



Imputation of Incomplete Multilevel Data with mice

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Abstract

Tutorial paper on imputing incomplete multilevel data with **mice**. Including methods for ignorable and non-ignorable missingness.

Keywords: missing data, multilevel, clustering, **mice**, R.

1. Introduction

1.1. Multilevel data

We talk of multilevel data when there is some kind of hierarchy or clustering in a dataset. In the typical case, individuals are nested within groups, but there are many different types of multilevel data. In the medical field, clustering occurs at e.g., the hospitals/center level in registry data, or at the study-level in meta-analyses (IPDMA). In the social sciences and official statistics we can find clustering e.g. at the country-level, or as imposed by the sampling design. In this paper, we will refer to the grouping variable as ‘cluster’, and the grouped variable as ‘(sample) unit’.¹ For reasons of brevity, we only discuss clustering between units, not within units (such as in timeseries or longitudinal data).

Analyzing multilevel data requires special care, compared to ‘regular’, single level data. The

¹Add that we’ll only discuss two levels?

cluster to which a unit belongs may influence the unit-level observations, and since clusters are made up of units, clusters depend on units as well (Hox, Moerbeek, and van de Schoot 2017). These relations can and should be taken into account when developing analysis models for multilevel data.² Multilevel models typically include separate intercepts for each cluster, which relieves one restriction imposed by single-level models: equal group means across clusters. Additionally, there may be random predictor effects and/or random error terms (residual error variances), see e.g. Hox *et al.* (2017) and de Jong, Moons, Eijkemans, Riley, and Debray (2021).³ There are many names for models that take clustering into account. Some popular examples are ‘multilevel models’, ‘hierarchical models’, ‘mixed effect models’ and ‘random effect models’.

1.2. Missing data

Multilevel data is not spared the ubiquitous problem of missing information. Just as in single level data, missingness may occur at the unit level. But with multiple levels of data comes the potential for missingness at multiple levels. Missingness in multilevel data can be categorized into two general patterns: systematic missingness and sporadic missingness, see Resche-Rigon, White, Bartlett, Peters, Thompson, and Group (2013). In figure 1, we show a dataset with units in the rows and variables in the columns, there are 5 units nested within 2 clusters, and 3 variables of interest. Variable X1 is completely observed. Variable X2 is systematically missing, X3 is sporadically missing.⁴ Systematic missingness can be further subdivided into unobserved constants (same value per cluster) and non-measured random variables (which may differ per unit within clusters). In Figure 1, the former implies that the unobserved values for units 4 and 5 on variable X2 would be equal. With the latter, the values may differ. Depending on the missing data pattern, there are more or less optimal way of accommodating the missingness.

Ignoring missing data in research endeavors is almost never a good idea. Complete case analysis (i.e., excluding all units with one or more missing entries) can introduce bias in statistical inference and lowers statistical power. Instead, the missingness should be accommodated *before* or *within* the analysis of scientific interest. Especially the former is very generic and popular. Imputing (i.e., filling in) the missing values splits the missing data problem from the scientific problem. The R package **mice** has become the de-facto standard for imputation by chained equations, which solves the missingness one variable at a time, iteratively. **mice** is known to yield valid inferences under many different missing data circumstances (Van Buuren 2018). In this paper, we’ll discuss how to use **mice** in the context of multilevel data, under varying missing data mechanisms.⁵

²Explain ICC here? The percentage of variance attributed to the cluster-level is expressed by the intra-class coefficient (ICC). The ICC can also be interpreted as the expected correlation between two randomly sampled units in same cluster. So if the ICC is high, a lot of variability in a variable is due to the clustering, which should be modeled accordingly.

³Add that heterogeneity refers to variability within clusters.

⁴Explain why.

⁵Discuss missingness mechanisms before this point, add references Yucel (2008) and Hox, van Buuren, and Jolani (2015).

unit	cluster	X1	X2	X3
1	1			
2	1			
3	1			
4	2			
5	2			

observed
 missing

1.3. Aim of this paper

This paper serves as a tutorial for imputing incomplete multilevel data with **mice**. We provide practical guidelines and code snippets for different missing data situations. For reasons of brevity, we focus on imputation by chained equations, although JOMO is available in **mice** as well. Other useful packages for incomplete multilevel data include: **mitml**, **miceadds**, **mdmb**.⁶

We structure this tutorial around three case studies:

- **mice::popmis** (simulated data on school kids, with MNAR/MAR mixture);
- **metamisc::impact** (real IPD on traumatic brain injuries, without NAs);
- **GJRM::hiv** (simulated patient data on HIV, without NAs)

For each case study we focus on a different aspect to illustrate how to impute incomplete multilevel data.

