EP16: Missing Values in Clinical Research: Multiple Imputation

7. Convergence & Diagnostics

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Setting

In this section, we use imputed data from the following set-up:

```r
library("mice")
imp0 <- mice(NHANES, maxit = 0,
             defaultMethod = c("norm", "logreg", "polyreg", "polr"))

meth <- imp0$method
meth["HyperMed"] <- ""
meth["BMI"] <- "~I(weight/height^2)"

pred <- imp0$predictorMatrix
pred[, "HyperMed"] <- 0

post <- imp0$post
post["creat"] <- "imp[[j]][,i] <- squeeze(imp[[j]][,i], c(0, 100))"
```

Setting

Knowing that we “forgot” to change the predictor matrix to prevent feedback from `BMI` to `height` and `weight`, we use the resulting `mids` object `imp3` for demonstratin purposes:

```r
imp3 <- mice(NHANES, method = meth, predictorMatrix = pred, post = post)
```

Setting

Knowing that we “forgot” to change the predictor matrix to prevent feedback from `BMI` to `height` and `weight`, we use the resulting `mids` object `imp3` for demonstratin purposes:

```r
imp3 <- mice(NHANES, method = meth, predictorMatrix = pred, post = post)
```

Additionally, we work with the improved imputation using the following additional settings:

```r
pred[c("weight", "height"), "BMI"] <- 0
```

```r
imp4 <- mice(NHANES, method = meth, predictorMatrix = pred, post = post,
             maxit = 30)
```

Logged Events

Information on the automatic changes that were done by **mice** is returned as `loggedEvents`, which is part of the `mids` object.

`loggedEvents` is a `data.frame` and has the following columns:

`it`	iteration number
`im`	imputation number
`dep`	dependent variable
`meth`	imputation method used
`out`	names of altered or removed predictors

It can be obtained as

```r
imp3$loggedEvents
```

Logged Events

Neither `imp3` nor `imp4` had any logged events.

To demonstrate `loggedEvents` we create a small dataset with some “mistakes” in it:

```r
demo <- NHANES[, 1:5]                  # first 5 variables from NHANES
demo$dupl <- demo[, 4]                 # create a duplicate variable
demo$const <- 1                        # create a constant variable
demo$age[demo$gender == 'male'] <- NA  # set age missing for all males
```

```r
demoimp <- mice(demo)
```

```
## Warning: Number of logged events: 8
```

Logged Events

```r
head(demoimp$loggedEvents)
```

```
##   it im dep      meth          out
## 1  0  0      constant        const
## 2  0  0     collinear         dupl
## 3  1  1 age       pmm genderfemale
## 4  1  2 age       pmm genderfemale
## 5  1  3 age       pmm genderfemale
## 6  2  1 age       pmm genderfemale
```

Before imputation (iteration 0):

- the constant variable was removed
- the duplicate variable was identified as collinear and removed.

During imputation:

- gender was removed from the model for age

Convergence

From a previous section of this course we know that **mice** uses an **iterative algorithm** and imputations from the first few iterations may not be samples from the "correct" distributions.

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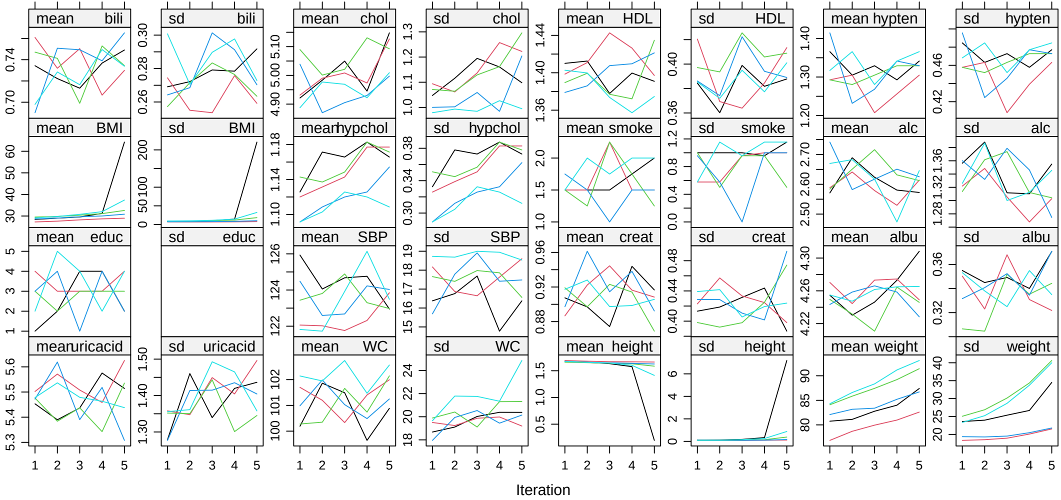
Traceplots can be used to visually assess **convergence**.

