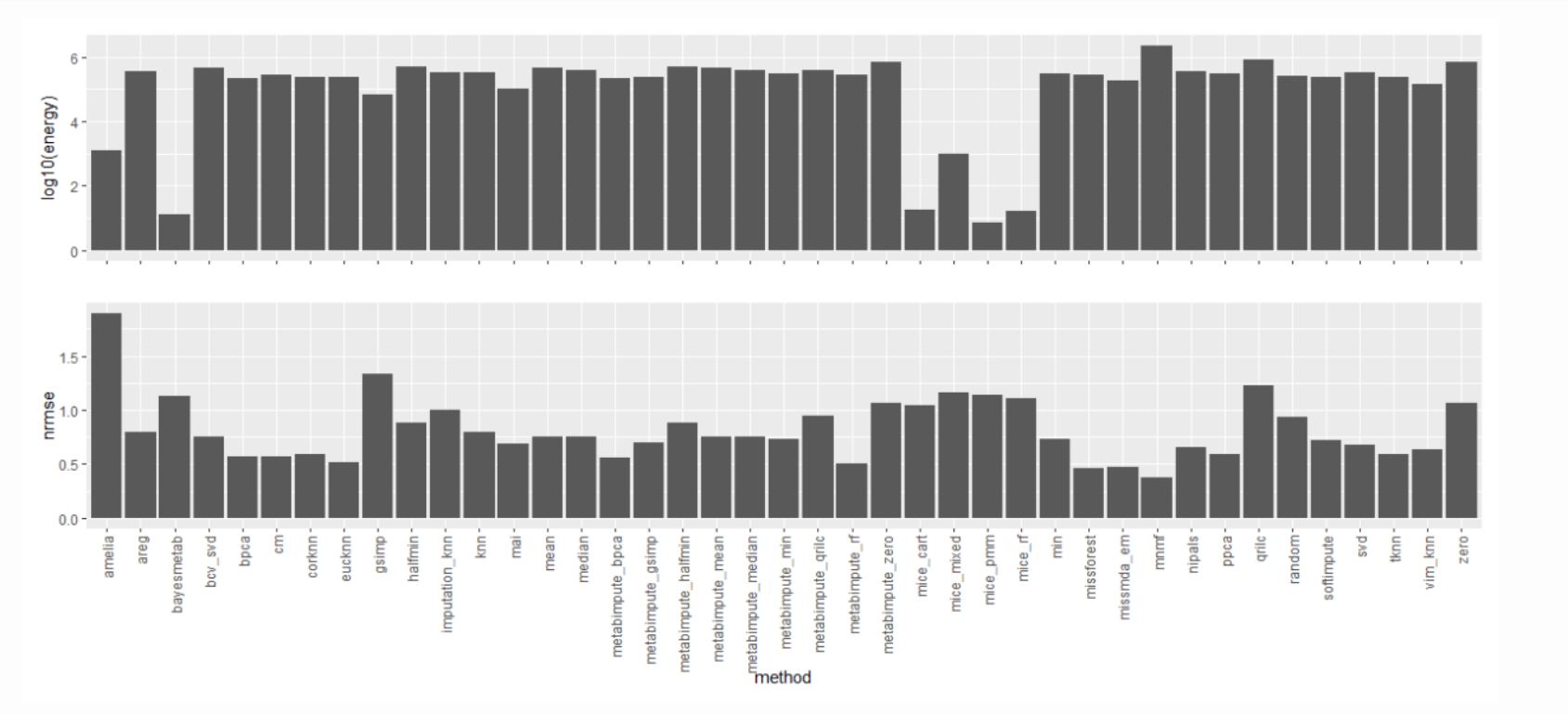


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# Conclusion

- Non-parametric PMM view of missing (different environments) helps understand non-parametric imputation under MAR
- Identification result for FCS: the right conditional distributions are identifiable under MAR with no parametric assumption
- Identification under the weakest MAR assumption.[23] Link between all MAR (MAR is broad): CIMAR, Extended MAR (EMAR), PMM-MAR

