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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

- What is clustering/multilevel data? In this paper, we discuss grouped observations, not longitudinal data (within-patient clustering). -> ADD: timeseries also in Discussion section.
- What do we mean by clustering? In the medical field: Clustering by studies (IPDMA), hospitals in registries, multi-center studies etc. In other fields: e.g. official stats clustering at country-level, or social sciences clustering at school-level (related to the sampling design).
- What is heterogeneity? I.e. variability within studies vs. variability between studies

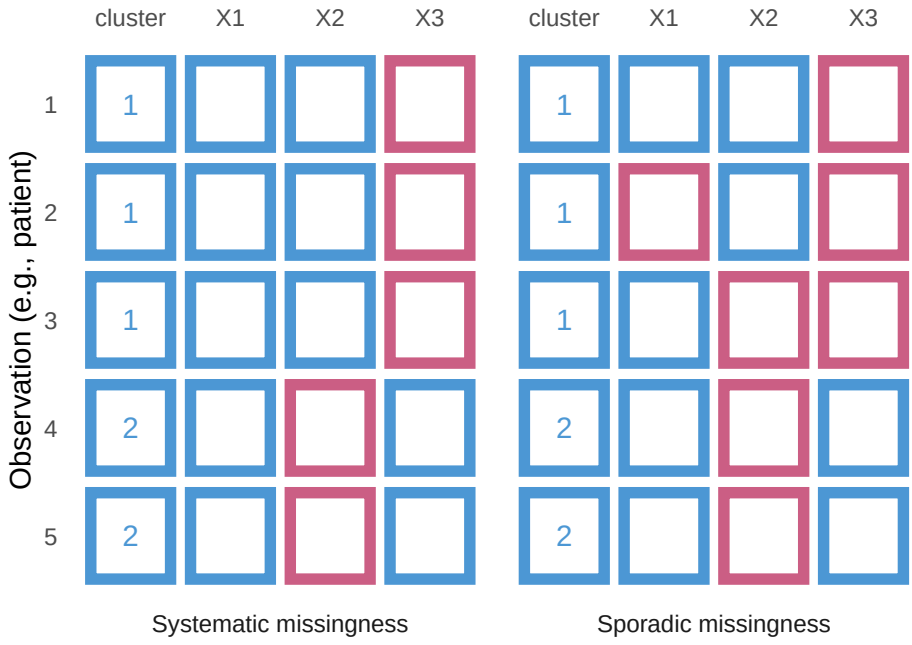
- What does multilevel data look like? ADD: figure to show difference between patient-level datapoints vs cluster-level datapoints. Maybe also add different data frame formats (or just explain in text that there's long and wide formats).

- What methods are required to analyze multilevel data? Add references, e.g. Hox, Moerbeek, and van de Schoot (b) and de Jong, Moons, Eijkemans, Riley, and Debray. At least explain difference random effects for intercept term, predictor effects, and/or variance residual error.

1.2. Missing data

- Why/where does missingness occur in multilevel data? I.e., not only patient-level but also cluster-level.

- How can we categorize this? Systematic vs sporadic missingness, see Resche-Rigon, White, Bartlett, Peters, Thompson, and Group. ADD: visualization of systematic vs sporadic missingness. Within systematic we have always missing (same value per cluster) and non-measured variables (may differ per patient). TODO: adjust md pattern to match text. -> syst may vary or same for all patients (observations/participants).



- What kinds of missingness are there? ADD: missingness mechanisms here. See e.g. Yucel and Hox, van Buuren, and Jolani (a).

- Why are standard (ad hoc) missing data methods not well suited?

- What types of multilevel methods are available? General overview of approaches, see Audigier, White, Jolani, Debray, Quartagno, Carpenter, van Buuren, and Resche-Rigon and Grund, Lüdtke, and Robitzsch. E.g., imputation of study level versus patient-level covariates, and one-stage imputation versus two-stage imputation methods.
- Additional difficulty that is addressed in this tutorial: MNAR data.

