

"How to" in **R**

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This document present ways to perform basic operations in **R**:

- importing data
- data management
- graphical displaying
- modeling
- loops and parallel computing
- generating data through simulation

Contents

1	Packages	5
2	Import/export data	6
2.1	Set the working directory	6
2.2	See which files are present in the current directory	7
2.3	Check that the file we want to import exists:	8
2.4	Display a file before importing it	9
2.5	Import a data from a file (.txt, .csv)	10
2.6	Import data from a specific format (e.g. excel files or outputs from SPSS/SAS)	11
2.7	Import data from a Github repository	12
2.8	Export data	13
2.9	Export table	14
2.10	Export graphs	15
3	Data management	16
3.1	Categorize age into groups	16
3.2	Convert list to array	17
3.3	Apply function for each element of a list	18
4	Data management using the <i>data.table</i> package	19
4.1	Introduction	19
4.2	Display a dataset	21
4.3	Extract row(s), i.e. all the variables relative to one or several observations	22
4.3.1	Extract row(s) using row numbers	22
4.3.2	Extract row(s) according to conditions	22
4.4	Extract column(s), i.e. all the observations relative to one or several variables	24
4.4.1	Extract column(s) using column numbers	24
4.4.2	Extract column(s) using column names	25
4.5	Work with categorical variables	26
4.5.1	Convert a numeric/character into a factor	26
4.5.2	Divide a continuous variable into categories	26
4.5.3	Redefine the levels of a factor variable	27
4.6	Extract simple features of a dataset	28
4.6.1	Number of rows and columns	28
4.6.2	Name of the columns	28
4.6.3	Type of the columns	28
4.6.4	Summary statistics by column	28
4.6.5	Number of missing values	29
4.6.6	Mean value of a column	29
4.6.7	Correlation between values of several columns	30
4.7	Performing operations on a group of rows	31
4.7.1	Computing the number of observations per subgroup	31
4.7.2	Computing the mean by subgroup	31
4.7.3	Computing the correlation matrix by subgroup	32

4.8	Sort a dataset according to one or several variables	34
4.9	Change the names of the column in a dataset	36
4.10	Converting a dataset from the wide format to the long format	37
4.10.1	Univariate melt	37
4.10.2	Multivariate melt	39
4.11	Converting a dataset from the long format to the wide format	40
4.11.1	Univariate	40
4.11.2	Multivariate	41
5	Graphical display	42
5.1	Descriptive plots	42
5.1.1	Spaguetti plot	42
5.1.2	Display the mean over time	46
5.1.3	Boxplot + points (non-overlapping)	47
5.2	Diagnostic plots	48
5.2.1	Histogram of the residuals	48
5.2.2	Forest plot	49
5.3	Customize graphic	50
5.3.1	Greek letter in facet	50
5.3.2	Modify the legend of a discrete scale (with greek letters)	50
5.3.3	Change the name of the legend	52
5.3.4	Increase the font size	52
5.3.5	Increase size of the legend labels	53
5.3.6	Put the legend at the bottom	53
5.3.7	Number of lines in the legend	55
5.3.8	Default ggplot color palette	55
5.3.9	Color blind palette	55
5.3.10	Rotate x-axis labels	55
5.3.11	Change tick mark labels	56
5.3.12	Combine ggplots	57
5.3.13	Symbols in facet names	58
5.4	Path diagram	59
5.5	Lexis diagram	60
6	Modeling	62
6.1	Test proportions	62
6.2	Compare proportions between groups	63
6.3	Estimate Mann Whitney parameter	66
6.4	Permutation t-test: 2 group comparison	67
6.5	Permutation t-test: multiple group comparison	68
6.6	Testing median	69
6.7	Testing linear hypotheses	71
6.7.1	Separate Wald tests of linear hypotheses	71
6.7.2	Confidence intervals associated with linear hypotheses	73
6.7.3	Joint test of linear hypotheses	73
6.8	Testing linearity assumptions in a linear model	75

6.9	Compute and display partial residuals in a linear model	76
6.10	Equivalence Poisson and Cox model	77
6.11	Displaying incidence rates with confidence intervals	80
6.12	Twin study	83
6.12.1	Data	83
6.12.2	REML solution	83
6.12.3	ML solution	86
7	Loops and parallel computations	88
7.1	Apply with progress bar	88
7.2	Parallel computation	89
7.2.1	Detect the number of cores	89
7.2.2	Start a cluster	89
7.2.3	Get the name of each core	89
7.2.4	Export element to cluster	89
7.2.5	Show progress bar (in console)	90
7.2.6	Show progress bar (external)	90
7.2.7	Stop a cluster	90
7.2.8	Parallel computation in C++	90
8	lava package	92
8.1	Generate repeated measurements	92
8.2	Generate data with heteroschadasticity	93
8.3	Generate survival time under non proportional hazard (non-PH)	94
8.4	Generate survival time with delayed treatment effect	96
8.5	Tune optimization parameters	98
8.6	Output correlation between two endogenous variables	99
8.7	Output correlation between two latent variables	101
8.8	Handling left, right, and interval censored data	103
8.9	LVM as a weighted mean	104
8.10	Standardized coefficients	106
9	Miscellaneous	108
9.1	Profile code R	108
9.2	Profile code C	109
9.3	Debug	110
9.4	Find all function names from a package	111
9.5	Install development version of R	112
9.6	Install suggested packages	113
9.7	R version	114
9.8	Install a package from a zip file (windows)	115
9.9	Install and load two version of the same package	116
9.10	CRAN check rocker	117

1 Packages

The following packages are necessary to run the code suggested in the document:

```
## importing data and data management
library(data.table)

## graphical display
library(ggplot2)
library(ggthemes)
library(abind) # convert list to array

## modeling
library(car)

library(prodlim) # survival analysis
library(survival) # survival analysis

## statistical inference
library(multcomp) # adjust for multiple comparisons
library(exactci) ## ci / p-values for proportions
library(exact2x2) ## compare proportions between groups
library(asht) ## test on the quantile
library(BuyseTest) ## wilcoxon-test with estimated effect size
library(perm) ## permutation tests
library(quantreg) ## quantile regression
library(butils) ## partial residuals (butils::install_github("bozenne/butils"))

## diagnostics
library(gof) ## devtools::install_github("kkholst/gof")

## loops and parallel computing
library(pbapply)
library(doSNOW)
library(parallel)

## simulation
library(lava)
```

2 Import/export data

2.1 Set the working directory

The working directory is where **R** will, by default, look for files to import and export data or pictures. The current working directory can be accessed using:

```
getwd()
```

```
[1] "c:/Users/hpl802/AppData/Roaming/R"
```

It can be changed using the function `setwd()`:

```
path <- "c:/Users/hpl802/Documents/GitHub/bozenne.github.io/doc/howTo-R/"  
setwd(path)
```

We can check that the working directory has indeed changed calling again `getwd()`:

```
getwd()
```

```
[1] "c:/Users/hpl802/Documents/GitHub/bozenne.github.io/doc/howTo-R"
```

2.2 See which files are present in the current directory

List all files in the current directory:

```
list.files()
```

```
[1] "#howTo-R.org#"      "figures"      "howTo-R.aux"  "howTo-R.log"
[5] "howTo-R.org"        "howTo-R.org_archive" "howTo-R.pdf"  "howTo-R.tex"
[9] "howTo-R.toc"        "mydata.csv"    "mydata.txt"   "myplot.png"
[13] "Table1.docx"
```

There are many files. To list files in the current directory with a given extension, e.g. `.txt` use:

```
list.files(pattern = ".txt")
```

```
[1] "mydata.txt"
```

There is only one file with a `.txt` extension, it is called `mydata.txt`.

2.3 Check that the file we want to import exists:

Test whether the file exists:

```
file.exists("./mydata.txt")
```

```
[1] TRUE
```


2.4 Display a file before importing it

Display the first three lines of the file we want to import

```
readLines("./mydata.txt")[1:3]
```

```
[1] "Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3"  
[2] "1 40 Male Yes 50 57 56 50.67 55.88 61.69"  
[3] "2 38 Female No 52 57 63 50.26 55.73 60.37"
```

```
readLines("./mydata.csv")[1:3]
```

```
[1] "Id;Age;Gender;Treatment;weight_t1;weight_t2;weight_t3;size_t1;size_t2;size_t3"  
[2] "1;40;Male;Yes;50;57;56;50,67;55,88;61,69"  
[3] "2;38;Female;No;52;57;63;50,26;55,73;60,37"
```

2.5 Import a data from a file (.txt, .csv)

Import a file and store the dataset into a `data.frame` object:

```
dfW.data <- read.table("./mydata.txt", header = TRUE, na.strings = ".")
```

Import a file and store the dataset into a `data.table` object:

```
dtW.data <- fread("./mydata.txt", header = TRUE, na.strings = ".")
```

In both cases, the argument `na.strings` specifies which character(s) in the dataset stands for missing values. The argument `header=TRUE` indicates that the first line of the dataset contains the name of the columns of the dataset (and not the data of an observation). See `?read.table` or `?fread` for further explanations about the arguments of these functions.

Note: `"./"` stands for current directory, e.g. `"./mydata.txt"` abbreviated in `"mydata.txt"`
 `"../"` stands for parent directory, e.g. `"../mydata.txt"`
 `"/"` stands for root directory, e.g. `"/mydata.txt"`

2.6 Import data from a specific format (e.g. excel files or outputs from SPSS/SAS)

There are many packages that can be used to read excel files, e.g.:

- **readxl** package (no dependency): function `read_excel`, `read_xls`, or `read_xlsx`.
- **xlsx** package: function `read.xlsx`.
- **gdata** package: function `read.xls`.
- **XLConnect** package: function `readWorksheet`.