2. Workflows

We introduce three case studies to illustrate the workflow. In the **mice::popmis** data, we show the advantages of including the multilevel structure of the data into the imputation

⁶Rephrase: Some level of knowledge on multilevel models is assumed. We're providing an overview of implementations. It's up-to the reader to decide which multilevel strategy suits their data. So we won't go into detail for the different methods (and equations). Refer to [Meng \(1994\)](#), an Audigier paper, and a paper by Grund on congeniality and random slopes. This paper is just a software tutorial. We'll keep it practical.

model. In the `metamisc::impact` data we'll show how to induce missingness and solve it in real-world data. In the `GJRM::hiv` we provide novel methodology⁷ for imputing MNAR missingness according to the Heckman model.

For each case study we'll look at least at: 1) the incomplete data; 2) the imputation model; 3) the imputed data; and 4) how to obtain pooled estimates for the analysis of scientific interest.

2.1. Case Study I: Popularity

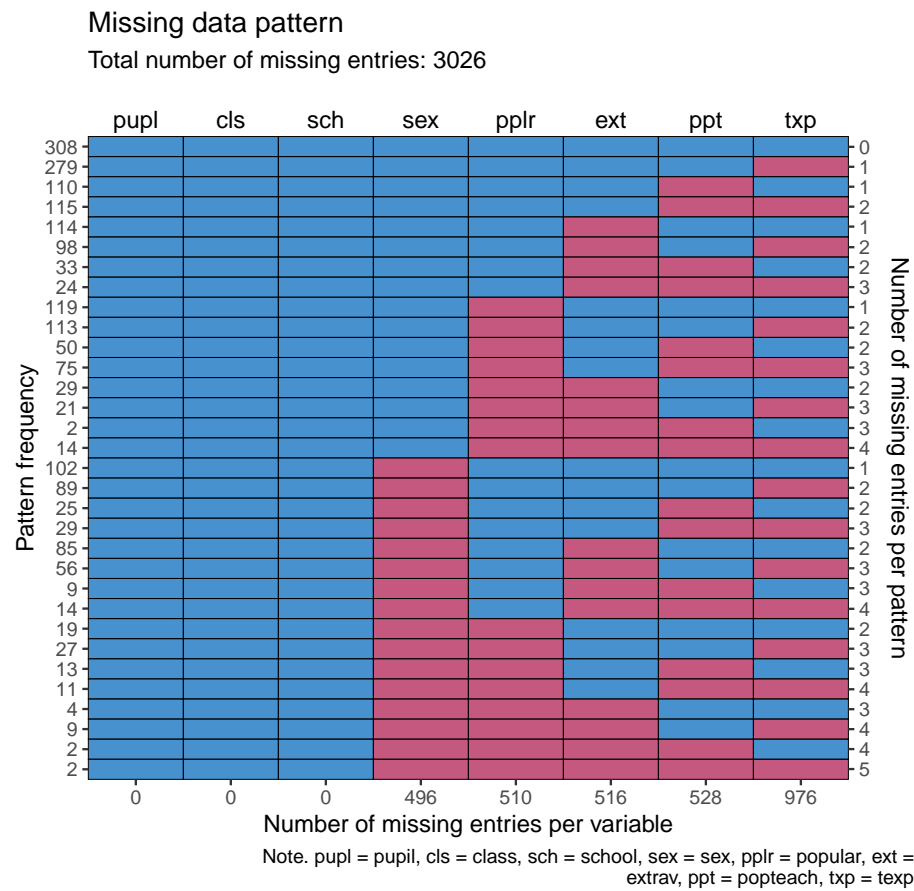
`popNCR` is a simulated dataset with pupils clustered in classes, $n_{\text{participants}} = 2000$, $n_{\text{clusters}} = 100$, on 7 variables:

- `pupil` Pupil number within class,
- `class` Class number,
- `extrav` Pupil extraversion,
- `sex` Pupil gender,
- `teexp` Teacher experience (years),
- `popular` Pupil popularity,
- `popteach` Teacher popularity.