In **mice**, the function `plot()` produces traceplots of the mean and standard deviation (across subjects) per incomplete variable.

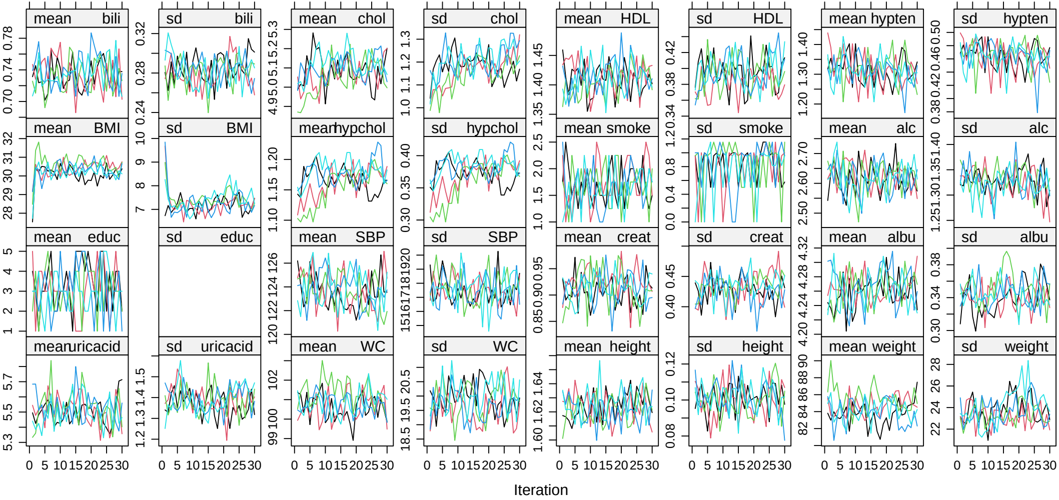
Convergence

```
plot(imp3, layout = c(8, 4))
```



Convergence

```
plot(imp4, layout = c(8, 4))
```



Convergence

Strong trends and traces that show **correlation** between variables indicate **problems of feedback**. This needs to be investigated and resolved in the specification of the `predictorMatrix`.

Weak trends may be artefacts that often disappear when the imputation is performed with more iterations.

Diagnostics

When MCMC chains have converged, the **distributions of the imputed and observed values** can be compared to investigate differences between observed and imputed data.

Note:
Plots usually show the **marginal** distributions of observed and imputed values, which do not have do be identical under MAR.

But:
The **conditional** distributions (given all the other variables in the imputation model) of the imputed values are assumed to be the same as the conditional distributions of the observed data.

Diagnostics

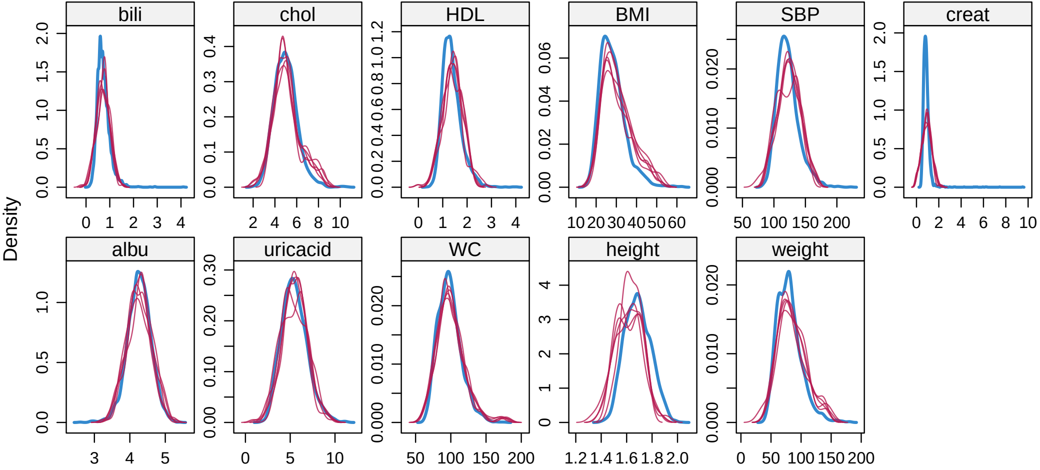
mice provides several functions for visual diagnosis of imputed values:

- `densityplot()` (for large datasets and variables with many NAs)
- `stripplot()` (for smaller datasets and/or variables with few NAs)
- `bwplot()`
- `xyplot()`

These functions create lattice graphics, which can be modified analogously to their parent functions from the **lattice** package.

Diagnostics

```
densityplot(imp4)
```

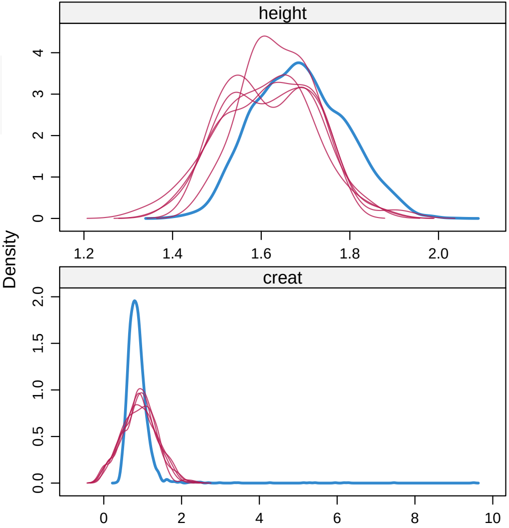


Diagnostics

```
densityplot(imp4, ~ height + creat,
            layout = c(1, 2))
```

The `densityplot()` shows that

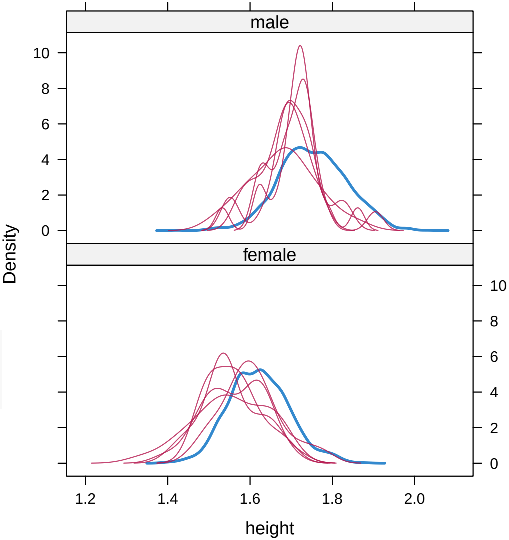
- imputed values of `height` are smaller than the observed values
- the distribution of the imputed values of `creat` is wider than the distribution of the observed values



Diagnostics

In some cases **differences** in distributions **can be explained by strata** in the data, however, here, `gender` does not explain the difference in observed and imputed values.

```
densityplot(imp4, ~height|gender,
                  layout = c(1, 2))
```



Diagnostics

As an alternative, we might consider `race` to explain the differences

```
densityplot(imp4, ~height|race)
```

```
## Error: need at least 2 points to select a bandwidth automatically
```

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```r
densityplot(imp4, ~height|race)
```

