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Imputation of Incomplete Multilevel Data with mice

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Abstract

This tutorial illustrates the imputation of incomplete multilevel data with the R packackage **mice**. We aim to submit at JSS, so there is no word count limit ("There is no page limit, nor a limit on the number of figures or tables").

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

1. Introduction

Many datasets include individuals that are clustered together, for example in geographic regions, or even different studies. In the simplest case, individuals (e.g., students) are nested within a single cluster (e.g., school classes). More complex clustered structures may occur when there are multiple hierarchical levels (e.g., students in different schools or patients within hospitals within regions across countries), or when the clustering is non-nested (e.g., electronic health record data from diverse settings and populations within large databases).

With clustered data we generally assume that individuals from the same cluster tend to be more similar than individuals from other clusters. In statistical terms, this implies that observations from the same cluster are not independent and may in fact be correlated. If this correlation is left unaddressed, estimates of p values, confidence intervals even model parameters are prone to bias (Localio, Berlin, Ten Have, and Kimmel 2001). Statistical methods for clustered data typically adopt hierarchical models that explicitly describe the grouping of observations. These models are also known as 'multilevel models', 'hierarchical models', 'mixed effect models', 'random effect models', and in the context of time-to-event data as 'frailty models'. Table ?? provides an overview of some key concepts in multilevel modeling.

Table 1: Concepts in multilevel methods

Concept	Details
Sample unit	Units of the population from which measurements are taken in a sample.
Hierarchical levels	Data are grouped into clusters at different levels. A three-level
Fixed effect	Here we assume that the values of an independent variable are fixed,
	i.e.,
	the values observed in the study are representative of all values in the in the dependent variable y e.g., blood pressure between treatments A and B.
Random effect	The values of an independent variable are assumed to be randomly drawn from
	admission we might select only certain hospitals that are representative of
	the difference of y between individual hospitals, but rather the variation of
ICC	The variability due to clustering is often measured by means of the intraclass coefficient (ICC). The ICC can be seen as the percentage of variance that can be attributed to the cluster-level, where a high ICC would indicate that a lot of variability is due to the cluster
	structure.
Random effect	Multilevel models typically accommodate for variability by including a separate group mean for each cluster. In addition to random intercepts, multilevel models can also include random coefficients and heterogeneous residual error variances across clusters [see e.g. Gelman and Hill (2006), Hox, Moerbeek, and van de Schoot (2017) and de Jong, Moons, Eijkemans, Riley, and Debray (2021)]. [TODO:

1.1. Missingness in multilevel data

As with any other dataset, clustered datasets may be impacted by missingness in much the same way. Several strategies can be used to handle missing data, including complete case analysis and imputation. We focus on the latter approach and discuss statistical methods

	cluster	X_1	X_2	X ₃	 X_p
1	1			NA	
2	1				
3	2		NA		
4	2		NA	NA	
5	3				
n	N				

Figure 1: Sporadic missingness in multilevel data

for replacing the missing data with one or more plausible values. Imputation separates the missing data problem from the analysis and the completed data can be analyzed as if it were completely observed. It is generally recommended to impute the missing values more than once to preserve uncertainty due to missingness and to allow for valid inferences (c.f. Rubin 1976).

With incomplete clustered datasets we can distinguish between two types of missing data: sporadic missingness and systematic missingness (Resche-Rigon, White, Bartlett, Peters, and Thompson 2013). Sporadic missingness arises when variables are missing for some but not all of the units in a cluster (Van Buuren 2018; Jolani 2018). For example, it is possible that test results are missing for several students in one or more classes. When all observations are missing within one or more clusters, data are said to be systematically missing.

Imputation of missing data requires consideration of the mechanism behind the missingness. Rubin proposed to distinguish between data that are missing completely at random (MCAR), data that are missing at random (MAR) and data that are missing not at random (MNAR; see Table ??). For each of these three missingness generating mechanisms, different imputation strategies are warranted (Yucel (2008) and Hox, van Buuren, and Jolani (2015)). We here consider the general case that data are MAR, and expand on certain MNAR situations.

Table 2: Concepts in missing data methods

Concept	Details
MCAR	Missing Completely At Random, where the probability to be missing is equal
	across all data entries
MAR	Missing At Random, where the probability to be missing depends on observed
	information
MNAR	Missing Not At Random (MNAR), where the probability to be missing depends on unrecorded information, making the missingness non-ignorable (Rubin 1976; Meng 1994).