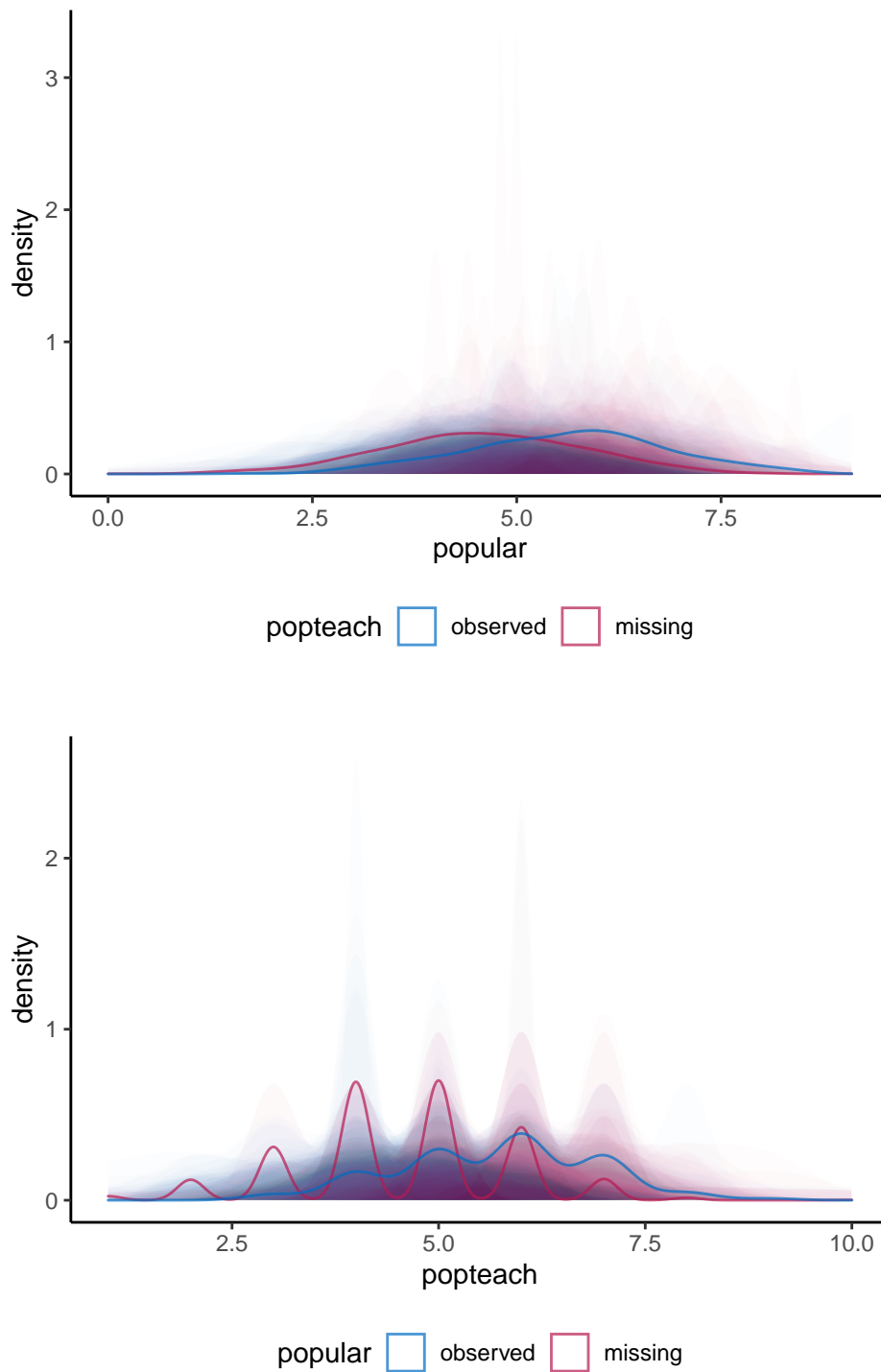
The incomplete data

- What does the missingness look like? Induced MAR/MNAR missingness. Missing data pattern:

⁷not really, the methods exist already, but how to show that this is something new and exciting?



- What are the ICCs? For **popular** the ICC is 0.33. For **popteach** it is 0.31. It would be wise to use multilevel modeling.
- Does the missing data of **popular** depend on **popteach**? Does the missingness in teacher popularity depend on pupil popularity? -> Check this by making a histogram of **popteach** separately for the pupils with known popularity and missing popularity, and the other way around.



- We do see that the distribution for the missing **popular** is further to the right than the distribution for observed **popular**. This would indicate a right-tailed MAR missingness. In fact this is exactly what happens, because we created the missingness in these data ourselves. But we made it observable by examining the relations between the missingness in **popular** and the observed data in **popteach**. There is also a dependency

between the missingness in teacher popularity and pupil popularity. The relation seems to be right-tailed as well.