```
## Error: need at least 2 points to select a bandwidth automatically
```

```r
with(NHANES, table(race = race, "height missing" = is.na(height)))
```

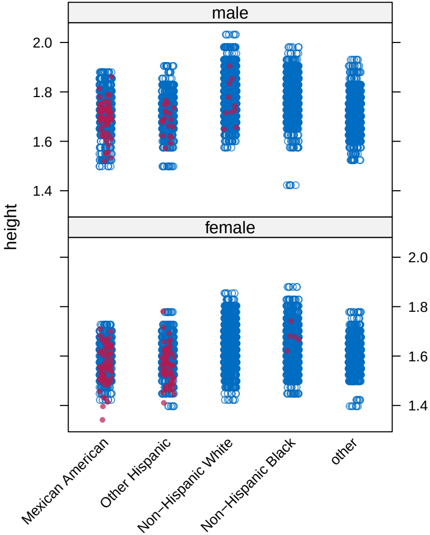
```
##                     height missing
## race                 FALSE TRUE
##   Mexican American     233   26
##   Other Hispanic       252   16
##   Non-Hispanic White   884    2
##   Non-Hispanic Black   618    1
##   other                451    0
```

There are not enough missing values of `height` per categories of `race` to estimate densities.

Diagnostics

In that case, a `stripplot()` may be better suited.

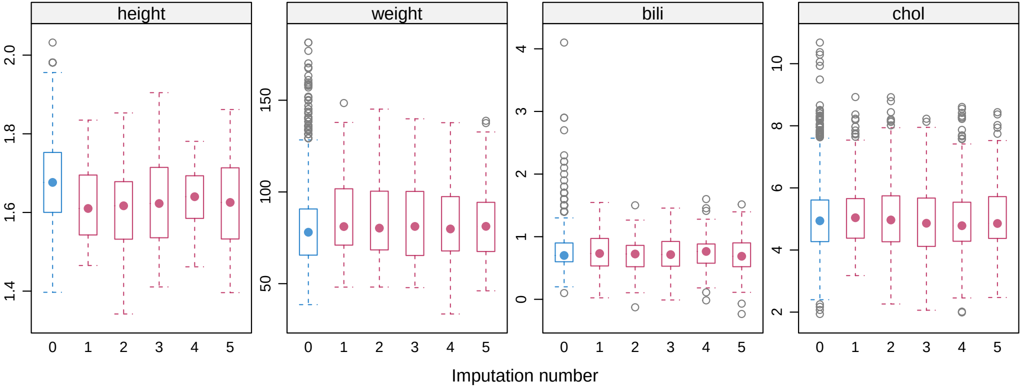
```
stripplot(imp4, height ~ race|gender,
          pch = c(1, 20), layout = c(1, 2),
          scales = list(x = list(rot = 45)))
```



Diagnostics

Alternatively, observed and imputed data can be represented by box-and-whisker plots:

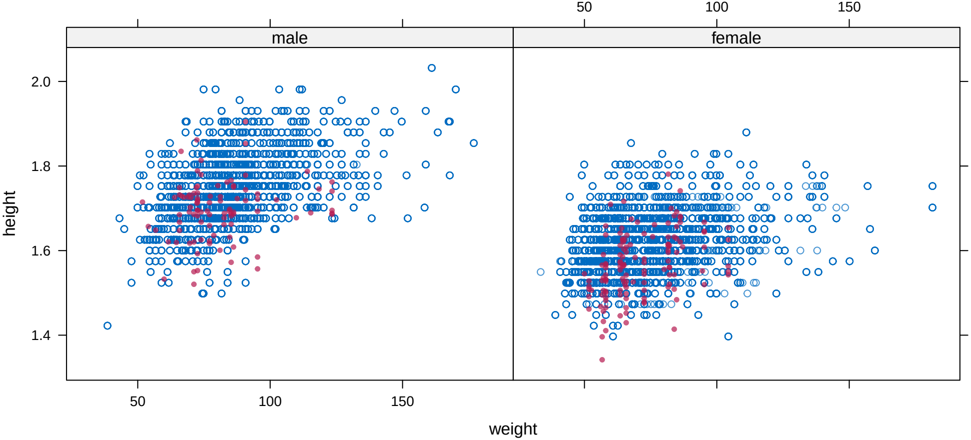
```
bwplot(imp4, height + weight + bili + chol ~.imp)
```



Diagnostics

The function `xyplot()` allows multivariate investigation of the imputed versus observed values.