The **foreign** package enable to read a variety for files, e.g.:

- `read.spss`: read an spss data file.
- `read.ssd`: obtain a data frame from a sas permanent dataset, via `read.xport`.

To load `.rds` files use `readRDS` and to load `.rdata` files use `load`.

2.7 Import data from a Github repository

```
urlfile="https://raw.githubusercontent.com/bozenne/repeated/master/data/calciumL.rda"
load(url(urlfile))
head(calciumL)
```

```
  girl grp visit bmd time.obs time.num time.fac
1  101  C    1 815      0        0 0 years
2  102  P    1 813      0        0 0 years
3  103  P    1 812      0        0 0 years
4  104  C    1 804      0        0 0 years
5  105  C    1 904      0        0 0 years
6  106  P    1 831      0        0 0 years
```

2.8 Export data

To export a `data.frame` to a file one can use:

- `write.csv` to export a `.csv` file
- `write.table` to export a `.txt` file
- `readxl::read_excel` to export a `.xlsx` file
- `data.table::fwrite`

```
fwrite(dtW.data, file = "./mydata.csv", sep = ";", dec = ",")  
fwrite(dtW.data, file = "./mydata.txt", sep = " ", dec = ".")
```

To export a single R object (can be anything) use `saveRDS`. To export several R object use `save`. To export the current workspace use `save.image`.

2.9 Export table

```
library(Publish)
myTable1 <- univariateTable(Treatment ~ Age + Gender + weight_t1, data = dtW.data)
```

Export to word:

```
library(officer)
myTable1.doc <- body_add_table(x = read_docx(),
  value = summary(myTable1))
print(myTable1.doc, target = "./Table1.docx")
```

```
[1] "c:/Users/hpl802/Documents/GitHub/bozenne.github.io/doc/howTo-R/Table1.docx"
```

2.10 Export graphs

The functions `pdf`, `png`, `postscript`, `svg`, `tiff` enables a graph to export to `.pdf`, `.png`, `.eps`, `.svg`, or `.tiff` file:

```
png("myplot.png")
plot(1:10)
dev.off()
```

```
null device
      1
```

```
file.exists("myplot.png")
```

```
[1] TRUE
```

For exporting graph generated by **ggplot2**, use **ggsave**.

3 Data management

3.1 Categorize age into groups

```
vec <- dfW.data$weight_t3  
vec
```

```
[1] 56 63 62 60 64 65 66 63 59 64 59 58 63 64 61 64 67 54 57 65 63 60 60 57 66 65 60 53 57 58 58  
[32] 58 59 63 64 58 64 58 59 59 60 59 57 62 61 63 63 63 65 55 59 65 71 64 62 62 64 58 61 61 65 64  
[63] 66 60 58 60 63 57 58 68 59 60 54 61 60 63 61 60 62 61 59 59 65 62 66 58 64 66 62 65 59 63 57  
[94] 62 64 59 63 57 62 59 55 68
```

```
cut(vec, breaks = seq(0,100,5))
```

```
[1] (55,60] (60,65] (60,65] (55,60] (60,65] (60,65] (65,70] (60,65] (55,60] (60,65] (55,60]  
[12] (55,60] (60,65] (60,65] (60,65] (60,65] (65,70] (50,55] (55,60] (60,65] (60,65] (55,60]  
[23] (55,60] (55,60] (65,70] (60,65] (55,60] (50,55] (55,60] (55,60] (55,60] (55,60] (55,60]  
[34] (60,65] (60,65] (55,60] (60,65] (55,60] (55,60] (55,60] (55,60] (55,60] (55,60] (60,65]  
[45] (60,65] (60,65] (60,65] (60,65] (60,65] (50,55] (55,60] (60,65] (70,75] (60,65] (60,65]  
[56] (60,65] (60,65] (55,60] (60,65] (60,65] (60,65] (60,65] (65,70] (55,60] (55,60] (55,60]  
[67] (60,65] (55,60] (55,60] (65,70] (55,60] (55,60] (50,55] (60,65] (55,60] (60,65] (60,65]  
[78] (55,60] (60,65] (60,65] (55,60] (55,60] (60,65] (60,65] (65,70] (55,60] (60,65] (65,70]  
[89] (60,65] (60,65] (55,60] (60,65] (55,60] (60,65] (60,65] (55,60] (60,65] (55,60] (60,65]  
[100] (55,60] (50,55] (65,70]  
20 Levels: (0,5] (5,10] (10,15] (15,20] (20,25] (25,30] (30,35] (35,40] (40,45] (45,50] ... (95,100]
```


3.2 Convert list to array

```
l1 <- list(matrix(1,2,2),  
            matrix(3,2,2),  
            matrix(9,2,2))  
do.call(abind, c(l1, list(along = 3)))
```

, , 1

	[,1]	[,2]
[1,]	1	1
[2,]	1	1

, , 2

	[,1]	[,2]
[1,]	3	3
[2,]	3	3

, , 3

	[,1]	[,2]
[1,]	9	9
[2,]	9	9

3.3 Apply function for each element of a list

```
l1 <- list(matrix(1,2,2),  
           matrix(3,2,2),  
           matrix(9,2,2))  
apply(do.call(abind, c(l1, list(along = 3))), 1:2, median)
```

```
      [,1] [,2]  
[1,]    3    3  
[2,]    3    3
```

4 Data management using the *data.table* package

4.1 Introduction

In **R**, data are usually stored in `data.frame` object since compared to matrices, it enables to store in a same object different types of variables (e.g. numeric, categorical, ...). Data management can be performed using the core R function, e.g. using `for` loops or the `apply`, `tapply`, `lapply` functions. However this approach will most often requires many lines of code to get the expected transformation. A faster and safer approach is to functions/packages suited to the structure of longitudinal data.

We present here how to use the *data.table* package to perform the most common operations in data management. The main benefit of using this package are:

- a concise and consistant syntax for performing the most common operations in data management.
- fast and memory efficient implementation (i.e. able to deal with dataset with millions of lines).
- share common features with the SQL terminology.

A concise summary of the features can be found at: <https://s3.amazonaws.com/assets.datacamp.com/img/blog/data+table+cheat+sheet.pdf>

Additional documentation can be found:

- in the documentation of the function `data.table`: type `?data.table` in **R**.
- on the webpage of the package: <https://github.com/Rdatatable/data.table/wiki>.
- in the vignettes of the package: <https://cran.r-project.org/web/packages/data.table/vignettes/datatable-intro.html>.

Note: the **wide format** denote a format where each line corresponds to a different individuals. Repeated measurements of the same quantity (e.g. weight) for a given individual are stored in different columns (e.g. `weight_t1`, `weight_t2`).

```
head(dtW.data)
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3
1:	1	40	Male	Yes	50	57	56	50.67	55.88	61.69
2:	2	38	Female	No	52	57	63	50.26	55.73	60.37
3:	3	41	Male	No	47	54	62	46.61	50.89	56.52
4:	4	41	Female	Yes	48	55	60	45.95	53.10	59.82
5:	5	42	Female	Yes	52	56	64	52.86	58.41	63.79
6:	6	38	Male	Yes	52	59	65	49.37	57.91	64.45

The **long** format denote a format where the same individual may appear on different lines but a given quantity is only stored in one column. In case of repeated measurement, an additional column encodes at which repetition the measurement was obtained (e.g. **time**):

```
head(dtL.data)
```

	Id	Gender	Treatment	Age	time	weight	size
1:	1	Male	Yes	40	1	50	50.67
2:	2	Female	No	38	1	52	50.26
3:	3	Male	No	41	1	47	46.61
4:	4	Female	Yes	41	1	48	45.95
5:	5	Female	Yes	42	1	52	52.86
6:	6	Male	Yes	38	1	52	49.37

4.2 Display a dataset

Using the print method:

```
print(dtW.data) # equivalent to just dtW.data
```

```
      Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:    1  40   Male      Yes        50        57        56  50.67  55.88  61.69
2:    2  38 Female      No         52        57        63  50.26  55.73  60.37
3:    3  41   Male      No         47        54        62  46.61  50.89  56.52
4:    4  41 Female      Yes         48        55        60  45.95  53.10  59.82
5:    5  42 Female      Yes         52        56        64  52.86  58.41  63.79
---
98:  98  39   Male      No         53        59        57  49.51  53.80  61.13
99:  99  42 Female      Yes         51        57        62  47.60  56.55  59.47
100: 100  40 Female      No         53        55        59  50.06  54.90  61.89
101: 101  38 Female      No         48        58        55  49.51  54.01  62.32
102: 102  39 Female      No         52        58        68  47.35  56.08  59.49
```

To print more lines use the argument `topn`:

```
print(dtW.data, topn = 6)
```

```
      Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:    1  40   Male      Yes        50        57        56  50.67  55.88  61.69
2:    2  38 Female      No         52        57        63  50.26  55.73  60.37
3:    3  41   Male      No         47        54        62  46.61  50.89  56.52
4:    4  41 Female      Yes         48        55        60  45.95  53.10  59.82
5:    5  42 Female      Yes         52        56        64  52.86  58.41  63.79
6:    6  38   Male      Yes         52        59        65  49.37  57.91  64.45
---
97:  97  39   Male      No         50        60        63  51.72  57.86  61.06
98:  98  39   Male      No         53        59        57  49.51  53.80  61.13
99:  99  42 Female      Yes         51        57        62  47.60  56.55  59.47
100: 100  40 Female      No         53        55        59  50.06  54.90  61.89
101: 101  38 Female      No         48        58        55  49.51  54.01  62.32
102: 102  39 Female      No         52        58        68  47.35  56.08  59.49
```

4.3 Extract row(s), i.e. all the variables relative to one or several observations

4.3.1 Extract row(s) using row numbers

Extract the third line:

```
dtW.data[3]
```

```
   Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:  3  41  Male        No         47         54         62  46.61  50.89  56.52
```

Extract line one to four:

```
dtW.data[1:4]
```

```
   Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:  1  40  Male        Yes         50         57         56  50.67  55.88  61.69
2:  2  38 Female        No         52         57         63  50.26  55.73  60.37
3:  3  41  Male        No         47         54         62  46.61  50.89  56.52
4:  4  41 Female        Yes         48         55         60  45.95  53.10  59.82
```

Extract line one, three, and five:

```
dtW.data[c(1,3,5)]
```

```
   Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:  1  40  Male        Yes         50         57         56  50.67  55.88  61.69
2:  3  41  Male        No         47         54         62  46.61  50.89  56.52
3:  5  42 Female        Yes         52         56         64  52.86  58.41  63.79
```

4.3.2 Extract row(s) according to conditions

Extract lines corresponding to the observations with Id equals to 1:

```
dtW.data[Id == 1]
```

```
   Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3
1:  1  40  Male        Yes         50         57         56  50.67  55.88  61.69
```

Extract lines corresponding to the males:

```
newdata <- dtW.data[Gender == "Male"]
head(newdata)
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3
1:	1	40	Male	Yes	50	57	56	50.67	55.88	61.69
2:	3	41	Male	No	47	54	62	46.61	50.89	56.52
3:	6	38	Male	Yes	52	59	65	49.37	57.91	64.45
4:	9	42	Male	Yes	46	52	59	49.53	52.84	60.54
5:	11	42	Male	No	55	58	59	50.03	55.09	60.94
6:	12	41	Male	Yes	50	52	58	48.66	52.73	55.86

Extract lines corresponding to the males whose age is inferior or equal to 38:

```
dtW.data[Gender == "Male" & Age <= 38]
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3
1:	6	38	Male	Yes	52	59	65	49.37	57.91	64.45
2:	41	37	Male	No	53	55	60	47.59	53.75	57.00
3:	76	38	Male	No	53	57	63	48.10	54.82	55.29
4:	91	38	Male	No	51	55	59	52.05	57.01	59.53

Extract lines corresponding to observations where Age is inferior or equal to 37, or greater or equal to 43 :

```
dtW.data[Age <= 37 | Age >= 43]
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3
1:	10	43	Female	Yes	52	57	64	53.22	57.25	62.94
2:	41	37	Male	No	53	55	60	47.59	53.75	57.00
3:	45	43	Female	Yes	48	51	61	49.88	54.41	56.18
4:	73	43	Male	Yes	46	53	54	48.44	52.74	60.93

4.4 Extract column(s), i.e. all the observations relative to one or several variables

4.4.1 Extract column(s) using column numbers

Extract the third column:

```
dtW.data[, 3, with = FALSE]
```

```
      Gender
1:   Male
2: Female
3:   Male
4: Female
5: Female
---
98:   Male
99: Female
100: Female
101: Female
102: Female
```

Alternatively:

```
dtW.data[[3]]
```

```
[1] "Male"  "Female" "Male"  "Female" "Female" "Male"  "Female" "Female" "Male"  "Female"
[11] "Male"  "Male"  "Female" "Female" "Female" "Female" "Female" "Female" "Male"  "Female"
[21] "Male"  "Male"  "Female" "Male"  "Female" "Male"  "Male"  "Male"  "Female" "Female"
[31] "Male"  "Male"  "Male"  "Male"  "Female" "Female" "Female" "Female" "Male"  "Male"
[41] "Male"  "Female" "Female" "Female" "Female" "Female" "Female" "Female" "Male"  "Male"
[51] "Female" "Male"  "Male"  "Male"  "Female" "Female" "Male"  "Male"  "Female" "Male"
[61] "Female" "Male"  "Male"  "Male"  "Female" "Male"  "Female" "Male"  "Male"  "Male"
[71] "Female" "Female" "Male"  "Female" "Female" "Male"  "Female" "Female" "Female" "Female"
[81] "Male"  "Male"  "Female" "Female" "Male"  "Female" "Female" "Female" "Female" "Female"
[91] "Male"  "Male"  "Male"  "Male"  "Male"  "Male"  "Male"  "Male"  "Female" "Female"
[101] "Female" "Female"
```

Extract column one, three, and five:

```
dtW.data[, c(1,3,5), with = FALSE]
```

```
      Id Gender weight_t1
1:    1   Male        50
2:    2 Female        52
3:    3   Male        47
4:    4 Female        48
5:    5 Female        52
---
98:  98   Male        53
```



```

99: 99 Female      51
100: 100 Female    53
101: 101 Female    48
102: 102 Female    52

```

4.4.2 Extract column(s) using column names

Extract one column, e.g. Id:

```
dtW.data[, Id] # similar to dtW.data[, "Id", with=FALSE]
```

```

[1] 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
[24] 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46
[47] 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69
[70] 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92
[93] 93 94 95 96 97 98 99 100 101 102

```

Extract several columns, e.g. Id and Age:

```

dtW.data[, .(Id, Age)]
# similar to dtW.data[, c("Id", "Age"), with = FALSE]
# similar to dtW.data[, .SD, .SDcols = c("Id", "Age")]

```

```

      Id Age
1:    1  40
2:    2  38
3:    3  41
4:    4  41
5:    5  42
---
98:  98  39
99:  99  42
100: 100  40
101: 101  38
102: 102  39

```

4.5 Work with categorical variables

4.5.1 Convert a numeric/character into a factor

```
class(dtW.data[,Gender])
```

```
[1] "character"
```

```
dtW.data[, Gender := as.factor(Gender)]  
class(dtW.data[,Gender])
```

```
[1] "factor"
```

```
class(dtW.data[,Id])
```

```
[1] "integer"
```

```
dtW.data[, Id := as.factor(Id)]  
class(dtW.data[,Id])
```

```
[1] "factor"
```

4.5.2 Divide a continuous variable into categories

```
dtW.data[, AgeCategory := cut(Age, breaks = c(0,38,40,42,100))]  
dtW.data[,.(Age, AgeCategory)]
```

```
      Age AgeCategory  
1:  40      (38,40]  
2:  38       (0,38]  
3:  41      (40,42]  
4:  41      (40,42]  
5:  42      (40,42]  
---  
98:  39      (38,40]  
99:  42      (40,42]  
100: 40      (38,40]  
101: 38       (0,38]  
102: 39      (38,40]
```

Alternatively:

```
dtW.data[, AgeCategory0 := findInterval(Age, vec = c(0,38,40,42,100))]  
dtW.data[,.(Age, AgeCategory0)]
```

	Age	AgeCategory0
1:	40	3
2:	38	2
3:	41	3
4:	41	3
5:	42	4

98:	39	2
99:	42	4
100:	40	3
101:	38	2
102:	39	2

The arguments `rightmost` and `left.open` can be used to decide what to do with the values equaling the breaks (i.e. one of the value of the argument `vec`). But it is often easier to modify `vec` such that no value equals the breaks, e.g. using `c(0,38,40,42,100)-1e12`.

4.5.3 Redefine the levels of a factor variable

```
dtW.data[,AgeCategory0 := factor(AgeCategory0,
  levels = 1:4,
  labels = c("[0-37)", "[38-39)", "[40-41)", "[42-100)"))]
dtW.data[,.(Age, AgeCategory0, AgeCategory)]
```

	Age	AgeCategory0	AgeCategory
1:	40	[40-41)	(38,40]
2:	38	[38-39)	(0,38]
3:	41	[40-41)	(40,42]
4:	41	[40-41)	(40,42]
5:	42	[42-100)	(40,42]

98:	39	[38-39)	(38,40]
99:	42	[42-100)	(40,42]
100:	40	[40-41)	(38,40]
101:	38	[38-39)	(0,38]
102:	39	[38-39)	(38,40]

4.6 Extract simple features of a dataset

4.6.1 Number of rows and columns

```
dim(dtW.data)
```

```
[1] 102 12
```

The dataset has 102 rows and 7 columns.