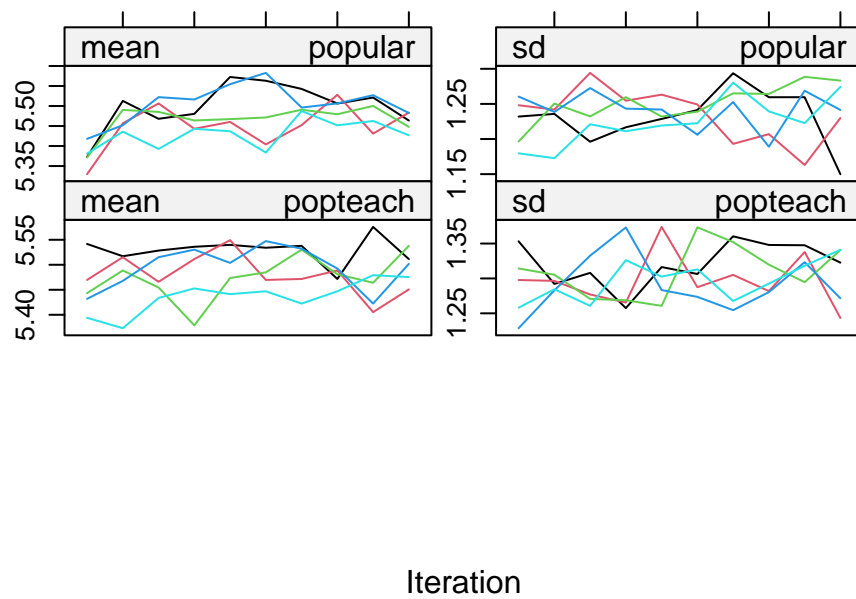
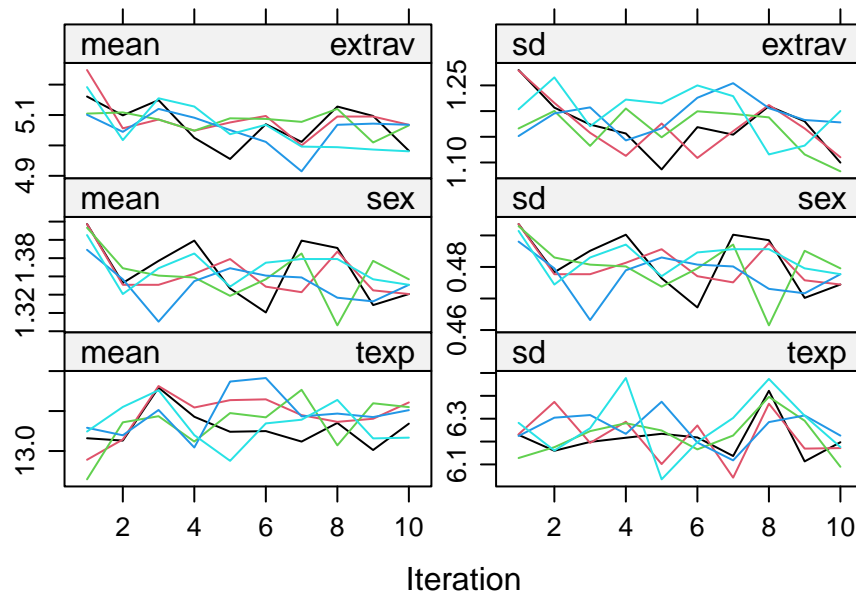
The imputation model

- We could ignore the multilevel structure of the data. This is likely invalid, given the high ICCs, but we'll do it anyways.
- We'll use predictive mean matching to impute the continuous variables (some appear to be somewhat ordinal), and logistic regression to impute the binary variable `sex`. We do not use the observation identifier `pupil` or cluster identifier `class` as predictors to impute other variables.

```
R> # dry run to get imputation parameters
R> ini <- mice(pop, maxit = 0)
R>
R> # extract predictor matrix and adjust
R> pred <- ini$pred
R> pred[, c("class", "pupil")] <- 0
R> pred
```