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- ▷ 5 points the ideal sequential imputation method should meet
- ▷ The quest for an imputation method meeting all 5 points is still open
- ▷ mice-DRF promising (code available)
- ▷ Imputation scores with missing values that are proper under MAR: ranking imputation methods

Impact for causal inference

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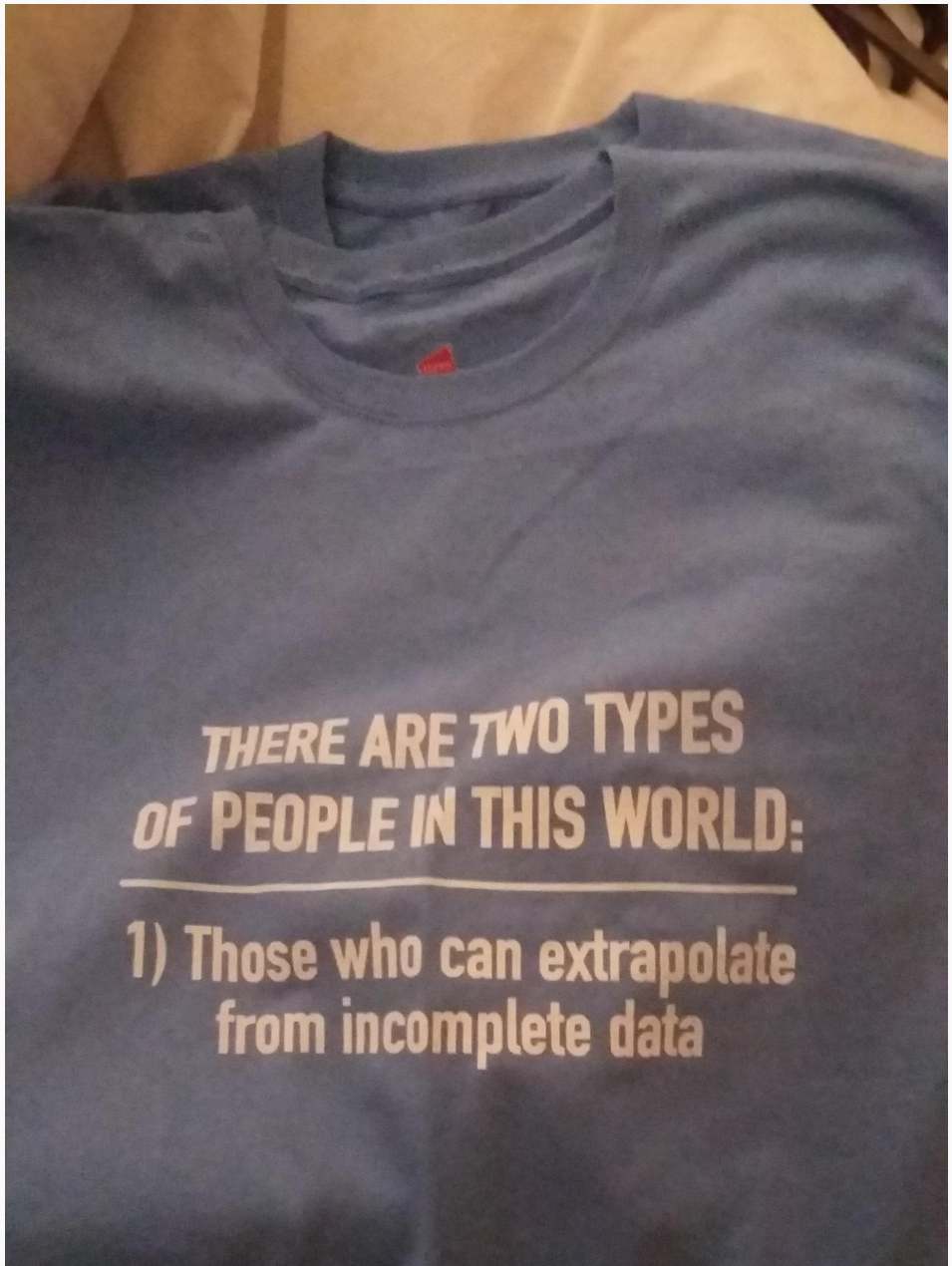
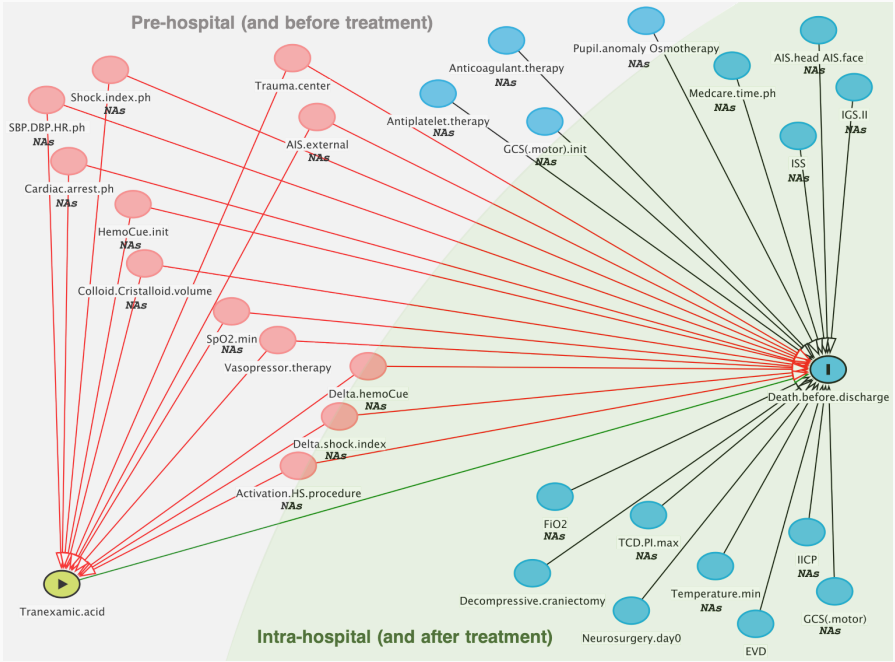
# Thank you