1.2. Aim of this paper

This papers serves as a tutorial for imputing incomplete multilevel data with **mice** in R. **mice** has become the de-facto standard for imputation by chained equations, which iteratively solves the missingness on a variable-by-variable basis. **mice** is known to yield valid inferences under many different missing data circumstances (Van Buuren 2018).

We provide practical guidelines and code snippets for different missing data situations, including non-ignorable mechanisms. For reasons of brevity, we focus on multilevel imputation by chained equations with **mice** exclusively; other imputation methods and packages (see e.g. Audigier, White, Jolani, Debray, Quartagno, Carpenter, van Buuren, and Resche-Rigon 2018, and Grund, Lüdtke, and Robitzsch (2018)) are outside the scope of this tutorial. Assumed knowledge includes basic familiarity with the **lme4** notation for multilevel models (see Table ??).

Table 3: Notation

Formula lme4	Details
y ~ x1 + (1 g1)	Fixed x1 predictor with random intercept
y~x1*x2+ (1 g1)	varying among $g1$ Interactions of $x1$ and $x2$ only in fixed effect
y ~ x1*x2+ (x2 g1)	Interactions of $x1$ and $x2$ only in fixed effect
y ~ x1*x2+ (x1*x2 g1)	with slope of x2 randomly varying among g1 variance-covariance matrix estimated only with
y ~ x1*x2+ (x1 g1)+ (x2 g1)	the variance terms of intercept, slope of x1, slope of x2 and interaction x1*x2 variance-covariance matrix estimated separately, i.e, one for intercept and x1 and another
y ~ x1 + (x1 g1) or 1 + x1 + (1 + x1 g1)	for intercept and x2 Fixed x1 with correlated random intercept and random slope of x
y ~ x1 + (x1 g1) or 1 + x1 + (1 g1) + (0 + x1 g1)	Fixed x1 with uncorrelated random intercept
y ~ (1 g1) + (1 g2)	and random slope of x1 Random intercept varying among g1 and among g2 $ y \sim (1 - 1) $

We illustrate imputation of incomplete multilevel data using three case studies:

- popmis from the mice package (simulated data on perceived popularity, n=2,000 pupils across N=100 schools with data that are MAR, van Buuren and Groothuis-Oudshoorn 2021);
- impact from the metamisc package (empirical data on traumatic brain injuries, n = 11,022 patients across N = 15 studies with data that are MAR, Debray and de Jong 2021);
- obesity from the miceheckman package [simulated data on obesity, n = 2,111 patients across N = 5 regions with data that are MNAR].

For each of these datasets, we discuss the nature of the missingness, choose one or more imputation models and evaluate the imputed data, but we will also highlight one specific aspect of the imputation workflow.

This tutorial is dedicated to readers who are unfamiliar with multiple imputation. More experienced readers can skip the introduction (case study 1) and directly head to practical applications of multilevel imputation under MAR conditions (case study 2) or under MNAR conditions (case study 3).

1.3. Setup

Install non-CRAN packages if necessary:

```
R> devtools::install_github("amices/ggmice")
R> devtools::install_github("hanneoberman/miceheckman")
```

Set up the R environment and load the necessary packages:

```
R> set.seed(2022)
                         # for reproducibility
R> library(mice)
                         # for imputation
R> library(miceadds)
                         # for additional imputation routines
R> library(ggmice)
                         # for incomplete/imputed data visualization
R> library(ggplot2)
                         # for visualization
R> library(dplyr)
                         # for data wrangling
R> library(lme4)
                         # for multilevel modeling
                         # for multilevel parameter pooling
R> library(mitml)
R> library(miceheckman) # for imputation cf heckman models
```

2. Case study I: popularity data

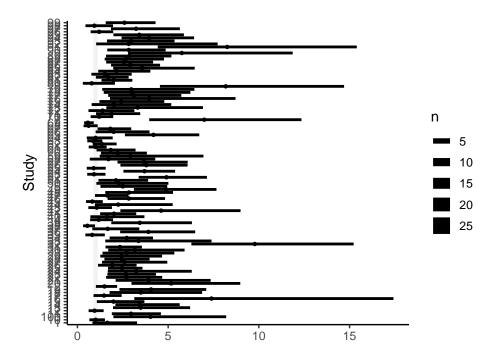
In this section we'll go over the different steps involved with imputing incomplete multilevel data with the R package mice. We consider the simulated popmis dataset, which included pupils (n=2000) clustered within schools (N=100). The following variables are of primary interest:

- school, school identification number (clustering variable);
- popular, pupil popularity (self-rating between 0 and 10; unit-level);

- sex, pupil sex (0=boy, 1=girl; unit-level);
- texp, teacher experience (in years; cluster-level).