	pupil	class	extrav	sex	texp	popular	popteach	school
pupil	0	0	1	1	1	1	1	1
class	0	0	1	1	1	1	1	1
extrav	0	0	0	1	1	1	1	1
sex	0	0	1	0	1	1	1	1
texp	0	0	1	1	0	1	1	1
popular	0	0	1	1	1	0	1	1
popteach	0	0	1	1	1	1	0	1
school	0	0	1	1	1	1	1	0

```
R> # impute the data, ignoring the cluster structure
R> imp_ignored <- mice(pop, maxit = 10, pred = pred, print = FALSE)
R>
R> # check convergence of the imputation model
R> plot(imp_ignored)
```



```
R> # compare descriptives before and after imputation
```

```
R> psych::describe(pop)[, c("n", "mean", "median", "min", "max", "sd")]
```

	n	mean	median	min	max	sd
pupil	2000	10.65	11.0	1	26.0	5.97


```

class* 2000 50.37 51.0 1 100.0 29.08
extrav 1484 5.31 5.0 1 10.0 1.29
sex* 1504 1.56 2.0 1 2.0 0.50
texp 1024 11.80 12.0 2 25.0 6.26
popular 1490 4.83 4.8 0 9.1 1.34
popteach 1472 4.83 5.0 1 10.0 1.36
school 2000 5.54 6.0 1 10.0 2.89

```

```
R> psych::describe(mice::complete(imp_ignored))[, c("n", "mean", "median", "min", "max", "sd", "fmi")]
```

```

      n mean median min  max  sd
pupil 2000 10.65    11  1 26.0 5.97
class* 2000 50.37    51  1 100.0 29.08
extrav 2000 5.23     5  1 10.0 1.25
sex* 2000 1.51     2  1  2.0 0.50
texp 2000 12.55    12  2 25.0 6.27
popular 2000 4.99     5  0  9.1 1.32
popteach 2000 5.01     5  1 10.0 1.38
school 2000 5.54     6  1 10.0 2.89

```

```
R> # TODO: add stripplot with boxplot overlay instead of the tables (make pooled one thick)
```

```
R> # TODO: pool mean median and sd
```

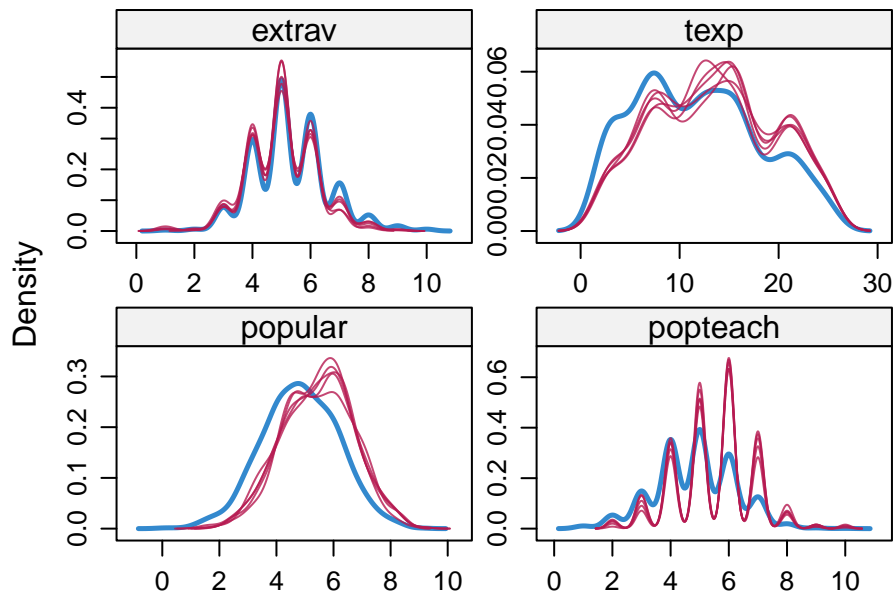
```
R> # feedback Stef: numbers, continuous statistics such as means, and uncertainty estimates
```

```
R> # TODO: add FMI for each of the estimates? at least for the mean
```

```
R>
```

```
R> # further inspection of the imputations
```

```
R> densityplot(imp_ignored)
```



```
R> # compare ICCs before and after imputation
R> ICCs <- data.frame(
+   vars = c("popular", "popteach", "texp"),
+   incomplete = c(multilevel::ICC1(aov(popular ~ class, pop)),
+                   multilevel::ICC1(aov(popteach ~ class, pop)),
+                   multilevel::ICC1(aov(texp ~ class, pop))),
+   ignored = c(multilevel::ICC1(aov(popular ~ class, complete(imp_ignored))),
+               multilevel::ICC1(aov(popteach ~ class, complete(imp_ignored))),
+               multilevel::ICC1(aov(texp ~ class, complete(imp_ignored))))
+ )
R> ICCs
```

```
      vars incomplete  ignored
1 popular  0.3280070 0.2754195
2 popteach 0.3138658 0.2467415
3   texp    1.0000000 0.4443760
```

