EP16: Missing Values in Clinical Research: Multiple Imputation

5. Know Your Data

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Missing Data Pattern

To demonstrate the **work flow** when performing **multiple imputation** with the **mice** package, we use data from the National Health and Nutrition Examination Survey (NHANES).

There are several packages in R that provide functions to investigate **the missing data pattern**.

Examples are:
mice, **JointAI**, **VIM**, **Amelia**, **visdat**, **naniar**, . . .

Missing Data Pattern

```
mdp <- mice::md.pattern(NHANES, plot = FALSE)
head(mdp[, -c(7:14)]) # omit some columns to fit it on the slide
```

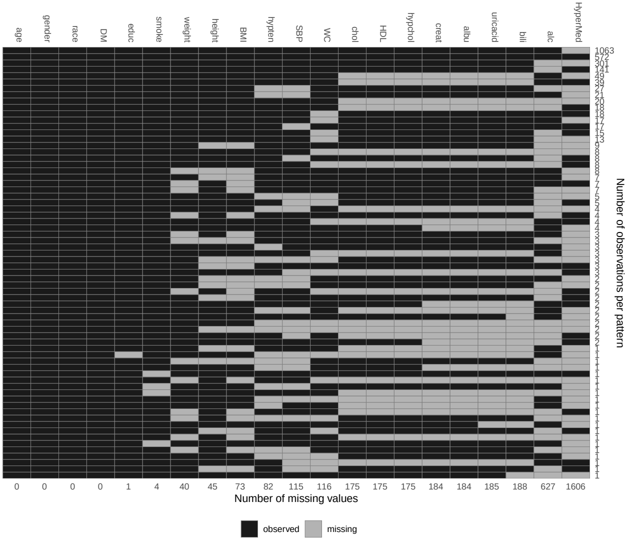
```
##      age gender race DM educ smoke hypchol creat albu uricacid bili alc HyperMed  
## 572    1      1    1  1    1     1       1     1    1        1    1   1        1 0
## 1063   1      1    1  1    1     1       1     1    1        1    1   1        0 1
## 141    1      1    1  1    1     1       1     1    1        1    1   0        1 1
## 301    1      1    1  1    1     1       1     1    1        1    1   0        0 2
## 2      1      1    1  1    1     1       1     1    1        1    0   1        0 2
## 1      1      1    1  1    1     1       1     1    1        1    0   0        0 3
```

```
tail(mdp[, -c(7:14)])
```

```
##   age gender race DM educ smoke hypchol creat albu uricacid bili alc HyperMed     
## 1   1      1    1  1    1     0       1     1    1        1    1   1        1    1
## 1   1      1    1  1    1     0       1     1    1        1    1   1        0    2
## 1   1      1    1  1    1     0       0     0    0        0    0   0        0   10
## 1   1      1    1  1    1     0       1     1    1        1    1   1        0    4
## 1   1      1    1  1    0     1       0     0    0        0    0   1        0   12
##     0      0    0  0    1     4     175   184  184      185  188 627     1606 3975
```

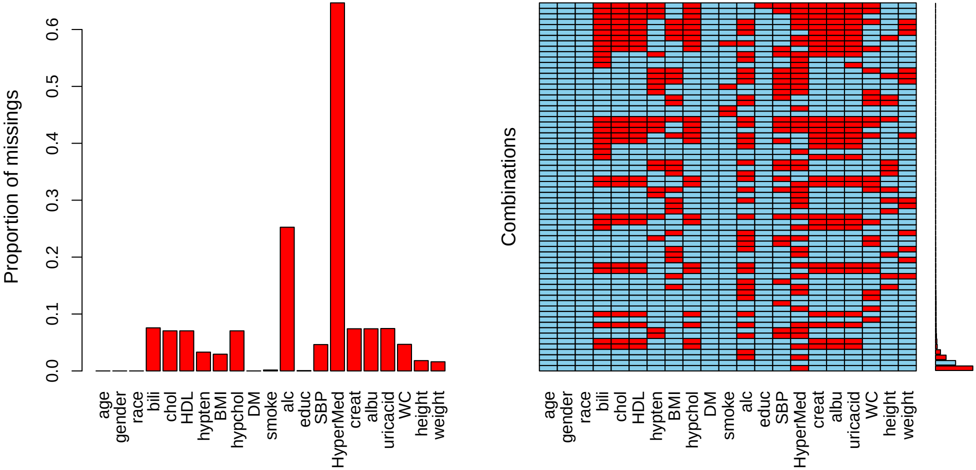
Missing Data Pattern

```
JointAI::md_pattern(NHANES)
```



Missing Data Pattern

```
VIM::aggr(NHANES, prop = TRUE)
```



Missing Data Pattern

We are also interested in the number and proportion of (in)complete cases ...

```
cctab <- table(complete.cases(NHANES))
cbind(
  "#" = setNames(cctab, c('incomplete', 'complete')),
  "%" = round(100 * cctab/nrow(NHANES), 2)
)
```

```
##               #     %
## incomplete 1911 76.96
## complete    572 23.04
```

Missing Data Pattern

… and the proportion of missing values per variable:

```
cbind("# NA" = sort(colSums(is.na(NHANES))),
      "% NA" = round(sort(colMeans(is.na(NHANES))) * 100, 2))
```

```
##        # NA % NA     ##        # NA % NA      ##          # NA  % NA
## age       0 0.00     ## height   45 1.81      ## hypchol   175  7.05
## gender    0 0.00     ## BMI      73 2.94      ## creat     184  7.41
## race      0 0.00     ## hypten   82 3.30      ## albu      184  7.41
## DM        0 0.00     ## SBP     115 4.63      ## uricacid  185  7.45
## educ      1 0.04     ## WC      116 4.67      ## bili      188  7.57
## smoke     4 0.16     ## chol    175 7.05      ## alc       627 25.25
## weight   40 1.61     ## HDL     175 7.05      ## HyperMed 1606 64.68
```