4.6.2 Name of the columns

```
names(dtW.data)
```

```
[1] "Id"          "Age"          "Gender"        "Treatment"     "weight_t1"     "weight_t2"
[7] "weight_t3"   "size_t1"      "size_t2"      "size_t3"      "AgeCategory"   "AgeCategory0"
```

4.6.3 Type of the columns

```
str(dtW.data)
```

```
Classes 'data.table' and 'data.frame':      102 obs. of  12 variables:
 $ Id          : Factor w/ 102 levels "1","2","3","4",...: 1 2 3 4 5 6 7 8 9 10 ...
 $ Age         : num  40 38 41 41 42 38 42 40 42 43 ...
 $ Gender      : Factor w/ 2 levels "Female","Male": 2 1 2 1 1 2 1 1 2 1 ...
 $ Treatment   : chr   "Yes" "No" "No" "Yes" ...
 $ weight_t1   : num   50 52 47 48 52 52 52 51 46 52 ...
 $ weight_t2   : int    57 57 54 55 56 59 63 52 52 57 ...
 $ weight_t3   : int    56 63 62 60 64 65 66 63 59 64 ...
 $ size_t1     : num   50.7 50.3 46.6 46 52.9 ...
 $ size_t2     : num   55.9 55.7 50.9 53.1 58.4 ...
 $ size_t3     : num   61.7 60.4 56.5 59.8 63.8 ...
 $ AgeCategory : Factor w/ 4 levels "(0,38)","(38,40)",...: 2 1 3 3 3 1 3 2 3 4 ...
 $ AgeCategory0: Factor w/ 4 levels "[0-37)","[38-39)",...: 3 2 3 3 4 2 4 3 4 4 ...
 - attr(*, ".internal.selfref")=<externalptr>
 - attr(*, "index")= int
```

The column **Gender** contains a factor variable with two levels "Yes" and "No".

The column **Id** contains integers while the columns **weight_t3** contains numeric numbers.

4.6.4 Summary statistics by column

```
summary(dtW.data)
```


Then compute the mean:

```
mean(vec.tempo)
```

```
[1] 40.26471
```

Alternatively:

```
dtW.data[,mean(Age)]
```

```
[1] 40.26471
```

4.6.7 Correlation between values of several columns

First extract the columns:

```
dt.tempo <- dtW.data[,.(weight_t1,weight_t2,weight_t3)]
```

Then compute the correlation:

```
cor(dt.tempo)
```

```
      weight_t1 weight_t2 weight_t3  
weight_t1 1.0000000 0.1882809 0.3179175  
weight_t2 0.1882809 1.0000000 0.2374259  
weight_t3 0.3179175 0.2374259 1.0000000
```

Alternatively:

```
dtW.data[,cor(cbind(weight_t1,weight_t2,weight_t3))]
```

```
      weight_t1 weight_t2 weight_t3  
weight_t1 1.0000000 0.1882809 0.3179175  
weight_t2 0.1882809 1.0000000 0.2374259  
weight_t3 0.3179175 0.2374259 1.0000000
```

4.7 Performing operations on a group of rows

4.7.1 Computing the number of observations per subgroup

Compute the number of observation per gender:

```
dtW.data[, .N, by = "Gender"]
```

```
Gender N
1: Male 48
2: Female 54
```

Alternatively:

```
dtW.data[, NROW(.SD), by = "Gender"]
```

```
Gender V1
1: Male 48
2: Female 54
```

4.7.2 Computing the mean by subgroup

Compute the mean weight at time 1 by gender:

```
dtW.data[, mean(weight_t1), by = "Gender"]
```

```
Gender V1
1: Male 50.45833
2: Female 51.24074
```

Alternative display:

```
dtW.data[, .(mean = mean(weight_t1)), by = "Gender"]
```

```
Gender mean
1: Male 50.45833
2: Female 51.24074
```

Compute the mean weight at time 1 to 3 by gender:

```
dtW.data[, .(mean_t1 = mean(weight_t1),
  mean_t2 = mean(weight_t2),
  mean_t3 = mean(weight_t3)),
  by = "Gender"]
```

```
Gender mean_t1 mean_t2 mean_t3
1: Male 50.45833 55.81250 60.64583
2: Female 51.24074 56.72222 61.68519
```

Compute the mean weight at time 1 to 3 by gender and treatment group:

```
dtW.data[, .(mean_t1 = mean(weight_t1),
             mean_t2 = mean(weight_t2),
             mean_t3 = mean(weight_t3)),
           by = c("Gender", "Treatment")]
```

```
   Gender Treatment mean_t1 mean_t2 mean_t3
1:   Male      Yes 50.42857 55.09524 60.23810
2: Female      No 51.65517 56.93103 61.75862
3:   Male      No 50.48148 56.37037 60.96296
4: Female      Yes 50.76000 56.48000 61.60000
```

4.7.3 Computing the correlation matrix by subgroup

We create a matrix containing the variables of interest, compute the correlation matrix and print it.

```
null.result <- dtW.data[, print(cor(cbind(weight_t1, weight_t2, weight_t3))),
                          by = "Gender"]
```

```
           weight_t1 weight_t2 weight_t3
weight_t1 1.0000000 0.2867753 0.2886667
weight_t2 0.2867753 1.0000000 0.2740567
weight_t3 0.2886667 0.2740567 1.0000000
           weight_t1 weight_t2 weight_t3
weight_t1 1.00000000 0.03214955 0.3148578
weight_t2 0.03214955 1.00000000 0.1551156
weight_t3 0.31485784 0.15511561 1.0000000
```

If we want to store the correlation matrix we need to wrap it into `.()` to keep the matrix format:

```
result <- dtW.data[, .(cor = .(cor(cbind(weight_t1, weight_t2, weight_t3)))),
                    by = "Gender"]
result[, cor]
```

```
[[1]]
           weight_t1 weight_t2 weight_t3
weight_t1 1.0000000 0.2867753 0.2886667
weight_t2 0.2867753 1.0000000 0.2740567
weight_t3 0.2886667 0.2740567 1.0000000

[[2]]
           weight_t1 weight_t2 weight_t3
weight_t1 1.00000000 0.03214955 0.3148578
weight_t2 0.03214955 1.00000000 0.1551156
weight_t3 0.31485784 0.15511561 1.0000000
```

Alternatively:


```
null.result <- dtW.data[, print(cor(.SD)),  
  .SDcols = c("weight_t1", "weight_t2", "weight_t3"),  
  by = "Gender"]
```

```
      weight_t1 weight_t2 weight_t3  
weight_t1 1.0000000 0.2867753 0.2886667  
weight_t2 0.2867753 1.0000000 0.2740567  
weight_t3 0.2886667 0.2740567 1.0000000  
      weight_t1 weight_t2 weight_t3  
weight_t1 1.00000000 0.03214955 0.3148578  
weight_t2 0.03214955 1.00000000 0.1551156  
weight_t3 0.31485784 0.15511561 1.0000000
```

4.8 Sort a dataset according to one or several variables

Sort the dataset according to Age:

```
setkeyv(dtW.data, c("Age"))
dtW.data
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3	AgeCategory
1:	41	37	Male	No	53	55	60	47.59	53.75	57.00	(0,38]
2:	2	38	Female	No	52	57	63	50.26	55.73	60.37	(0,38]
3:	6	38	Male	Yes	52	59	65	49.37	57.91	64.45	(0,38]
4:	46	38	Female	No	53	57	63	49.27	61.45	66.59	(0,38]
5:	48	38	Female	No	52	57	63	54.27	57.71	65.63	(0,38]

98:	95	42	Male	Yes	51	55	64	51.05	56.48	60.30	(40,42]
99:	99	42	Female	Yes	51	57	62	47.60	56.55	59.47	(40,42]
100:	10	43	Female	Yes	52	57	64	53.22	57.25	62.94	(42,100]
101:	45	43	Female	Yes	48	51	61	49.88	54.41	56.18	(42,100]
102:	73	43	Male	Yes	46	53	54	48.44	52.74	60.93	(42,100]
AgeCategory0											
1:	[0-37)										
2:	[38-39)										
3:	[38-39)										
4:	[38-39)										
5:	[38-39)										

98:	[42-100)										
99:	[42-100)										
100:	[42-100)										
101:	[42-100)										
102:	[42-100)										

Sort the dataset according to Age and then weight_t1:

```
setkeyv(dtW.data, cols = c("Age", "weight_t1"))
dtW.data
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3	AgeCategory
1:	41	37	Male	No	53	55	60	47.59	53.75	57.00	(0,38]
2:	101	38	Female	No	48	58	55	49.51	54.01	62.32	(0,38]
3:	59	38	Female	Yes	49	60	61	51.08	53.77	60.75	(0,38]
4:	91	38	Male	No	51	55	59	52.05	57.01	59.53	(0,38]
5:	2	38	Female	No	52	57	63	50.26	55.73	60.37	(0,38]

98:	11	42	Male	No	55	58	59	50.03	55.09	60.94	(40,42]
99:	54	42	Male	Yes	57	60	64	58.75	57.57	63.98	(40,42]
100:	73	43	Male	Yes	46	53	54	48.44	52.74	60.93	(42,100]
101:	45	43	Female	Yes	48	51	61	49.88	54.41	56.18	(42,100]
102:	10	43	Female	Yes	52	57	64	53.22	57.25	62.94	(42,100]
AgeCategory0											

1:	[0-37)
2:	[38-39)
3:	[38-39)
4:	[38-39)
5:	[38-39)

98:	[42-100)
99:	[42-100)
100:	[42-100)
101:	[42-100)
102:	[42-100)

4.9 Change the names of the column in a dataset

Use a small dataset

```
dt.simple <- dtW.data[,.(Age,Gender,Id,Treatment)]
head(dt.simple)
```

	Age	Gender	Id	Treatment
1:	37	Male	41	No
2:	38	Female	101	No
3:	38	Female	59	Yes
4:	38	Male	91	No
5:	38	Female	2	No
6:	38	Male	6	Yes

Change all names:

```
setnames(dt.simple, c("AgeXX","GenderYY","IdZZ","Treat"))
head(dt.simple)
```

	AgeXX	GenderYY	IdZZ	Treat
1:	37	Male	41	No
2:	38	Female	101	No
3:	38	Female	59	Yes
4:	38	Male	91	No
5:	38	Female	2	No
6:	38	Male	6	Yes