- As the original ICCs show, 100% of the variance in `texp` can be attributed to the clustering variable `class`. This tells us that the multilevel structure of the data should be taken into account. If we don't, we'll end up with incorrect imputations, biasing the effect of the clusters towards zero.
- We can also observe that the teacher experience increases slightly after imputation. This is due to the MNAR missingness in `texp`. Higher values for `texp` have a larger probability to be missing. This may not a problem, however, if at least one pupil in each class has teacher experience recorded, we can deductively impute the correct (i.e. true) value for every pupil in the class.
- We'll now use `class` as a predictor to impute all other variables.

```
R> # adjust the predictor matrix
R> pred <- ini$pred
R> pred[, "pupil"] <- 0
R> pred
```

```
      pupil class extrav sex texp popular popteach school
pupil      0     1     1   1   1       1         1       1
class      0     0     1   1   1       1         1       1
extrav     0     1     0   1   1       1         1       1
sex        0     1     1   0   1       1         1       1
texp       0     1     1   1   0       1         1       1
popular    0     1     1   1   1       0         1       1
popteach   0     1     1   1   1       1         0       1
school     0     1     1   1   1       1         1       0
```

```
R> # impute the data, cluster as predictor
R> imp_predictor <- mice(pop, maxit = 10, pred = pred, print = FALSE)
```

Warning: Number of logged events: 312

```
R> # check logged events
R> head(imp_predictor$loggedEvents)
```

	it	im	dep	meth
1	1	1	extrav	pmm
2	1	1	sex	logreg
3	1	1	texp	pmm
4	1	1	popular	pmm
5	1	1	popular	pmm
6	1	1	popteach	pmm

1

2

3

4

5 mice detected that your data are (nearly) multi-collinear.\nIt applied a ridge penalty to