1.3. Aim of this paper

- Provide practical guidelines with code snippets for imputation of incomplete multilevel data.
- We focus on the workflow for conditional modeling (not JOMO) in `mice`. Refer to other packages: `mitml`, `miceadds`, `mdmb`.
- Case study options: `metamisc::impact` (real IPD on traumatic brain injuries, without `NA`s), `mice::popularity` (simulated data on school kids, with MNAR/MAR mixture). TODO: Check example data Gelman.
- Introduce case study and set scope of this tutorial: We're providing an overview of implementations. It's up-to the reader to decide which strategy suits their data. So we won't go into detail for the different methods (and equations). This paper is just a software tutorial. We'll keep it practical. -> ADD: some kind of help function that suggests a suitable predictor matrix to the user, given a certain analysis model.

2. Workflows

We'll use the IMPACT data (`metamisc::impact`) and a MAR/MNAR version of the `mice::popmis` data (i.e., a variation on the Hox (2010) popularity data, where the missingness in the variables is either missing at random (MAR) or missing not at random (MNAR)). -> ask whether we can use the Heckman repo data or simulate data ourselves

Heckman options:

- leiden85
- GJRM::hiv (https://rdrr.io/github/egeminiani/GJRM/man/hiv.html)
- simulating
- IMPACT

2.1. Case study I: IMPACT

- What does the data look like? `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).

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==>  V <==  No need for mice. This data set is completely observed.
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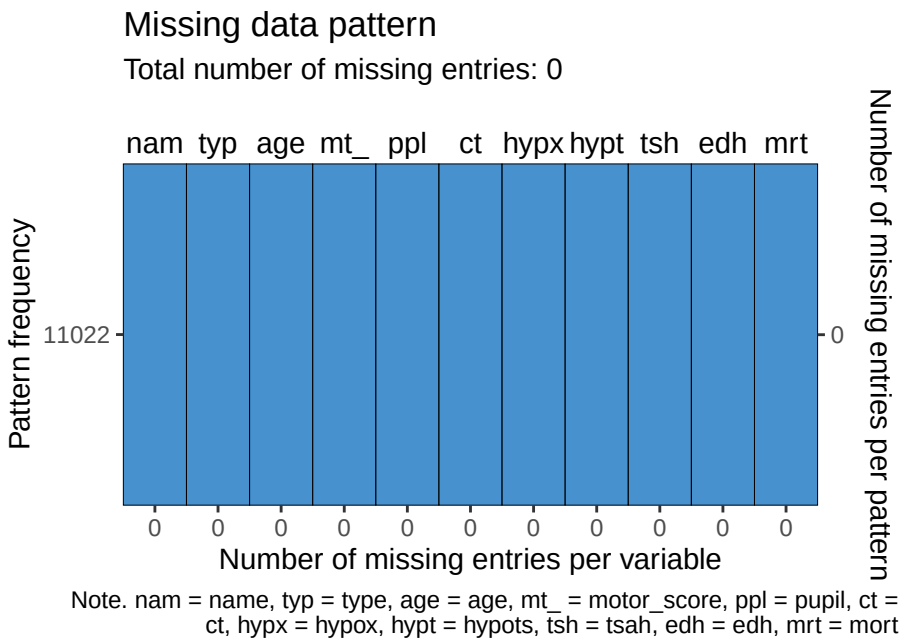


-> Why are there no missings? According to the vignette, the data is already imputed (Steyerberg et al, 2008).

- MAR miss varying by cluster. Obs data patt differ per cluster. E.g., in cluster 1 miss depends on age but not in cluster two. Split the dataframe and run `ampute()` on each cluster. -> TODO: also make MNAR missingness to heckman model. Maybe based on `ct`

variable? Inclusion-selection variable. -> otherwise: use `leiden85` data on blood pressure with MNAR. Then run cox regression like the boshuizen article but with living situation as clusters. -> TODO: get analyses from https://www.gerkovink.com/mimp/Contents/Exercises/Day%203%20-%20Wednesday/Sensitivity_analysis/Sensitivity_analysis.html.

