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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

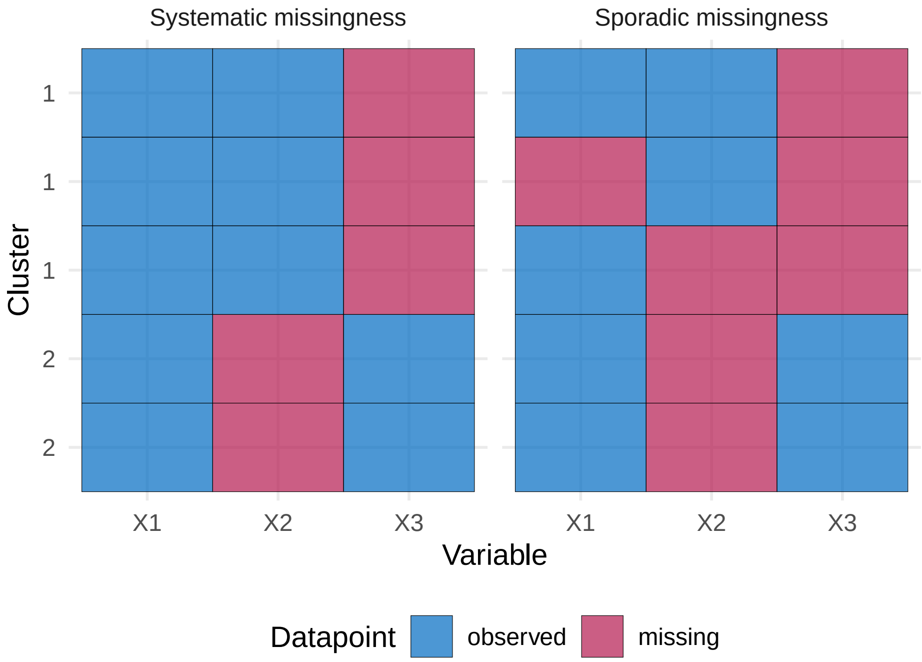
1.1. Multilevel data

- 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. **?**. 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.
- 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 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`.
- Case study options: `metamisc::impact` (real data on traumatic brain injuries, IPD), `mice::popularity` (simulated data with MNAR/MAR mixture, schools). -> Check Gelman's data/NSRI data.
- 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 pred matrix to the user, given a certain analysis model.

2. Workflows

2.1. Case study

- 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)).
- `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).

```
R> # load data
R> data("impact")
R> # # descriptive statistics
R> # by(impact, impact$name, summary)
R> # psych::describe(impact)[,c(2:5,8:9)]
R> # missingness
R> md_pat(impact)
```

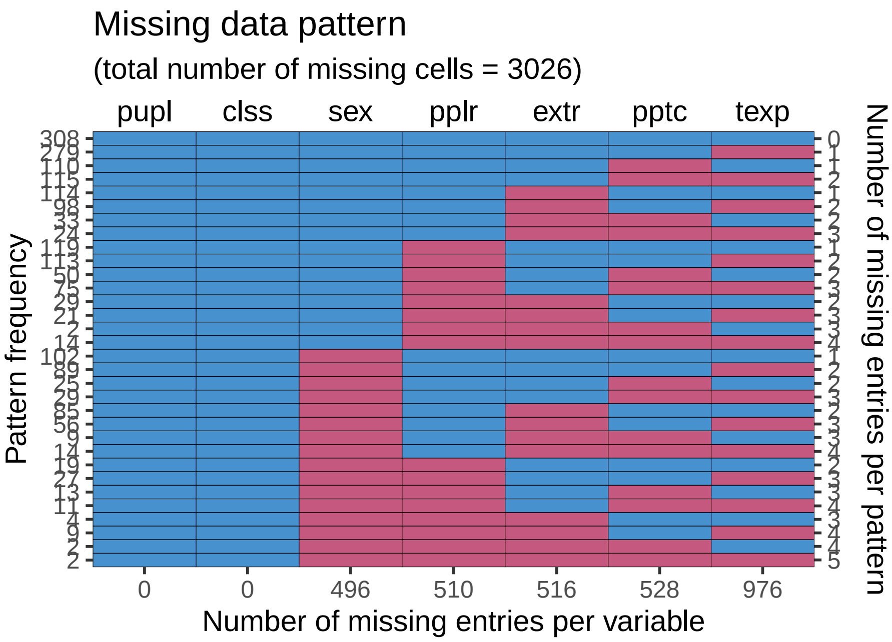
```
 /\     /\
{  `---'  }
{  O   O  }
==>  V <==  No need for mice. This data set is completely observed.
 \  \|/  /
  `-----'
```

```
      name type age motor_score pupil ct hypox hypots tsah edh mort
11022    1    1   1           1     1  1     1      1    1   1    1 0
         0    0   0           0     0  0     0      0    0   0    0 0
```

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

- 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.

```
R> # load data
R> pop <- readRDS("../Data/popNCR.RDS")
R> # missingness
R> md_pat(pop)
```



2.2. 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, Vincent, and a paper by Grund on congeniality and random slopes.
- Step 0: study as a predictor, AKA multilevel imputation for dummies. Doesn't work for syst missing.

2.3. Conditional models

- How to define the imputation model(s) in `mice`?
- What do the different implementations look like?
- Step 1: Intercept
- Step 2: Slope

- Step 3: Residuals
- Heckman model for MNAR

2.4. Pooling

- Analysis of scientific interest.
- Pooling using `mitml`.
- Pooling 'regular' parameters vs more 'exotic' parameters (SE of residual errors, or autocorreletion)
- 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.

References

Audigier V, White IR, Jolani S, Debray TPA, Quartagno M, Carpenter J, van Buuren S, Resche-Rigon M (????). "Multiple Imputation for Multilevel Data with Continuous and Binary Variables." **33**(2), 160–183. ISSN 0883-4237, 2168-8745. doi:10.1214/18-STS646. 1702.00971, URL https://projecteuclid.org/journals/statistical-science/volume-33/issue-2/Multiple-Imputation-for-Multilevel-Data-with-Continuous-and-Binary-Variables/10.1214/18-STS646.full.

Grund S, Lüdtke O, Robitzsch A (????). "Multiple Imputation of Missing Data for Multilevel Models: Simulations and Recommendations." **21**(1), 111–149. ISSN 1094-4281. doi:10.1177/1094428117703686. URL https://doi.org/10.1177/1094428117703686.

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