The research objective of the popmis dataset is to predict the pupils' popularity based on their gender and the experience of the teacher. The analysis model corresponding to this dataset is multilevel regression with random intercepts, random slopes and a cross-level interaction. The outcome variable is popular, which is predicted from the unit-level variable sex and the cluster-level variable texp:

The true effect is:



Load the data into the environment and select the relevant variables:

Plot the missing data pattern:

The missingness is univariate and sporadic, which is illustrated in the missing data pattern in Figure 2.

To develop the best imputation model for the incomplete variable popular, we need to know whether the observed values of popular are related to observed values of other variables. Plot the pair-wise complete correlations in the incomplete data:

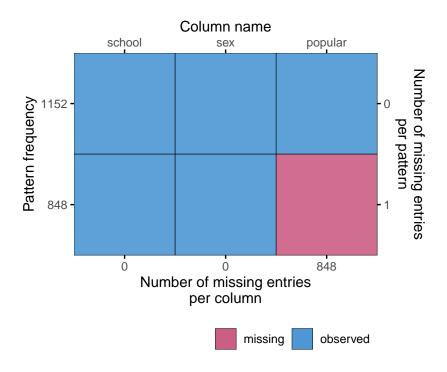
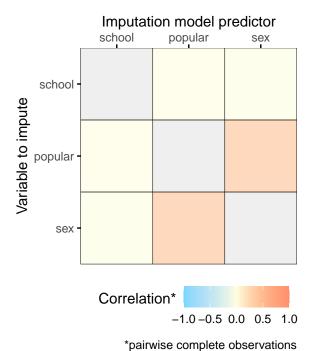


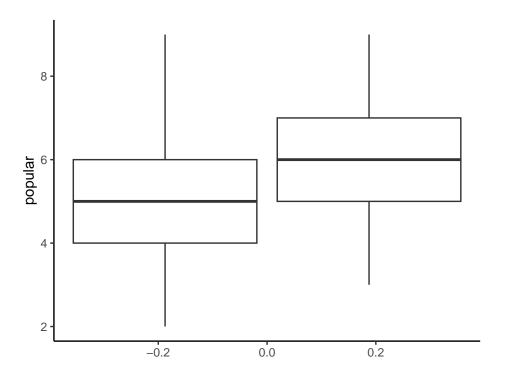
Figure 2: Missing data pattern in the popularity data

R> plot_corr(popmis)



This shows us that sex may be a useful imputation model predictor. Moreover, the missingness in popular may depend on the observed values of other variables.

```
R> # ggmice(popmis, aes(sex)) +
R> # geom_histogram(fill = "white") +
R> # facet_grid(. ~ is.na(popular), scales = "free", labeller = label_both)
R>
R> ggplot(popmis, aes(y = popular, group = sex)) +
+ geom_boxplot() +
+ theme_classic()
```

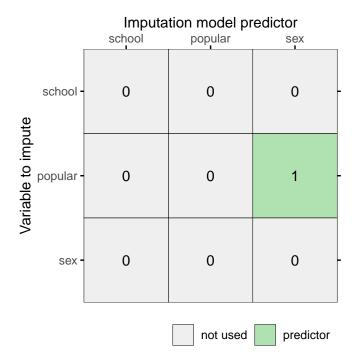


Imputation ignoring the cluster variable (not recommended)

The first imputation model that we'll use is likely to be invalid. We do <u>not</u> use the cluster identifier school as imputation model predictor. With this model, we ignore the multilevel structure of the data, despite the high ICC. This assumes exchangeability between units. We include it purely to illustrate the effects of ignoring the clustering in our imputation effort.

Create a methods vector and predictor matrix for popular, and make sure school is not included as predictor:

```
R> meth <- make.method(popmis) # methods vector
R> pred <- quickpred(popmis) # predictor matrix
R> plot_pred(pred)
```



Impute the data, ignoring the cluster structure:

Analyze the imputations:

Print the estimates:

R> testEstimates(as.mitml.result(fit), extra.pars = TRUE)

Call:

testEstimates(model = as.mitml.result(fit), extra.pars = TRUE)

Final parameter estimates and inferences obtained from 5 imputed data sets.