Change one or several names (less memory efficient):

```
names(dt.simple)[1:2] <- c("Age","Gender")
head(dt.simple)
```

	Age	Gender	IdZZ	Treat
1:	37	Male	41	No
2:	38	Female	101	No
3:	38	Female	59	Yes
4:	38	Male	91	No
5:	38	Female	2	No
6:	38	Male	6	Yes

4.10 Converting a dataset from the wide format to the long format

4.10.1 Univariate melt

Data in the wide format:

```
head(dtW.data)
```

```
      Id Age Gender Treatment weight_t1 weight_t2 weight_t3 size_t1 size_t2 size_t3 AgeCategory
1:   41  37  Male       No         53         55         60  47.59  53.75  57.00      (0,38]
2:  101  38 Female       No         48         58         55  49.51  54.01  62.32      (0,38]
3:   59  38 Female      Yes         49         60         61  51.08  53.77  60.75      (0,38]
4:   91  38  Male       No         51         55         59  52.05  57.01  59.53      (0,38]
5:    2  38 Female       No         52         57         63  50.26  55.73  60.37      (0,38]
6:    6  38  Male      Yes         52         59         65  49.37  57.91  64.45      (0,38]
      AgeCategory0
1:           [0-37)
2:           [38-39)
3:           [38-39)
4:           [38-39)
5:           [38-39)
6:           [38-39)
```

The conversion can be done naming explicitly the columns or using **patterns**:

```
dtL.data <- melt(dtW.data, id.vars = c("Id", "Gender", "Treatment", "Age"),
  measure=c("weight_t1", "weight_t2", "weight_t3"),
  variable.name = "time", value.name = "weight")

dtL.data.bis <- melt(dtW.data, id.vars = c("Id", "Gender", "Treatment", "Age"),
  measure=patterns("weight_t"),
  variable.name = "time", value.name = "weight")

identical(dtL.data, dtL.data.bis)
```

Warning message:

```
In melt.data.table(dtW.data, id.vars = c("Id", "Gender", "Treatment", "Age"),
  'measure.vars' [weight_t1, weight_t2, weight_t3] are not all of the same type. By order of hierarchy, the mol
Warning message:
In melt.data.table(dtW.data, id.vars = c("Id", "Gender", "Treatment", "Age"),
  'measure.vars' [weight_t1, weight_t2, weight_t3] are not all of the same type. By order of hierarchy, the mol
[1] TRUE
```

Arguments (see `?melt.data.table` for more details):

- **id.vars**: name of the column(s) that are kept constant over the repetitions
- **measure.vars**: name of the columns to be melted in a single one (i.e. repeated measurements).

Data in the long format:

```
head(dtL.data)
```

	Id	Gender	Treatment	Age	time	weight
1:	41	Male	No	37	weight_t1	53
2:	101	Female	No	38	weight_t1	48
3:	59	Female	Yes	38	weight_t1	49
4:	91	Male	No	38	weight_t1	51
5:	2	Female	No	38	weight_t1	52
6:	6	Male	Yes	38	weight_t1	52

Reorder the data by Id and time:

```
setkeyv(dtL.data, c("Id","time"))  
head(dtL.data)
```

	Id	Gender	Treatment	Age	time	weight
1:	1	Male	Yes	40	weight_t1	50
2:	1	Male	Yes	40	weight_t2	57
3:	1	Male	Yes	40	weight_t3	56
4:	2	Female	No	38	weight_t1	52
5:	2	Female	No	38	weight_t2	57
6:	2	Female	No	38	weight_t3	63

4.10.2 Multivariate melt

Use a list of vectors each containing a vector with the columns to be melted:

```
dtL.data <- melt(dtW.data, id.vars = c("Id","Gender","Treatment","Age"),
  measure=list(c("weight_t1","weight_t2","weight_t3"),
    c("size_t1","size_t2","size_t3")),
  variable.name = "time", value.name = c("weight","size"))

dtL.data.bis <- melt(dtW.data, id.vars = c("Id","Gender","Treatment","Age"),
  measure=patterns("weight_t","size_t"),
  variable.name = "time", value.name = c("weight","size"))

identical(dtL.data,dtL.data.bis)
```

```
[1] TRUE
```

```
dtL.data
```

```
      Id Gender Treatment Age time weight  size
1:   41  Male        No  37   1    53 47.59
2:  101 Female        No  38   1    48 49.51
3:   59 Female        Yes  38   1    49 51.08
4:   91  Male        No  38   1    51 52.05
5:    2 Female        No  38   1    52 50.26
---
302:  11  Male        No  42   3    59 60.94
303:  54  Male        Yes  42   3    64 63.98
304:  73  Male        Yes  43   3    54 60.93
305:  45 Female        Yes  43   3    61 56.18
306:  10 Female        Yes  43   3    64 62.94
```

4.11 Converting a dataset from the long format to the wide format

4.11.1 Univariate

Data in the long format:

```
head(dtL.data)
```

```
      Id Gender Treatment Age time weight  size
1:   41  Male        No  37   1    53 47.59
2:  101 Female        No  38   1    48 49.51
3:   59 Female       Yes  38   1    49 51.08
4:   91  Male        No  38   1    51 52.05
5:    2 Female        No  38   1    52 50.26
6:    6  Male       Yes  38   1    52 49.37
```

The conversion can be done using a formula:

- left side: variables that do not vary
- right side: variable indexing the repetition whose values will be used to name the new columns.

```
dtW.data <- dcast(dtL.data, value.var = c("weight"),
  formula = Id + Gender + Treatment + Age ~ time)
```

Data in the wide format:

```
setnames(dtW.data, old = c("1","2","3"), new = paste0("weight_t",1:3))
dtW.data
```

```
      Id Gender Treatment Age weight_t1 weight_t2 weight_t3
1:    1  Male       Yes  40         50         57         56
2:    2 Female       No  38         52         57         63
3:    3  Male       No  41         47         54         62
4:    4 Female      Yes  41         48         55         60
5:    5 Female      Yes  42         52         56         64
---
98:  98  Male       No  39         53         59         57
99:  99 Female      Yes  42         51         57         62
100: 100 Female       No  40         53         55         59
101: 101 Female       No  38         48         58         55
102: 102 Female       No  39         52         58         68
```


4.11.2 Multivariate

Same as before but with several elements in the argument `value.var`. Note that the repetition index (here `time`) must be the same for both variables:

```
dtW.data <- dcast(dtL.data, value.var = c("weight", "size"),  
  formula = Id + Gender + Treatment + Age ~ time)
```

Data in the wide format:

```
dtW.data
```

```
      Id Gender Treatment Age weight_1 weight_2 weight_3 size_1 size_2 size_3  
1:    1  Male      Yes  40      50      57      56  50.67  55.88  61.69  
2:    2 Female     No  38      52      57      63  50.26  55.73  60.37  
3:    3  Male     No  41      47      54      62  46.61  50.89  56.52  
4:    4 Female    Yes  41      48      55      60  45.95  53.10  59.82  
5:    5 Female    Yes  42      52      56      64  52.86  58.41  63.79  
---  
98:  98  Male     No  39      53      59      57  49.51  53.80  61.13  
99:  99 Female    Yes  42      51      57      62  47.60  56.55  59.47  
100: 100 Female    No  40      53      55      59  50.06  54.90  61.89  
101: 101 Female    No  38      48      58      55  49.51  54.01  62.32  
102: 102 Female    No  39      52      58      68  47.35  56.08  59.49
```

5 Graphical display

5.1 Descriptive plots

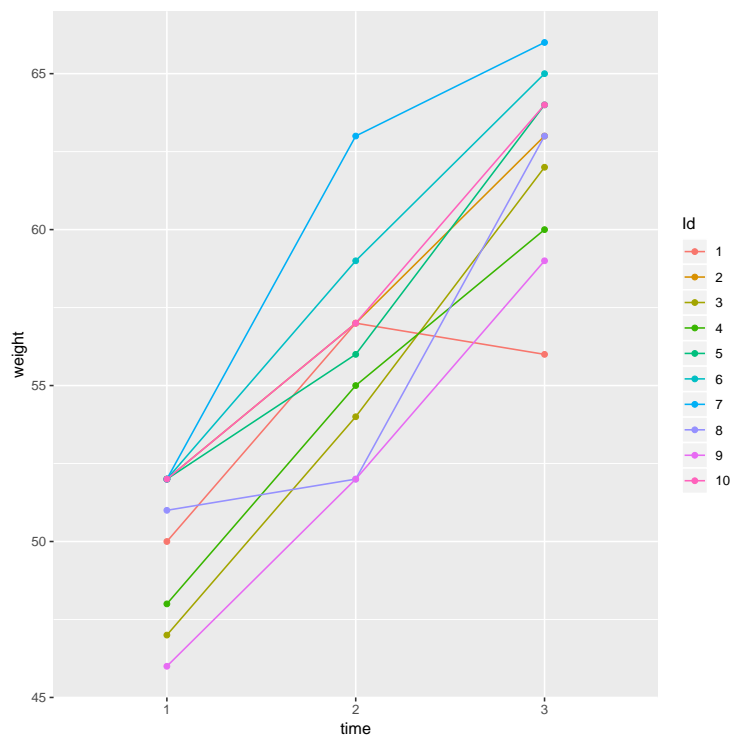
```
head(dtL.data)
```

	Id	Gender	Treatment	Age	time	weight	size
1:	1	Male	Yes	40	1	50	50.67
2:	2	Female	No	38	1	52	50.26
3:	3	Male	No	41	1	47	46.61
4:	4	Female	Yes	41	1	48	45.95
5:	5	Female	Yes	42	1	52	52.86
6:	6	Male	Yes	38	1	52	49.37