THERE ARE TWO TYPES
OF PEOPLE IN THIS WORLD:
1) Those who can extrapolate
from incomplete data

# Causal identifiability assumptions adapted to missing values

http://www.dagitty.net/




| Covariates | | | Treatment | Outcome(s) | |
|---|---|---|---|---|---|
| $X_1$ | $X_2$ | $X_3$ | W | Y(0) | Y(1) |
| NA | 20 | F | 1 | ? | 200 |
| -6 | 45 | NA | 0 | 10 | ? |
| 0 | NA | M | 1 | ? | 150 |
| NA | 32 | F | 1 | ? | 100 |
| 1 | 63 | M | 1 | 15 | ? |
| -2 | NA | M | 0 | 20 | ? |

**Unconfoundedness**: $\{Y_i(1), Y_i(0)\} \perp\!\!\!\perp W_i \mid X^\star$

$\Rightarrow$ Doctors give us the DAG (do not ask for the complete graph only for a sufficient adjustment set), obtained by a Delphi method

**Unconfoundedness with missing values**: $\{Y_i(1), Y_i(0)\} \perp\!\!\!\perp W_i \mid X$

$X = (1 - M) \odot X^\star + M \odot NA$; with $M_{ij} = 1$ if $X_{ij}$ is missing, 0 otherwise

$\Rightarrow$ Doctors decide to treat a patient based on what they observe/record. We have access to the same information as the doctors

# 2. Augmented IPW under unconfoundeness with missing values

## Augmented IPW[24] with missing values

$$\hat{\tau} = \frac{1}{n}\sum_i \left( \widehat{\mu_{(1)}}(X_i) - \widehat{\mu_{(0)}}(X_i) + W_i \frac{Y_i - \widehat{\mu_{(1)}}(X_i)}{\widehat{e}(X_i)} - (1 - W_i)\frac{Y_i - \widehat{\mu_{(0)}}(X_i)}{1 - \widehat{e}(X_i)} \right)$$