	Estimate	Std.Error	t.value	df	P(> t)	RIV	FMI
(Intercept)	5.012	0.295	16.994	4.362	0.000	22.587	0.969
sex	0.695	0.251	2.768	4.287	0.047	28.390	0.975

 ${\tt Estimate}$

Intercept~~Intercept|school 0.266

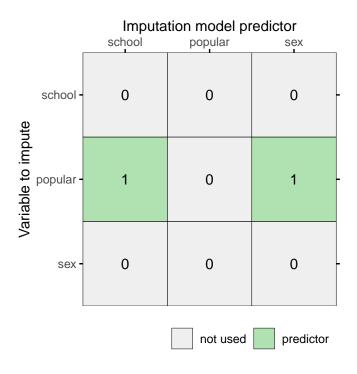
```
Residual~~Residual 1.035
ICC|school 0.208
```

Unadjusted hypothesis test as appropriate in larger samples.

Imputation with the cluster variable as predictor (not recommended)

We'll now use school as a predictor to impute all other variables. This is still not recommended practice, since it only works under certain circumstances and results may be biased (Drechsler 2015; Enders, Mistler, and Keller 2016). But at least, it includes some multilevel aspect. This method is also called 'fixed cluster imputation', and uses N-1 indicator variables representing allocation of N clusters as a fixed factor in the model (Reiter, Raghunathan, and Kinney 2006; Enders et al. 2016). Colloquially, this is 'multilevel imputation for dummies'.

```
R> # adjust the predictor matrix
R> pred["popular", "school"] <- 1
R> plot_pred(pred)
```



```
R> # impute the data, cluster as predictor
R> imp <- mice(popmis, pred = pred, print = FALSE)</pre>
```

Analyze the imputations:

Print the estimates:

R> testEstimates(as.mitml.result(fit), extra.pars = TRUE)

Call:

testEstimates(model = as.mitml.result(fit), extra.pars = TRUE)

Final parameter estimates and inferences obtained from 5 imputed data sets.

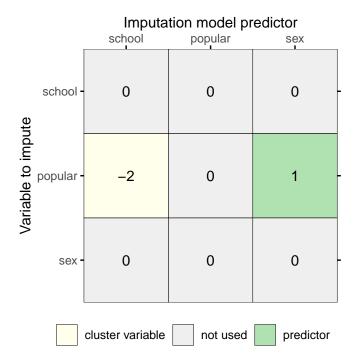
	Estimate	Std.Error	t.value	df	P(> t)	RIV	FMI
(Intercept)	4.808	0.197	24.354	5.072	0.000	7.930	0.916
sex	1.086	0.135	8.056	5.271	0.000	6.761	0.902

	Estimate
${\tt Intercept^{\tt \sim}Intercept school}$	0.324
Residual~~Residual	1.130
TCClschool	0.226

Unadjusted hypothesis test as appropriate in larger samples.

Imputation with multilevel model

```
R> # adjust the predictor matrix
R> pred["popular", "school"] <- -2
R> plot_pred(pred)
```



R> # impute the data, cluster as predictor
R> imp <- mice(popmis, pred = pred, print = FALSE)</pre>

Analyze the imputations:

Print the estimates:

R> testEstimates(as.mitml.result(fit), extra.pars = TRUE)

Call:

testEstimates(model = as.mitml.result(fit), extra.pars = TRUE)

Final parameter estimates and inferences obtained from 5 imputed data sets.

	Estimate	Std.Error	t.value	df	P(> t)	RIV	FMI
(Intercept)	4.808	0.197	24.354	5.072	0.000	7.930	0.916
sex	1.086	0.135	8.056	5.271	0.000	6.761	0.902

Residual~~Residual 1.130

ICC|school 0.226

Unadjusted hypothesis test as appropriate in larger samples.