5.1.1 Spaguetti plot

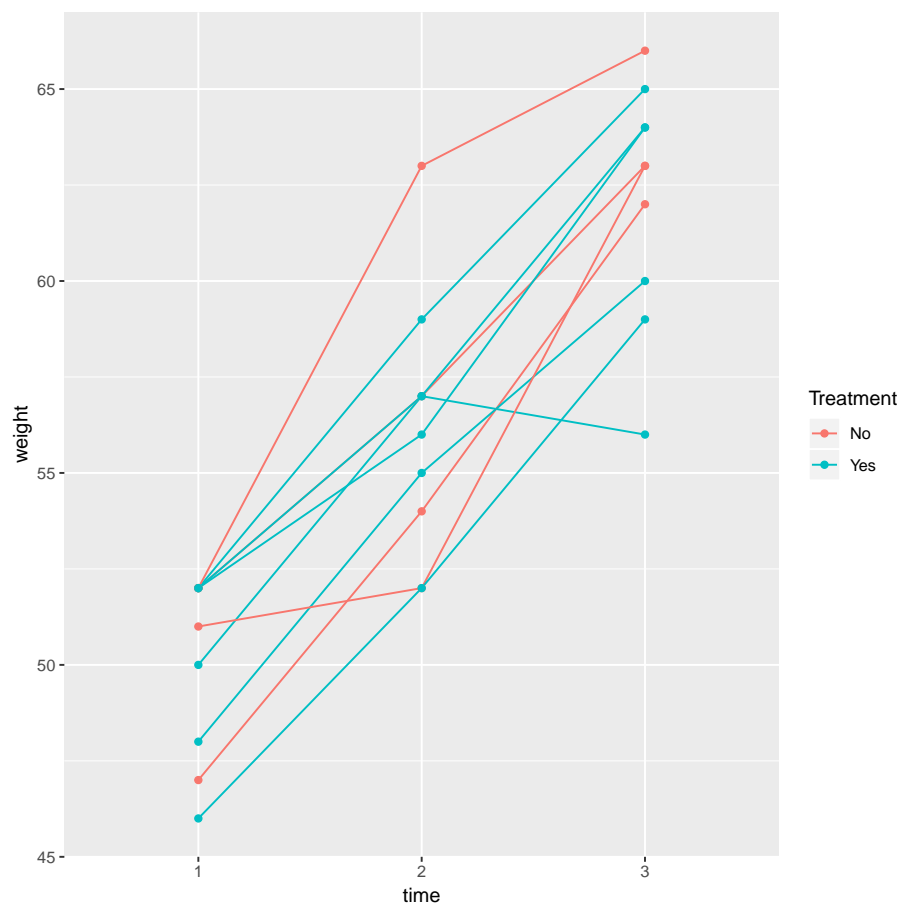
1. color by individual (first ten individuals)

```
gg.spaguetti1 <- ggplot(dtL.data[Id %in% 1:10],  
  aes(x = time, y = weight, color = Id, group = Id))  
gg.spaguetti1 <- gg.spaguetti1 + geom_line() + geom_point()  
gg.spaguetti1
```



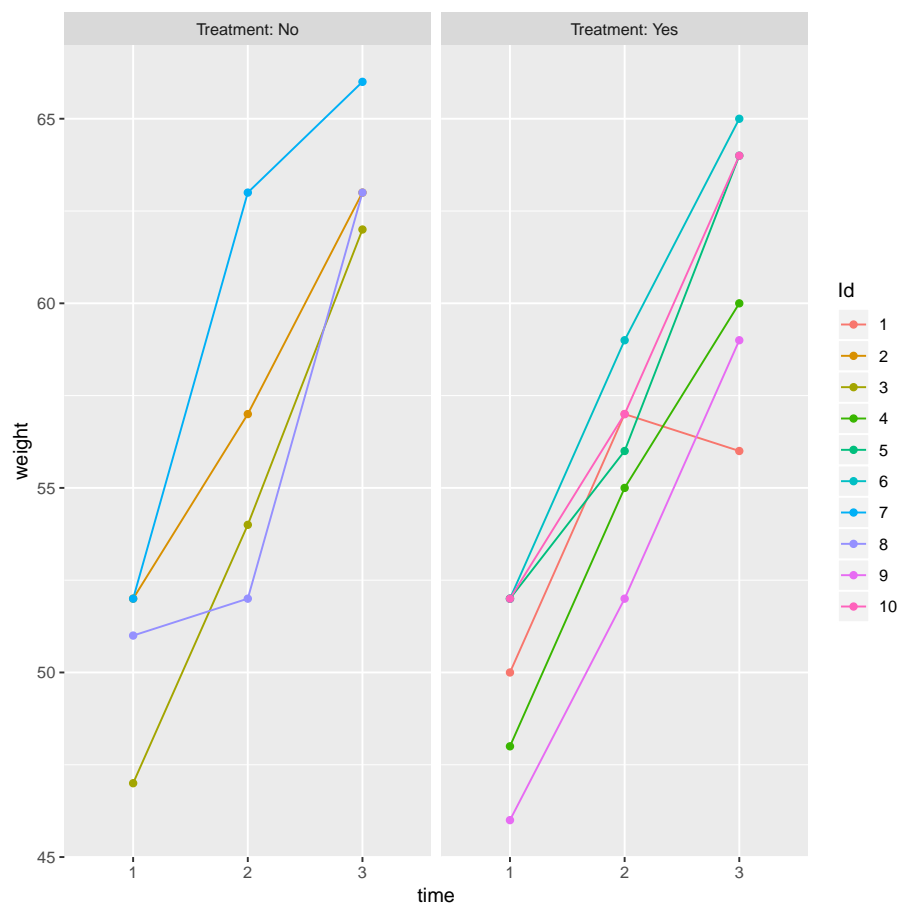
2. color by treatment group (first ten individuals)

```
gg.spaguetti2 <- ggplot(dtL.data[Id %in% 1:10],  
  aes(x = time, y = weight, color = Treatment, group = Id))  
gg.spaguetti2 <- gg.spaguetti2 + geom_line() + geom_point()  
gg.spaguetti2
```



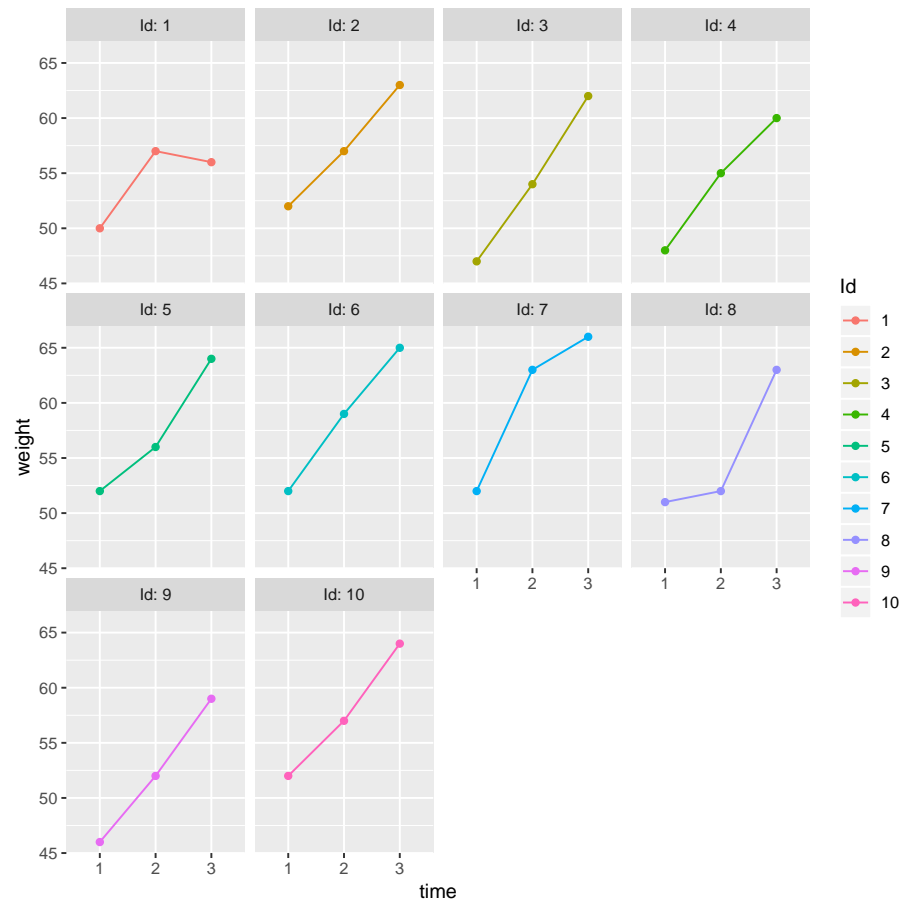
3. pannel for each treatment group (first ten individuals)

```
gg.spaguetti3 <- ggplot(dtL.data[Id %in% 1:10],  
  aes(x = time, y = weight, color = Id, group = Id))  
gg.spaguetti3 <- gg.spaguetti3 + geom_line() + geom_point()  
gg.spaguetti3 <- gg.spaguetti3 + facet_wrap(~ Treatment, labeller = label_both)  
gg.spaguetti3
```