```
xyplot(imp4, height ~ weight | gender, pch = c(1, 20))
```



Diagnostics

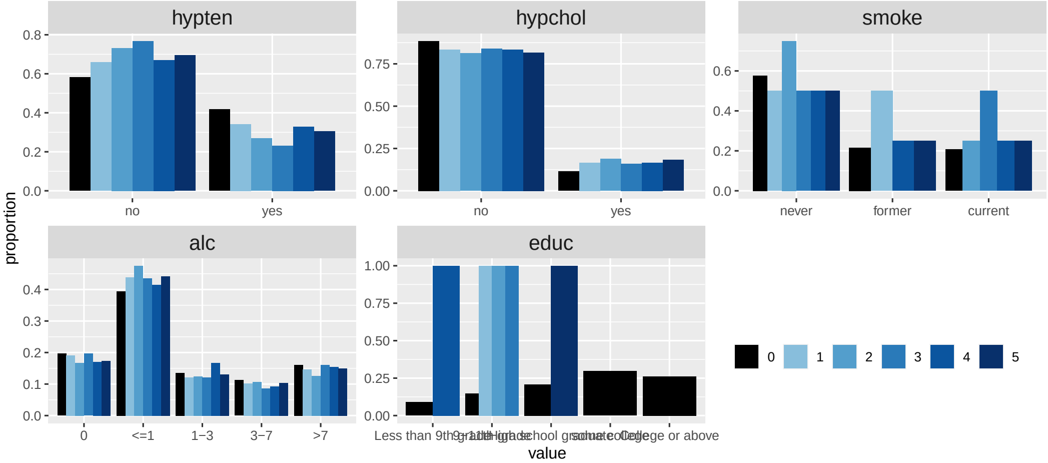
All of the above graphs displayed only continuous imputed variables.

For categorical variables we can compare the proportion of values in each category.

mice does not provide a function to do this, but we can write one ourselves, as for instance the function `propplot()`, for which the syntax can be found here: https://gist.github.com/NErler/0d00375da460dd33839b98faeee2fdab

Diagnostics

```r
propplot(imp4)
```



Diagnostics

`smoke` and `educ` have **very few missing values** (4 and 1)
➡ no need to worry about differences

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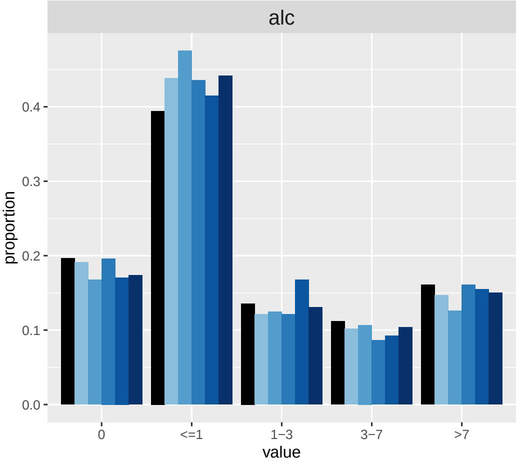
`alc`: missing values are imputed in the category "<=1" more often than we would expect from the observed data

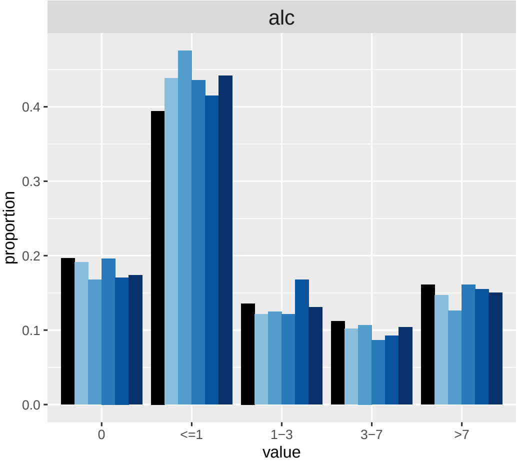


Diagnostics

`smoke` and `educ` have **very few missing values** (4 and 1)
➡ no need to worry about differences

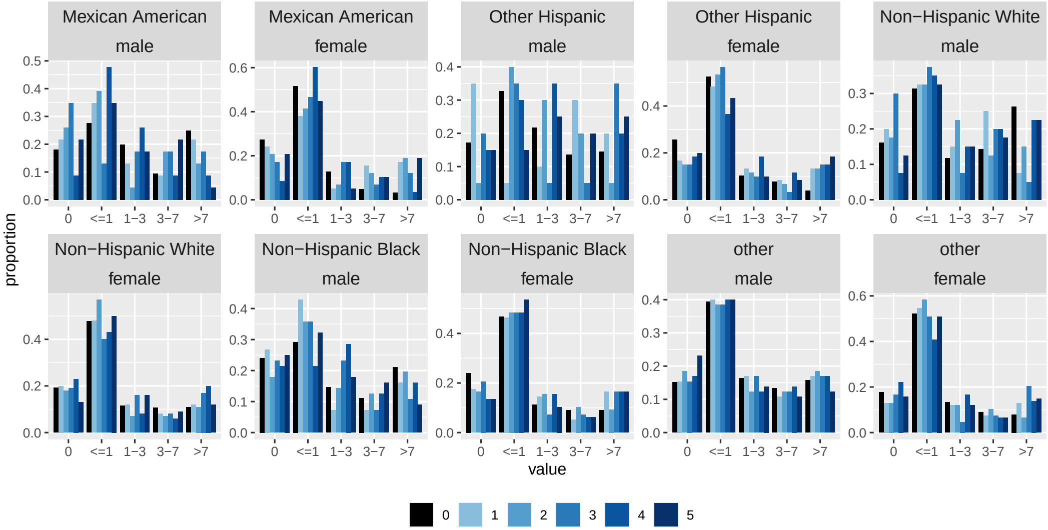
`alc`: missing values are imputed in the category “<=1” more often than we would expect from the observed data

If we expect that `gender` and `race` might explain the differences for `alc`, we can include those factors into the plot.



Diagnostics

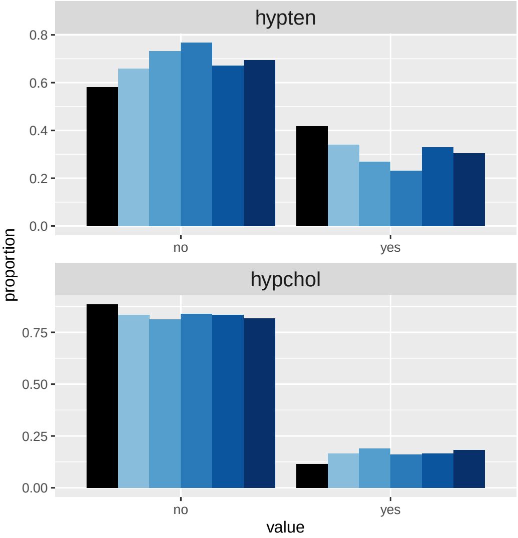
```r
propplot(imp4, formula = alc ~ race + gender)
```



Diagnostics

We also see that

- `hypten` is less frequent and
- `hypchol` a bit more frequent, in the imputed data compared to the observed.



Diagnostics

Since hypertension is more common in older individuals, we may want to investigate if age can explain the differences in imputed values of hypten.