3. Case study II: IMPACT data (syst missingness, pred matrix)

We illustrate how to impute incomplete multilevel data by means of a case study: impact from the **metamisc** package (empirical data on traumatic brain injuries, n=11,022 units across N=15 clusters, Debray and de Jong 2021). The impact data set contains traumatic brain injury data on n=11022 patients clustered in N=15 studies with 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 analysis model for this dataset is a prediction model with mort as the outcome. In this tutorial we'll estimate the adjusted prognostic effect of ct on mortality outcomes. The estimand is the adjusted odds ratio for ct, after including type, age motor_score and pupil into the analysis model:

```
R> mod <- mort ~ 1 + type + age + motor_score + pupil + ct + (1 | name)
```

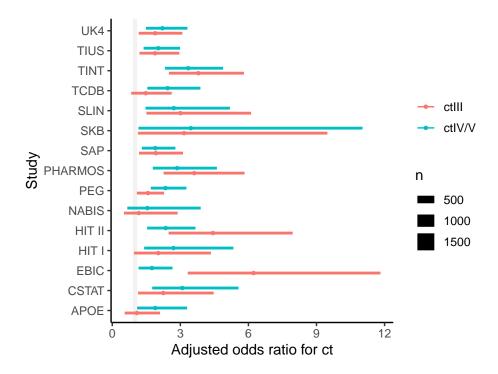
Note that variables hypots, hypox, tsah and edh are not part of the analysis model, and may thus serve as auxiliary variables for imputation.

The impact data included in the **metamisc** package is a complete data set. The original data has already been imputed once (Steyerberg et al, 2008). For the purpose of this tutorial we have induced missingness (mimicking the missing data in the original data set before imputation). The resulting incomplete data can be accessed from zenodo link to be created.

Load the complete and incomplete data into the R workspace:

```
R> data("impact", package = "metamisc")  # complete data
R> dat <- read.table("link/to/the/data.txt") # incomplete data</pre>
```

The estimated effects in the complete data are visualized in Figure ??.

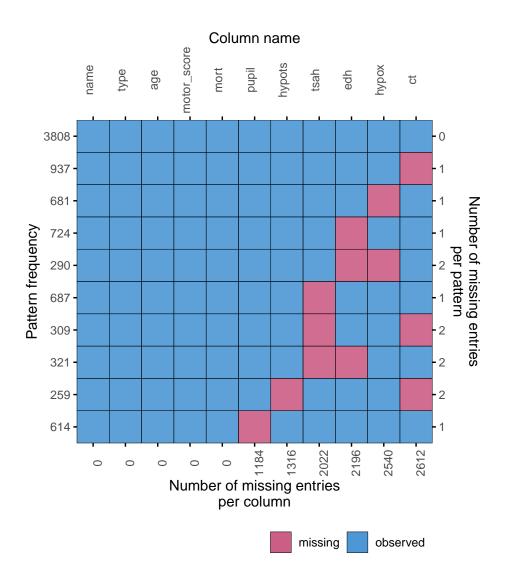


```
R> # fit <- glmer(mod, family = "binomial", data = impact) # fit the model
R> # tidy(fit, conf.int = TRUE, exponentiate = TRUE) # print estimates
```

3.1. Missingness

To explore the missingness, it is wise to look at the missing data pattern. The ten most frequent missingness patterns are shown:

R> plot_pattern(dat, rotate = TRUE, npat = 10L) # plot missingness pattern

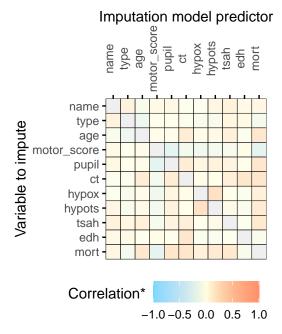


This shows that we need to impute ct and pupil.

To develop the best imputation model, we need to investigate the relations between the observed values of the incomplete variables and the observed values of other variables, and the relation between the missingness indicators of the incomplete variables and the observed values of the other variables. To see whether the missingness depends on the observed values of other variables, we can test this statistically or use visual inspection (e.g. a histogram faceted by the missingness indicator).

We should impute the variables ct and pupil and any auxiliary variables we might want to use to impute these incomplete analysis model variables. We can evaluate which variables may be useful auxiliaries by plotting the pairwise complete correlations:

R> plot_corr(dat, rotate = TRUE) # plot correlations



*pairwise complete observations

This shows us that hypox and hypot would not be useful auxiliary variables for imputing ct. Depending on the minimum required correlation, tsah could be useful, while edh has the strongest correlation with ct out of all the variables in the data and should definitely be included in the imputation model. For the imputation of pupil, none of the potential auxiliary variables has a very strong relation, but hypots could be used. We conclude that we can exclude hypox from the data, since this is neither an analysis model variable nor an auxiliary variable for imputation:

R> dat <- select(dat, !hypox) # remove variable

3.2. Complete case analysis

As previously stated, complete case analysis lowers statistical power and may bias results. The complete case analysis estimates are:

```
<dbl>
                                                                    <dbl>
                                                                            <dbl>
   <chr>
            <chr> <chr>
                                <dbl>
                                                  <dbl>
                                                            <dbl>
 1 fixed
                                       0.0182
            <NA>
                               0.0863
                                                 -11.6
                                                         2.99e-31
                                                                   0.0571
                                                                            0.130
                  (Intercept)
2 fixed
                                       0.137
                                                  -1.54 1.22e- 1
                                                                            1.08
            <NA>
                  typeRCT
                               0.757
                                                                   0.531
3 fixed
            <NA>
                  age
                               1.03
                                       0.00265
                                                  12.9
                                                         7.40e-38
                                                                   1.03
                                                                            1.04
 4 fixed
            <NA> motor scor~
                               0.651
                                       0.0732
                                                  -3.82 1.34e- 4
                                                                   0.522
                                                                            0.811
5 fixed
                                                  -6.30 2.97e-10
            <NA> motor_scor~
                               0.489
                                       0.0555
                                                                   0.391
                                                                            0.611
6 fixed
            <NA> motor_scor~
                               0.274
                                       0.0321
                                                 -11.0
                                                         2.28e-28
                                                                   0.218
                                                                            0.345
7 fixed
                               3.20
                                       0.317
                                                  11.7
                                                         8.18e-32
                                                                            3.88
            <NA> pupilNone
                                                                   2.63
8 fixed
            <NA>
                 pupilOne
                               1.75
                                       0.195
                                                   5.06 4.27e- 7
                                                                   1.41
                                                                            2.18
9 fixed
            <NA>
                 ctIII
                               2.41
                                       0.268
                                                   7.89 3.05e-15
                                                                   1.94
                                                                            2.99
10 fixed
            <NA>
                 ctIV/V
                               2.30
                                       0.214
                                                   8.95 3.55e-19
                                                                   1.92
                                                                            2.76
11 ran_pars name sd__(Inter~ 0.230 NA
                                                        NA
                                                                  NA
                                                  NA
                                                                           NA
# ... with abbreviated variable names 1: estimate, 2: std.error, 3: statistic,
    4: conf.low, 5: conf.high
```

As we can see, a higher ct (Marshall Computerized Tomography classification) is associated with a lower odds of 6-month mortality, given by the odds ratio $\exp(0.42)$, CI ... to ..., when controlling for...

3.3. Imputation model

Mutate data to get the right data types for imputation (e.g. integer for clustering variable).

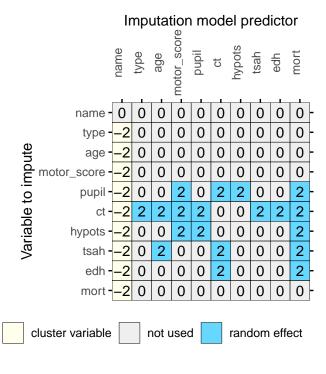
```
R> dat <- dat %>% mutate(across(everything(), as.integer))
```

Create a methods vector and predictor matrix, and make sure name is not included as predictor, but as clustering variable:

```
R> meth <- make.method(dat) # methods vector
R> pred <- quickpred(dat) # predictor matrix
R> plot_pred(pred, rotate = TRUE)
```

Imputation model predictor name - 0 0 0 0 0 0 type -Variable to impute 0 0 0 0 age -0 0 0 0 0 motor_score -0 1 pupil - 0 ct hypots - 0 1 0 tsah -edh mort - 0 0 0 0 0 not used predictor

```
R> pred[pred == 1] <- 2
R> pred["mort", ] <- 2
R> pred[, "mort"] <- 2
R> pred[c("name", "type", "age", "motor_score", "mort"), ] <- 0
R> pred[, "name"] <- -2
R> diag(pred) <- 0
R> plot_pred(pred, rotate = TRUE)
```



R> meth <- make.method(dat)
R> meth

name	type	age mot	or_score	pupil	ct
" "	11 11	11 11	" "	"pmm"	"pmm"
hypots	tsah	edh	mort		
"pmm"	"pmm"	"pmm"	11 11		