Missing Data Pattern

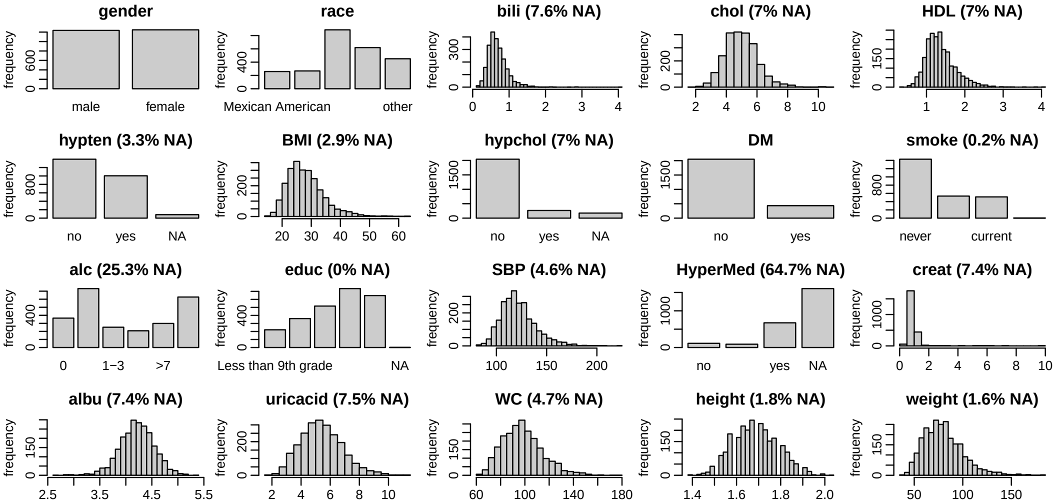
See also:

- `mice::md.pattern()`
- `visdat::vis_miss()`
- `visdat::vis_dat()`
- ...

- `naniar::prop_miss_case()`, `naniar::pct_miss_case()`
- `naniar::prop_complete_case()`, `naniar::pct_complete_case()`
- `naniar::miss_var_summary()`
- `mice::md.pairs()`
- ...

Data Distribution

```r
JointAI::plot_all(NHANES[, -1])  # exclude 1st column to fit on slide
```



Correlations & Patterns

A quick (and dirty) way to check for strong correlations between variables is:

```r
# re-code all variables as numeric and calculate spearman correlation
Corr <- cor(sapply(NHANES, as.numeric),
            use = "pairwise.complete.obs", method = "spearman")
```

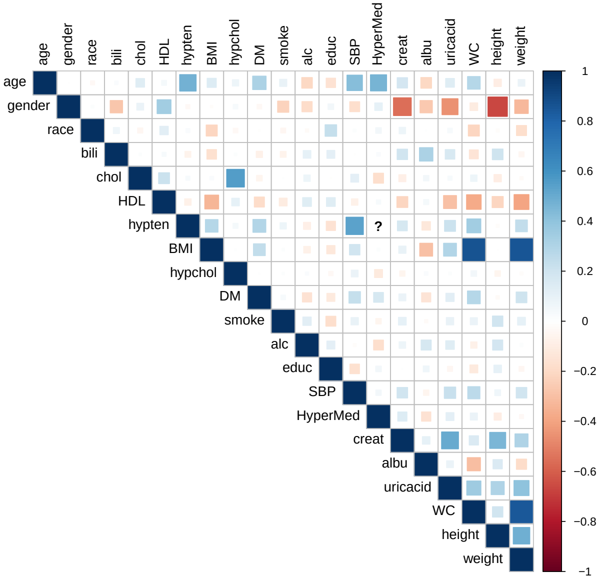
```
## Warning in cor(sapply(NHANES, as.numeric), use =
## "pairwise.complete.obs", : the standard deviation is zero
```

```r
corrplot::corrplot(Corr, method = "square", type = "upper",
                   tl.col = "black")
```

Note:

We only use the correlation coefficient for categorical variables for visualization, not as a statistical result!

Correlations & Patterns



Correlations & Patterns

Check out what the problem is with `hypertension` and `HyperMed`:

```r
table(hypertension = NHANES$hypten,
      HyperMed = NHANES$HyperMed, exclude = NULL)
```

```
##             HyperMed
## hypertension   no previous  yes <NA>
##          no     0        0    0 1397
##          yes  114       90  673  127
##          <NA>   0        0    0   82
```

Why are values missing?

Knowing your data also means being able to answer these questions:

- Do missing values in multiple variables always **occur together**? (e.g. blood measurements)
- Are there **structural missing values**? (e.g. pregnancy status in men)
- Are there **patterns** in the missing values? (e.g. only patients with hypertension have observations of `HyperMed`)
- Are values **missing by design**?
- Is the **assumption of ignorable missingness** (MAR or MCAR) justifiable?

Auxiliary Variables

Auxiliary variables are variables that are not part of the analysis but **can help during imputation**.

Good auxiliary variables

- are **related to the probability of missingness** in a variable, or
- are **related to the incomplete variable** itself,
- do **not have many missing values** themselves and
- are (mostly) **observed** when the incomplete variable of interest is missing.