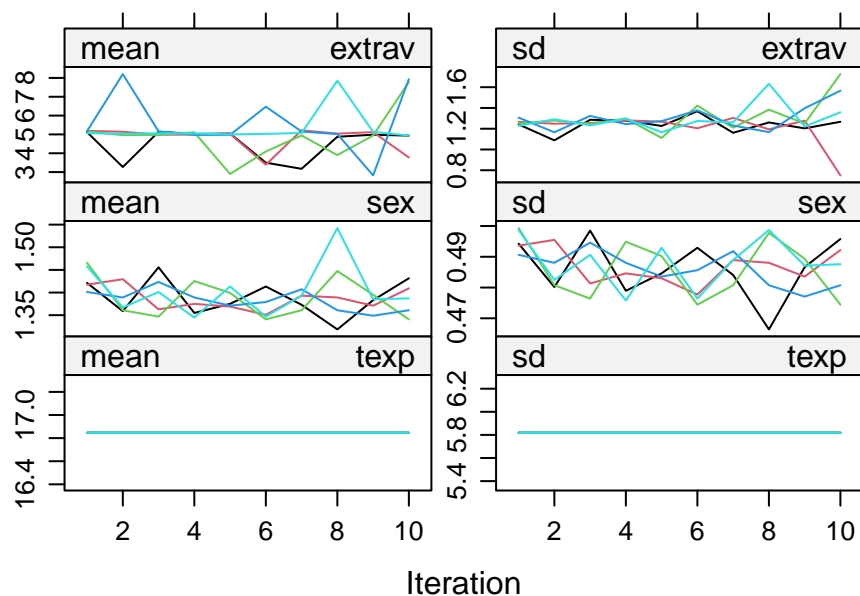
6

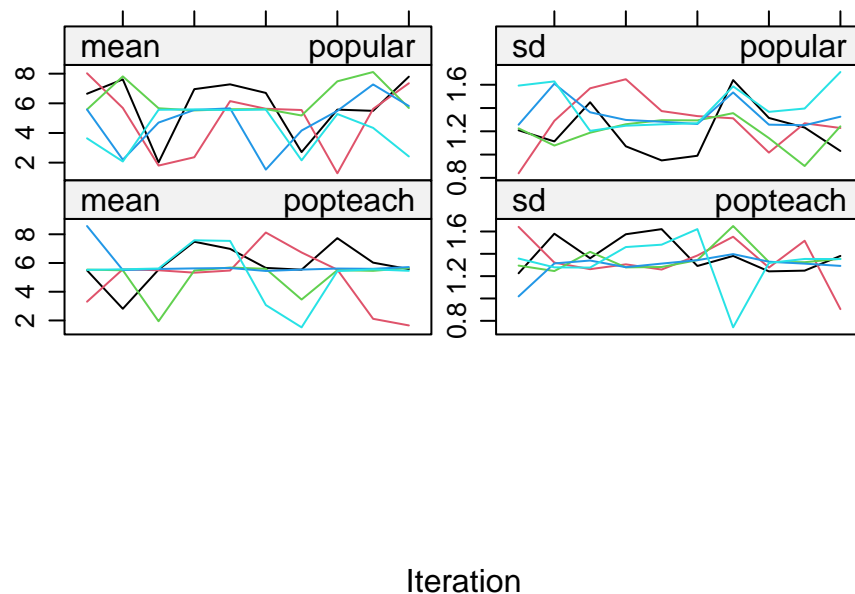
```
R> ## "The mice() function detects multicollinearity, and solves the problem by removing c
```

```
R>
```

```
R> # check convergence of the imputation model
```

```
R> plot(imp_predictor)
```





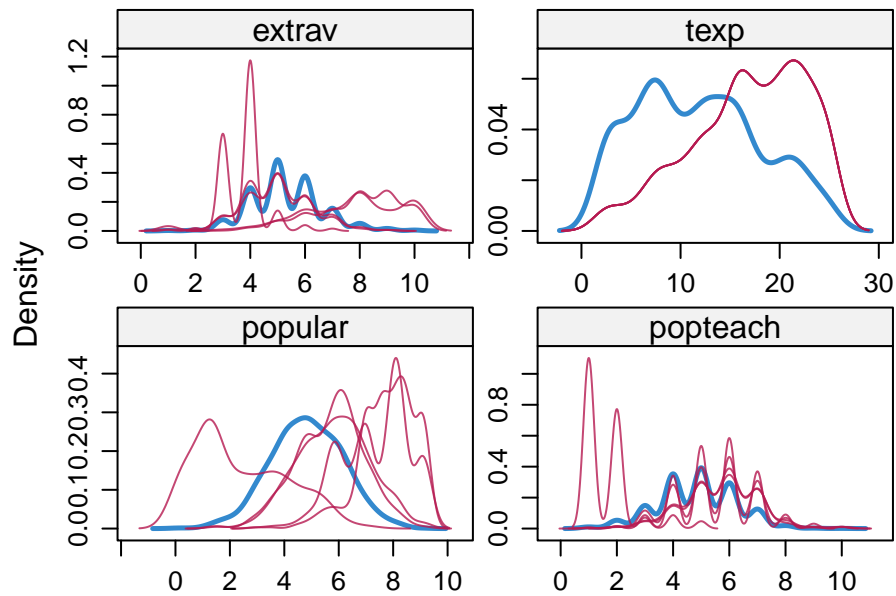
```
R> # compare descriptives before and after imputation
R> psych::describe(pop)[, c("n", "mean", "median", "min", "max", "sd")]
```

	n	mean	median	min	max	sd
pupil	2000	10.65	11.0	1	26.0	5.97
class*	2000	50.37	51.0	1	100.0	29.08
extrav	1484	5.31	5.0	1	10.0	1.29
sex*	1504	1.56	2.0	1	2.0	0.50
texp	1024	11.80	12.0	2	25.0	6.26
popular	1490	4.83	4.8	0	9.1	1.34
popoteach	1472	4.83	5.0	1	10.0	1.36
school	2000	5.54	6.0	1	10.0	2.89

```
R> psych::describe(mice::complete(imp_predictor))[, c("n", "mean", "median", "min", "max", "sd")]
```

	n	mean	median	min	max	sd
pupil	2000	10.65	11.0	1	26.0	5.97
class*	2000	50.37	51.0	1	100.0	29.08
extrav	2000	5.22	5.0	1	10.0	1.29
sex*	2000	1.53	2.0	1	2.0	0.50
texp	2000	14.26	15.0	2	25.0	6.55
popular	2000	5.59	5.4	0	9.1	1.81
popoteach	2000	5.03	5.0	1	10.0	1.40
school	2000	5.54	6.0	1	10.0	2.89

```
R> # further inspection of the imputations
R> densityplot(imp_predictor)
```



```
R> # compare ICCs before and after imputation
R> ICCs <- ICCs %>% cbind(
+   predictor = c(multilevel::ICC1(aov(popular ~ class, complete(imp_predictor)))
+                 multilevel::ICC1(aov(popteach ~ class, complete(imp_predictor)))
+                 multilevel::ICC1(aov(texp ~ class, complete(imp_predictor))))
+ )
R> ICCs
```

	vars	incomplete	ignored	predictor
1	popular	0.3280070	0.2754195	0.2496278
2	popteach	0.3138658	0.2467415	0.3483987
3	texp	1.0000000	0.4443760	1.0000000

- Now, we can clearly see that the imputed values of `texp` are higher than the observed values, which is in line with right-tailed MNAR.
- The ICCs are way more in line with the ICCs in the incomplete data. But this is a quick and dirty way of imputing multilevel data. We *should* be using a multilevel model.