Impute the incomplete data

```
R> imp <- mice(dat, method = meth, predictorMatrix = pred, printFlag = FALSE)

R> fit <- imp %>%
+ with(glmer(mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 | name), famil
R> tidy(pool(fit))
```

```
term
                            estimate
                                       std.error
                                                  statistic
                                                                 p.value
1
              (Intercept) -2.3054756 0.340854445
                                                  -6.763813 1.425704e-11
2
                                                  -2.322780 2.021049e-02
                     type -0.4200458 0.180837517
3
                      age 0.0302518 0.001561625
                                                  19.372002 0.000000e+00
4 as.factor(motor_score)2 -0.6619736 0.069527977
                                                  -9.520967 0.000000e+00
5 as.factor(motor_score)3 -1.0520025 0.070748986 -14.869507 0.000000e+00
6 as.factor(motor_score)4 -1.5087772 0.072240455 -20.885489 0.000000e+00
7
                    pupil 0.4731045 0.038187004 12.389150 0.000000e+00
8
                       ct 0.4291135 0.032126389
                                                 13.357041 0.000000e+00
                        df dfcom
             b
                                         fmi
                                                  lambda m
                                                                   riv
```

```
1 7.937082e-04 9227.60708 11013 0.008412824 0.008197930 5 0.008265691
2 1.386594e-04 10229.67142 11013 0.005282534 0.005088076 5 0.005114097
3 1.138007e-08 10083.78177 11013 0.005796971 0.005599802 5 0.005631337
4 1.427540e-04 2450.43742 11013 0.036222753 0.035436457 5 0.036738334
5 1.147119e-04 3540.28145 11013 0.028049975 0.027501049 5 0.028278744
6 1.377409e-04 2902.11217 11013 0.032339200 0.031672563 5 0.032708526
7 3.160434e-04 58.71181 11013 0.284053948 0.260073900 5 0.351486317
                74.37520 11013 0.250767587 0.230887509 5 0.300199921
8 1.985834e-04
          ubar
1 1.152293e-01
2 3.253582e-02
3 2.425016e-06
4 4.662835e-03
5 4.867765e-03
6 5.053394e-03
7 1.078995e-03
8 7.938047e-04
R> as.mitml.result(fit)
[[1]]
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial (logit)
Formula: mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 |
    name)
      AIC
                BIC
                       logLik deviance df.resid
10494.825 10560.593 -5238.412 10476.825
                                            11013
Random effects:
Groups Name
                   Std.Dev.
        (Intercept) 0.2917
Number of obs: 11022, groups: name, 15
Fixed Effects:
            (Intercept)
                                            type
                                                                      age
               -2.33693
                                        -0.43143
                                                                  0.03013
as.factor(motor_score)2 as.factor(motor_score)3 as.factor(motor_score)4
               -0.67764
                                        -1.05120
                                                                 -1.49989
                  pupil
                                              ct
                0.49336
                                         0.44123
optimizer (Nelder_Mead) convergence code: 0 (OK); 0 optimizer warnings; 2 lme4 warnings
[[2]]
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial (logit)
Formula: mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 |
    name)
```

```
BIC
                       logLik deviance df.resid
      ATC
10543.607 10609.376 -5262.803 10525.607
                                            11013
Random effects:
 Groups Name
                   Std.Dev.
 name (Intercept) 0.2937
Number of obs: 11022, groups: name, 15
Fixed Effects:
            (Intercept)
                                            type
                                                                      age
               -2.28159
                                        -0.42088
                                                                  0.03026
as.factor(motor_score)2 as.factor(motor_score)3 as.factor(motor_score)4
                                        -1.04928
               -0.65610
                                                                 -1.49432
                  pupil
                                              ct
                0.48055
                                         0.41014
optimizer (Nelder_Mead) convergence code: 0 (OK); 0 optimizer warnings; 1 lme4 warnings
[[3]]
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial (logit)
Formula: mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 |
    name)
      AIC
                BIC
                       logLik deviance df.resid
10543.170 10608.939 -5262.585 10525.170
                                            11013
Random effects:
Groups Name
                   Std.Dev.
        (Intercept) 0.2901
Number of obs: 11022, groups: name, 15
Fixed Effects:
            (Intercept)
                                            type
                                                                      age
               -2.29948
                                        -0.40181
                                                                  0.03038
as.factor(motor_score)2 as.factor(motor_score)3 as.factor(motor_score)4
               -0.65959
                                        -1.06391
                                                                -1.52075
                  pupil
                0.45837
                                         0.42186
optimizer (Nelder Mead) convergence code: 0 (OK); 0 optimizer warnings; 2 lme4 warnings
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial (logit)
Formula: mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 |
    name)
      ATC
                BIC
                       logLik deviance df.resid
10527.222 10592.991 -5254.611 10509.222
Random effects:
 Groups Name
                   Std.Dev.
        (Intercept) 0.2962
 name
```

```
Number of obs: 11022, groups: name, 15
Fixed Effects:
            (Intercept)
                                            type
                                                                       age
               -2.27660
                                        -0.42912
as.factor(motor score)2 as.factor(motor score)3 as.factor(motor score)4
               -0.66963
                                        -1.05952
                                                                 -1.51971
                  pupil
                                              ct
                0.45085
                                         0.44439
optimizer (Nelder_Mead) convergence code: 0 (OK); 0 optimizer warnings; 1 lme4 warnings
[[5]]
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial (logit)
Formula: mort ~ type + age + as.factor(motor_score) + pupil + ct + (1 |
    name)
      AIC
                BIC
                       logLik deviance df.resid
10519.178 10584.947 -5250.589 10501.178
                                            11013
Random effects:
                    Std.Dev.
 Groups Name
        (Intercept) 0.2897
Number of obs: 11022, groups: name, 15
Fixed Effects:
            (Intercept)
                                            type
                                                                       age
               -2.33278
                                        -0.41699
                                                                   0.03032
as.factor(motor_score)2 as.factor(motor_score)3 as.factor(motor_score)4
               -0.64691
                                        -1.03611
                                                                 -1.50921
                  pupil
                0.48240
                                         0.42794
optimizer (Nelder_Mead) convergence code: 0 (OK); 0 optimizer warnings; 1 lme4 warnings
attr(,"class")
[1] "mitml.result" "list"
R> # testEstimates(as.mitml.result(fit))
```