## Generalized propensity score[25]

$$e(x) = \mathbb{P}(W = 1 \,|\, X = x)$$

One model per pattern: $\sum_{m \in \{0,1\}^d} \mathbb{E}\left[W | X_{obs(m)}, M = m\right] \; \mathbb{1}_{M=m}$

$\Rightarrow$ Supervised learning with missing values[26,27]

- Learning with a universally consistent learner on (Mean) imputed data is Bayes consistent for **all missing data mechanism**
- Missing incorporate in attributes (MIA) for tree methods (grf package)

[24] Mayer, Wager, J. Doubly robust treat. effect estim. with incomplete confounders *AOAS*. 2020.
[25] Rosenbaum & Rubin. Reducing bias in observational studies *JASA*. (1984).
[26] **J.** et al. Consistency of supervised learning with missing values. *Stats Papers*. 2028-24.
[27] Le Morvan, **J.** et al. What's a good imputation to predict with missing values? *Neurips 2021*.

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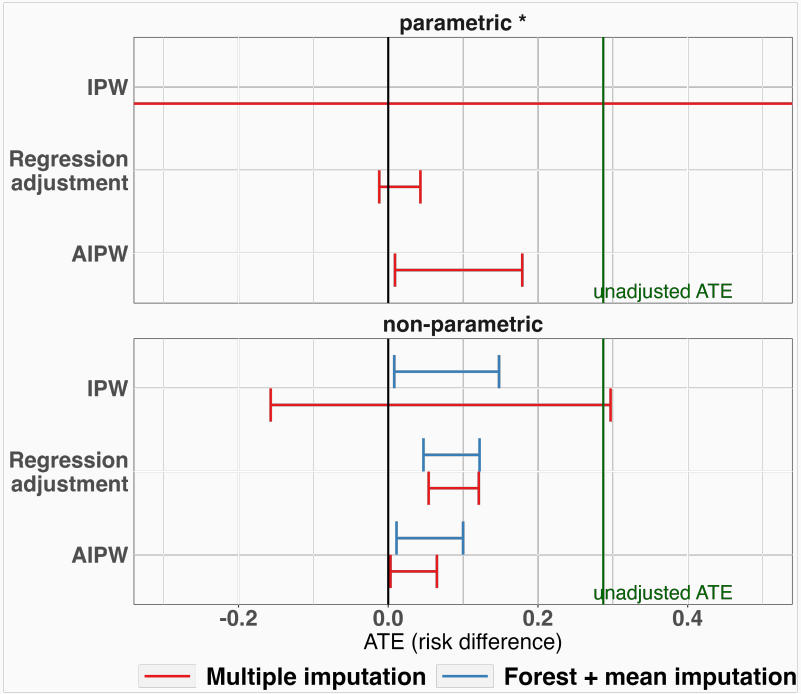
# ATE estimations: effect of tranexamic acid on in-ICU mortality

- 40 covariates, 18 confounders (categorical and quantitative). 8248 patients
- Multiple imputation assumes **MAR & classical unconfoundeness** while other **unconfoundeness with missing & (no) assumptions on missing mechanism**




$x$-axis: Estimat. of the ATE ($\times 100$), bootstrap CI, $y$-axis: Methods with logistic regression or forests for nuisances. Missing values handled with multiple imputation or MIA[25]

[25] Other estimators (latent confounding, Kallus 2018 or parametric models with EM algorithms Jiang, J. 2019) are available bur not displayed for clarity (all tend to a slightly detrimental effect)