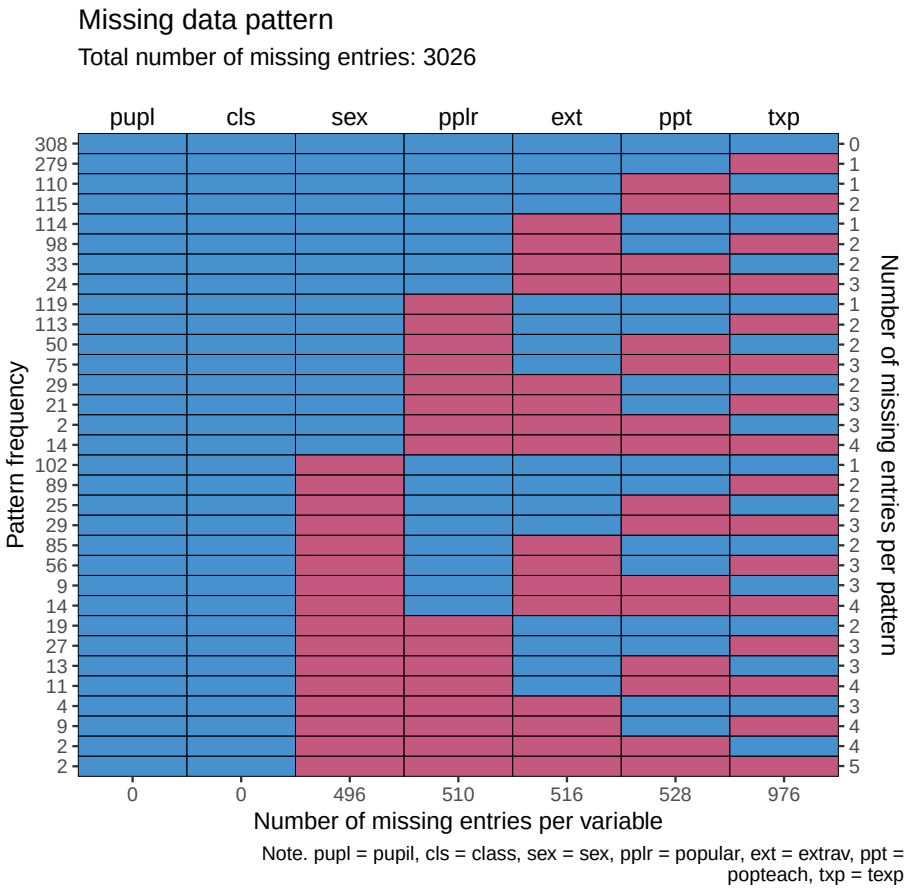
- ADD: `multilevel_ampute()` wrapper function in `mice`.

2.2. Case Study II: Popularity

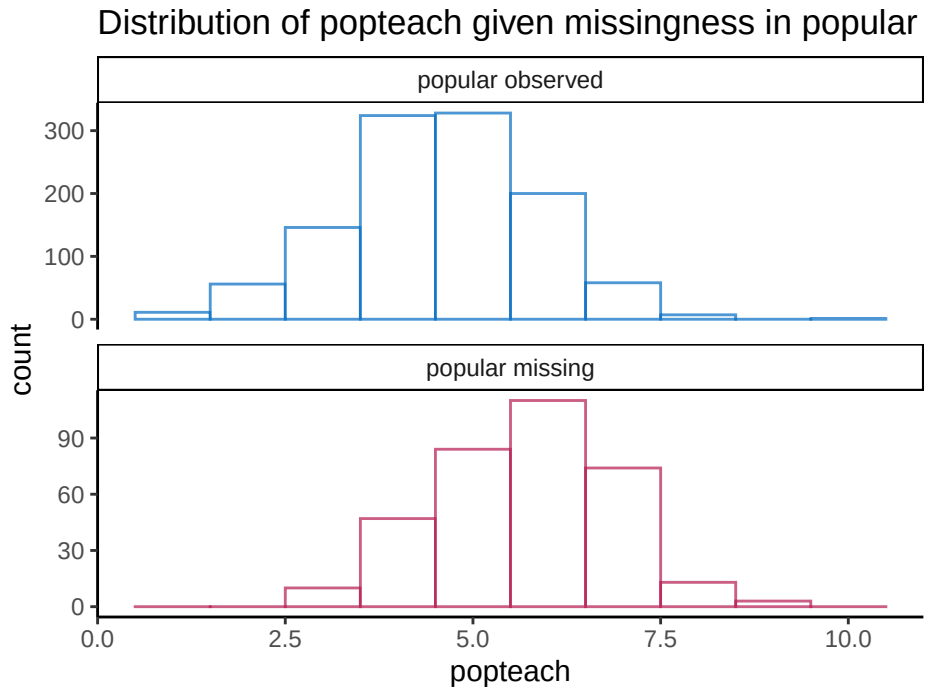
- What does the data look like? `popNCR` is a simulated dataset with pupils clustered in classes, $n_{\text{participants}} = 2000$, $n_{\text{clusters}} = 100$, on 7 variables:
  - `pupil` Pupil number within class,
  - `class` Class number,
  - `extrav` Pupil extraversion,
  - `sex` Pupil gender,
  - `texp` Teacher experience (years),
  - `popular` Pupil popularity,
  - `popteach` Teacher popularity.