4. Case study III: obesity data

Data are simulated and included in the miceheckman package. We will use the following variables:

- region Cluster variable,
- gender Gender (0=male, 1=female),
- age Age of the patient,
- height Height in meters,

- weight Weight in kilograms,
- 'rt" Response time in minutes (inclusion-restriction variable).

The imputation of these data is based on the IPDMA Heckman Github repo Load the data:

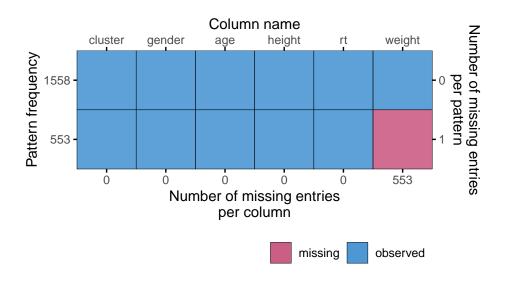
R> data("obesity", package = "miceheckman")

Select relevant variables:

R> dat <- select(obesity, -"bmi")</pre>

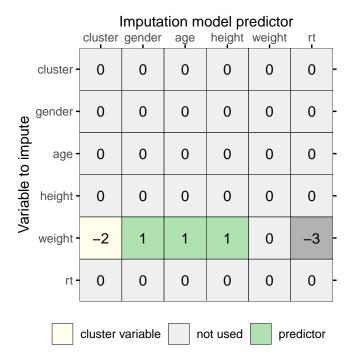
Visualize missing data pattern:

R> plot_pattern(dat)



Create predictor matrix:

```
R> pred <- quickpred(dat)  # predictor matrix
R> pred["weight","cluster"]<- -2 # clustering variable
R> pred["weight","rt"] <- -3 #inclusion-restriction variable
R> plot_pred(pred)
```



Set the Heckman model as imputation method:

```
R> meth <- make.method(dat) # methods vector
R> meth["weight"]<-"21.heckman"</pre>
```

Impute the missingness:

```
R> imp <- mice(
+ dat, # dataset with missing values
+ m = 5, # number of imputations
+ maxit = 10,
+ meth = meth, #imputation method vector
+ pred = pred, #imputation predictors matrix
+ meta_method = "reml",
+ printFlag = FALSE
+ )</pre>
```

5. Discussion

- Additional levels of clustering
- More complex data types: timeseries and polynomial relationship in the clustering.

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7. References

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