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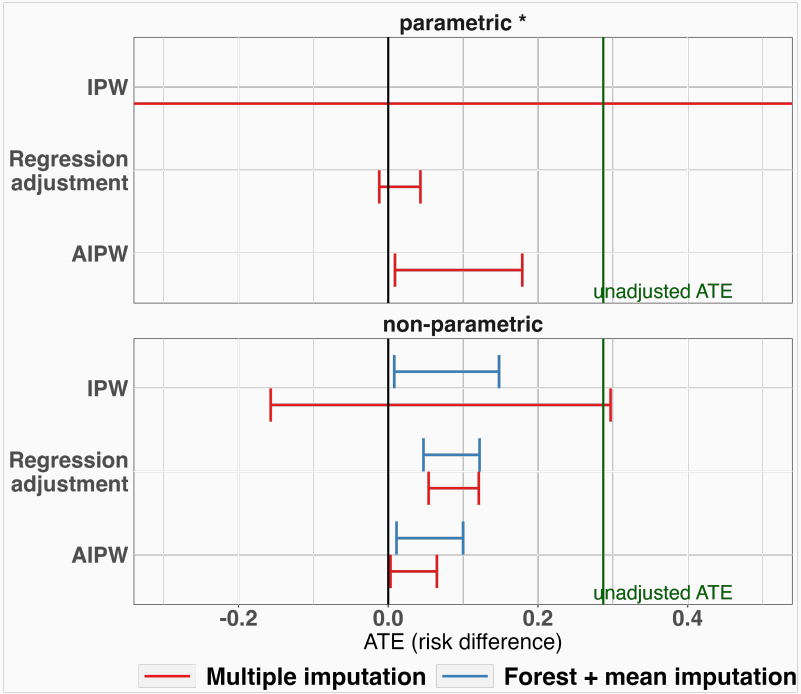


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# Imputing with a mixture of patterns

$$\mathbf{X} = \begin{pmatrix} x_{1,1} & x_{1,2} & x_{1,3} \\ x_{2,1} & NA & x_{2,3} \\ NA & x_{3,2} & x_{3,3} \end{pmatrix}, \mathbf{M} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \end{pmatrix} = \begin{pmatrix} m_1 \\ m_2 \\ m_3 \end{pmatrix}.$$

whereby $(X_1, X_2, X_3)$ are independently uniformly distributed on $[0, 1]$.

$$\begin{aligned} \mathbb{P}(M = m_1 \mid x) &= \mathbb{P}(M = m_1 \mid x_1) = x_1/3 \\ \mathbb{P}(M = m_2 \mid x) &= \mathbb{P}(M = m_2 \mid x_1) = 2/3 - x_1/3 \\ \mathbb{P}(M = m_3 \mid x) &= \mathbb{P}(M = m_3) = 1/3. \end{aligned}$$

# Imputing with a mixture of patterns

We want to impute $X_1$ in the third pattern (with $X_2$ and $X_3$ observed)

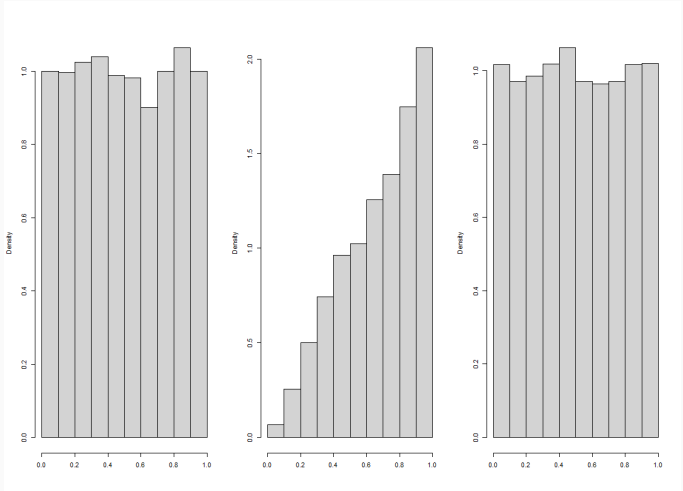


**Figure 3:** Distrib. of $X_1$ in different patterns. Left: Distrib. of $X_1 \mid M = m_3$. Middle: $(X_1 \mid M = m_1)$. Right: Distribution of all patterns for which $X_1$ is observed (Mixture of the distribution of $X_1$ in pattern 1 and 2).

• As the distrib. of $(X_2, X_3)$ in each patterns is the same, this shows the change of $X_1 \mid X_2, X_3$ from $m_3$ to $m_1$: PMM-MAR allows change in the conditional distrib. over patterns.

• Note that the distrib. $X_1 \mid X_2, X_3$ in $m_3$ corresponds to the mixture of distribution of $X_1 \mid X_2, X_3$ in the patterns where $X_1$ is observed.