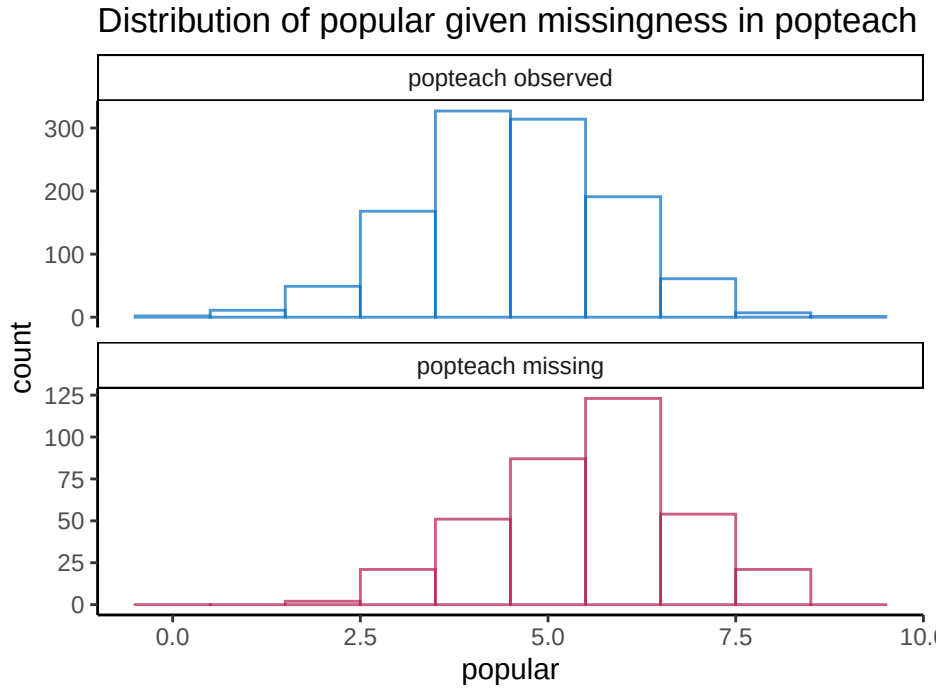
- What are the ICCs? For `popular` the ICC is 0.33. For `popteach` it is 0.31. It would be wise to use multilevel modeling.

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



- Does the missing data of `popular` depend on `popteach`? One could for example check this by making a histogram of `popteach` separately for the pupils with known popularity and missing popularity. And the other way around: Does the missingness in teacher popularity depend on pupil popularity?





- We do see that the histogram for the missing `popular` is further to the right than the histogram 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.

2.3. Amputation

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2.4. Modeling choices

- Which models will we discuss? We'll build the model to grow in complexity. The final model is the most complex but also the most versatile.
- Note on model complexity: Typically, we should at least use random intercepts, but often random slopes as well. Ideally we impute with random everything and heteroscedastic errors: most generic method (no worry about congeniality, but don't mention the term) -> Refer to other papers for background, we'll focus just on the software implementation of the situations mentioned there. Sometimes there's little reason to assume some variable is affected by heterogeneity. -> Refer to Meng, an Audigier paper, and a paper by Grund on congeniality and random slopes.
- Step 0: As predictor + CCA to scare off users
- Step 1: Random intercepts
- Step 2: Random slopes
- Step 3: Residuals
- Heckman model for MNAR
- What do the different implementations look like? How to define the imputation model(s) in `mice`?

2.5. Step 0

- AKA multilevel imputation for dummies.
- Doesn't work for systematic missingness.

2.6. Step 1-3 + MNAR

- TODO: fill in.

2.7. Pooling

- Analysis of scientific interest.
- Pooling using `mitml`.
- Pooling 'regular' parameters vs more 'exotic' parameters (SE of residual errors, or autocorrelation)
- ADD: export `mids` objects to other packages like `lme4` or `coxme`?

3. Discussion

- JOMO in `mice` –> on the side for now
- Additional levels of clustering
- Timeseries: and polynomial relationship in the clustering.

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