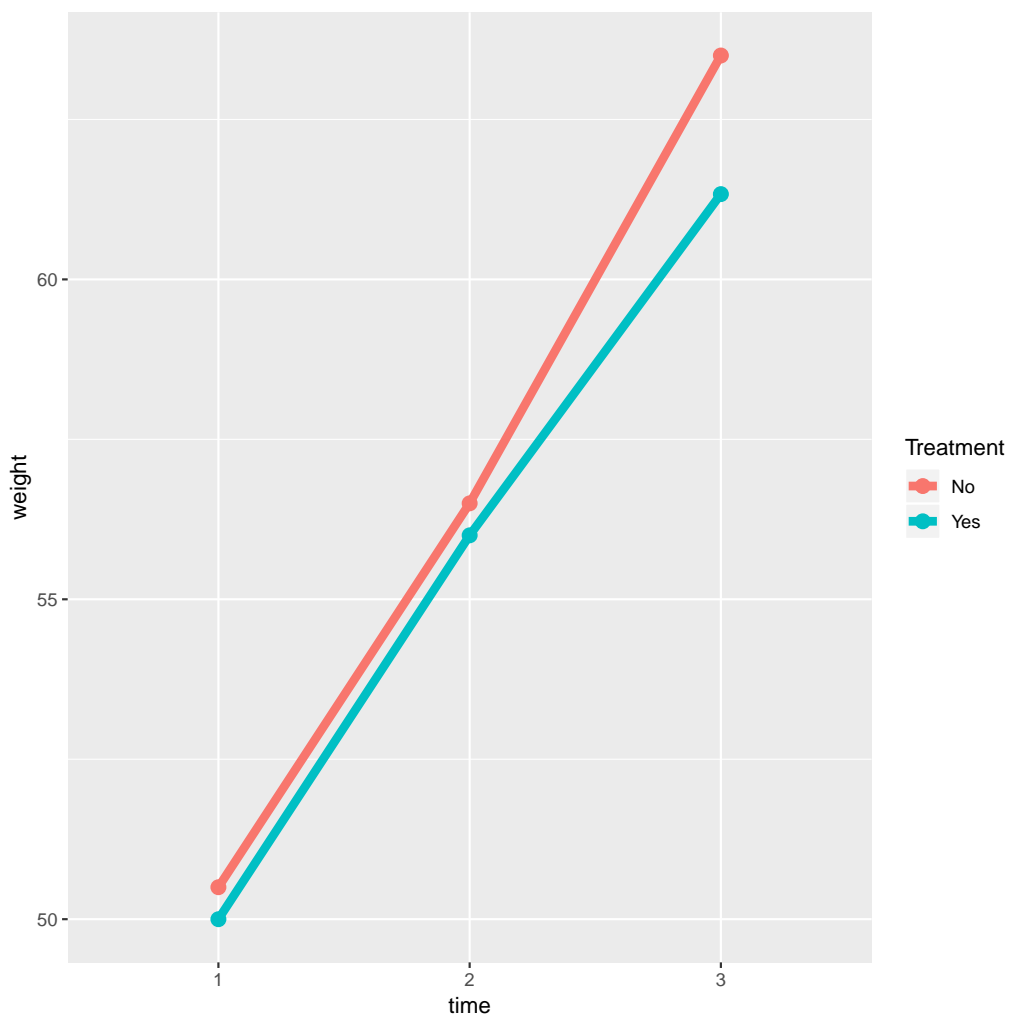
4. individual spaghetti plot (first ten individuals)

```
gg.spaguetti4 <- ggplot(dtL.data[Id %in% 1:10],  
  aes(x = time, y = weight, color = Id, group = Id))  
gg.spaguetti4 <- gg.spaguetti4 + geom_line() + geom_point()  
gg.spaguetti4 <- gg.spaguetti4 + facet_wrap(~ Id, labeller = label_both)  
gg.spaguetti4
```



5.1.2 Display the mean over time

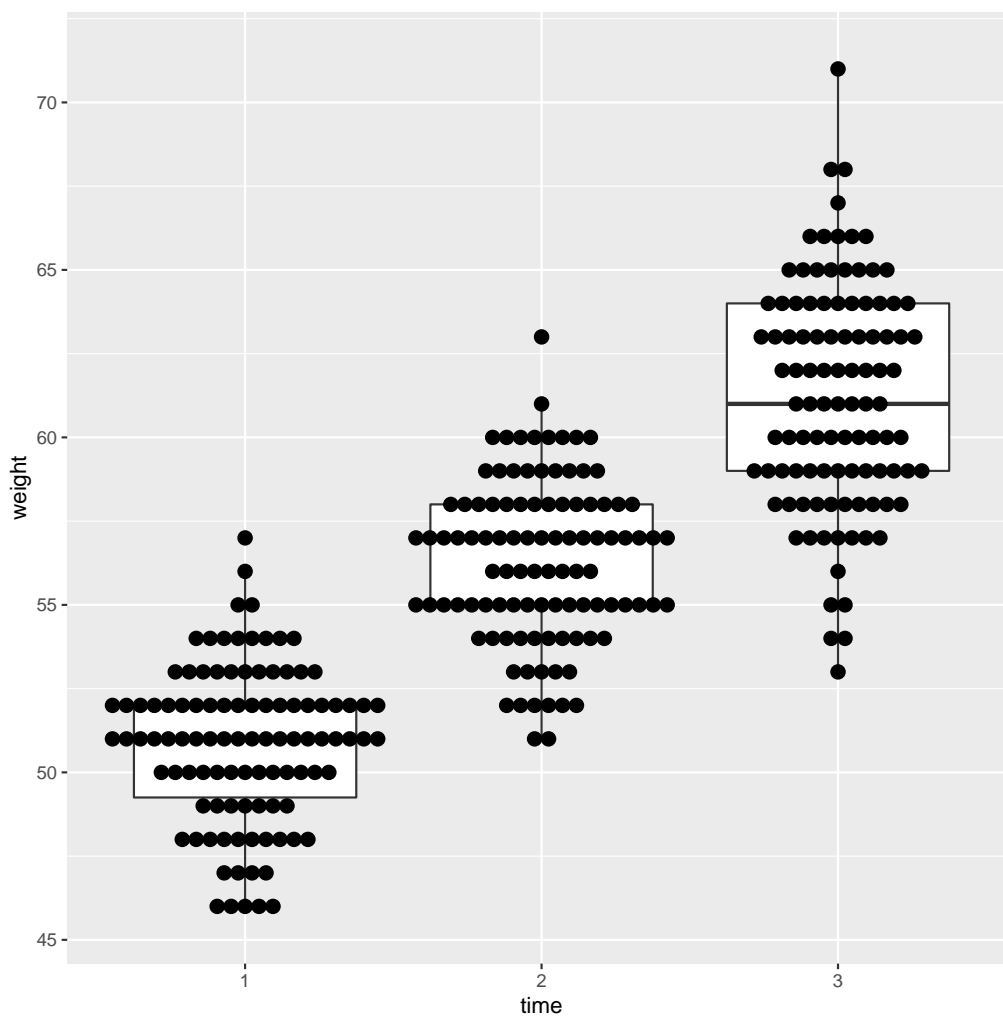
```
gg.mean <- ggplot(dtL.data[Id %in% 1:10], aes(x = time, y = weight))
gg.mean <- gg.mean + stat_summary(aes(group = Treatment, color = Treatment),
  geom = "line", fun.y = mean, size = 2)
gg.mean <- gg.mean + stat_summary(aes(group = Treatment, color = Treatment),
  geom = "point", fun.y = mean, size = 3)
```



5.1.3 Boxplot + points (non-overlapping)

```
gg.hist <- ggplot(dtL.data, aes(x = time, y = weight))
gg.hist <- gg.hist + geom_boxplot()
gg.hist <- gg.hist + geom_dotplot(binaxis = "y", stackdir = "center", dotsize = 0.5)
gg.hist
```

`'stat_bindot()'` using `'bins = 30'`. Pick better value with `'binwidth'`.