2.2. Case study II: IMPACT

`impact` is traumatic brain injury data with patients clustered in studies, $n_{\text{participants}} = 11022$ and $n_{\text{clusters}} = 15$, on the following 11 variables:

- **name** Name of the study,
- **type** Type of study (RCT: randomized controlled trial, OBS: observational cohort),

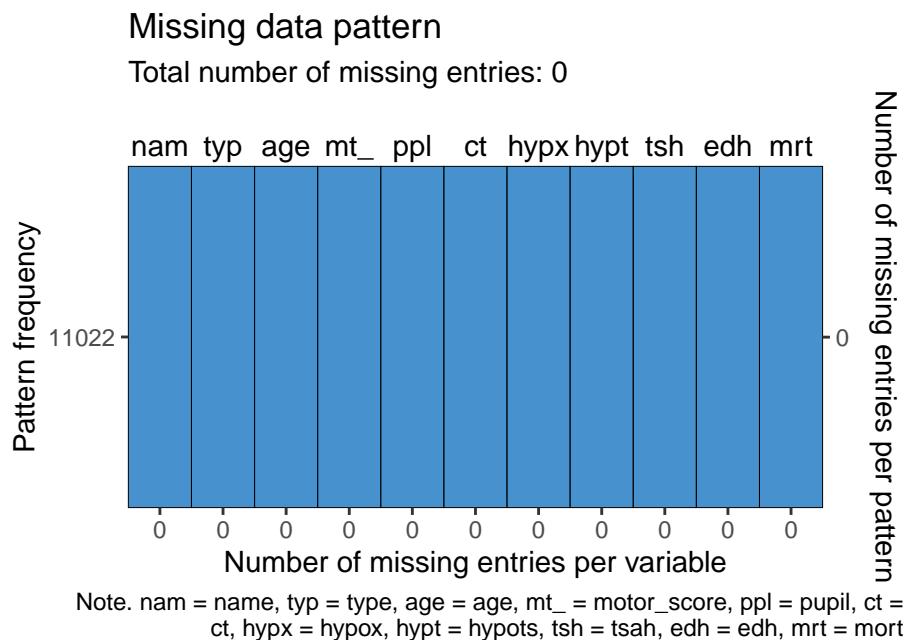
- `age` Age of the patient,
- `motor_score` Glasgow Coma Scale motor score,
- `pupil` Pupillary reactivity,
- `ct` Marshall Computerized Tomography classification,
- `hypox` Hypoxia (0=no, 1=yes),
- `hypots` Hypotension (0=no, 1=yes),
- `tsah` Traumatic subarachnoid hemorrhage (0=no, 1=yes),
- `edh` Epidural hematoma (0=no, 1=yes),
- `mort` 6-month mortality (0=alive, 1=dead).

The data is already imputed (Steyerberg et al, 2008), so we'll induce missingness ourselves. For example, MAR missingness varying by cluster.⁸

```

/\      /\
{ '---' }
{ 0    0 }
==> V <== No need for mice. This data set is completely observed.
\  \|/  /
'-----'

```



2.3. Pooling

- Analysis of scientific interest.

⁸Observed data pattern should differ per cluster. So, in cluster 1, the missingness would depend on age, but not in cluster two. Split the dataframe and run `ampute()` on each cluster.

- Pooling using `mitml`.
- Pooling ‘regular’ parameters vs more ‘exotic’ parameters (SE of residual errors, or autocorrelation)

3. Discussion

- JOMO in **mice** -> on the side for now
- Additional levels of clustering
- More complex data types: timeseries and polynomial relationship in the clustering.

4. Think about

- Adding some kind of help function to mice that suggests a suitable predictor matrix to the user, given a certain analysis model.
- Adding a `multilevel_ampute()` wrapper function in mice.
- Exporting `mids` objects to other packages like `lme4` or `coxme`?

References

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