```
round(sapply(split(NHANES[, "age"], addNA(NHANES$hypten)), summary), 1)
```

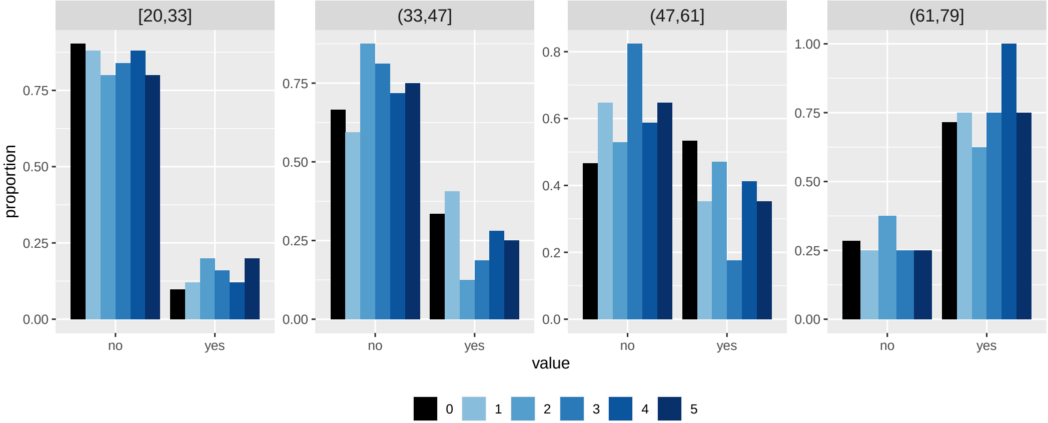
```
##           no  yes <NA>
## Min.    20.0 20.0 20.0
## 1st Qu. 28.0 47.0 30.0
## Median  38.0 59.0 38.5
## Mean    40.7 56.9 41.5
## 3rd Qu. 51.0 68.0 50.8
## Max.    79.0 79.0 78.0
```

The distribution of age in participants with missing hypten is very similar to the distribution of age in participants without hypten.

Diagnostics

Plotting the proportions of observed and imputed `hypten` separately per quartile of `age`:

```
propplot(imp4, formula = hypten ~ cut(age, quantile(age), include.lowest = T))
```


[20,33]
(33,47]
(47,61]
(61,79]
proportion
no
yes
value