5.2 Diagnostic plots

Consider the linear model:

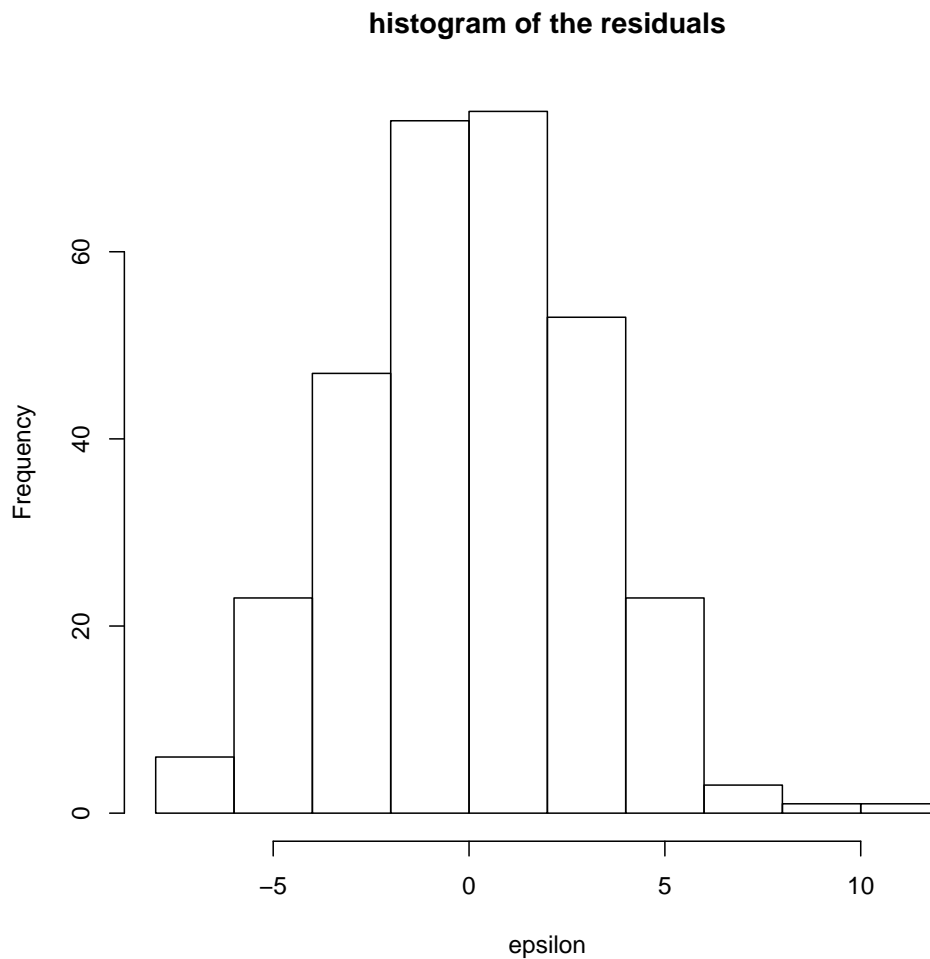
```
e.lm <- lm(weight ~ Age + Treatment + size,  
            data = dtL.data)
```

5.2.1 Histogram of the residuals

Extract the residuals:

```
epsilon <- residuals(e.lm, type = "response")
```

Display the histogram



5.2.2 Forest plot

```
## gg.forest <- ggplot(data=df.bcg, aes(x=label, y=Estimate, ymin=lower, ymax=upper))  
## gg.forest <- gg.forest + geom_pointrange()  
## gg.forest <- gg.forest + geom_hline(yintercept=1, lty=2) + coord_flip()  
## gg.forest <- gg.forest + xlab("Label") + ylab("Mean (95% CI)")
```

5.3 Customize graphic

5.3.1 Greek letter in facet

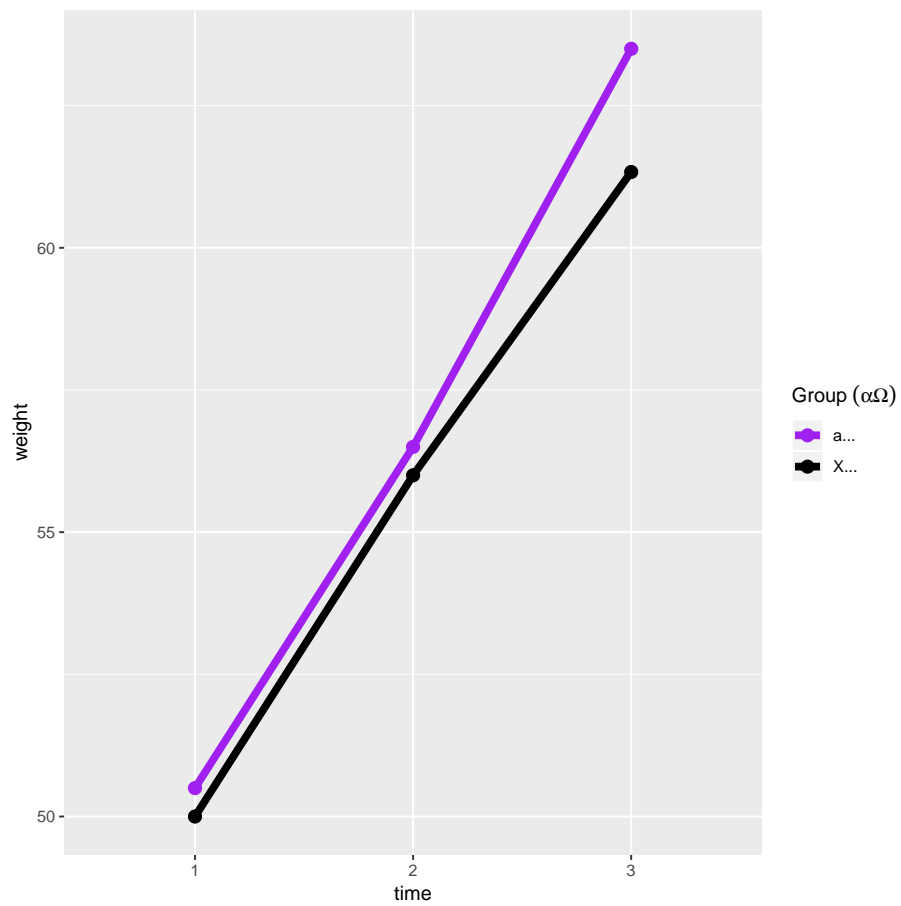
```
seqX <- 1:15
df <- rbind(data.frame(density = dpois(seqX,lambda = 1),
  lambda = 1,
  x = seqX),
  data.frame(density = dpois(seqX,lambda = 2),
    lambda = 2,
    x = seqX))

df$lambda <- factor(df$lambda, levels = c(1,2),
  labels=c(expression(paste(lambda,"=1")),
    expression(paste(lambda,"=2"))))
)

library(ggplot2)
gg <- ggplot(df, aes(y=density,x=x)) + geom_bar(stat="identity")
gg + facet_wrap(~lambda, nrow = 1, labeller = label_parsed)
```

5.3.2 Modify the legend of a discrete scale (with greek letters)

```
gg.mean2 <- gg.mean + scale_colour_manual(name = expression("Group"~(alpha*Omega)),
  labels = c("\u03b1\u2090", "X\u1D30"),
  values = c("No" = "purple",
    "Yes" = "black"))
```



See also:

- https://en.wikipedia.org/wiki/List_of_Unicode_characters
- https://en.wikipedia.org/wiki/Unicode_subscripts_and_superscripts
- <https://stackoverflow.com/questions/5293715/how-to-use-greek-symbols-in-ggplot2>

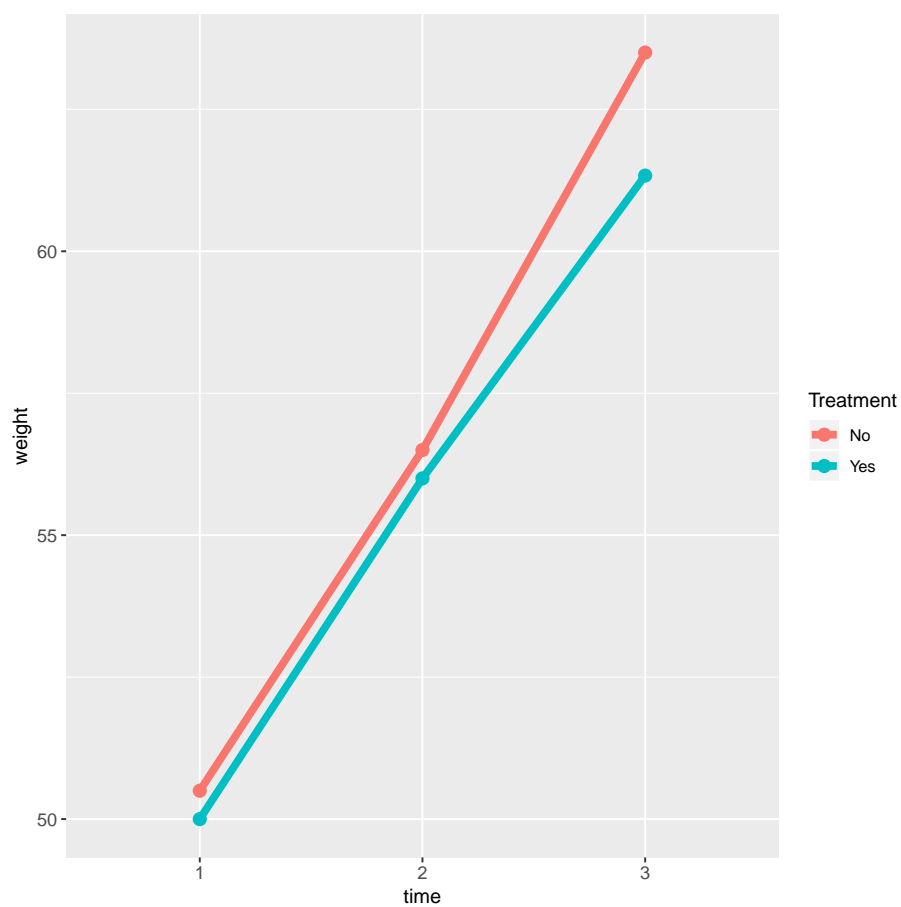
5.3.3 Change the name of the legend

```
gg.mean3 <- gg.mean2 + labs(colour="xyz")
```

5.3.4 Increase the font size

All text:

```
gg.mean3 <- gg.mean + theme(text = element_text(size=10))
```



Only x axis labels:

```
gg.mean3 <- gg.mean + theme(axis.text = element_text(size=10))
```

Only axis title:

```
gg.mean3 <- gg.mean + theme(axis.title = element_text(size=10))
```

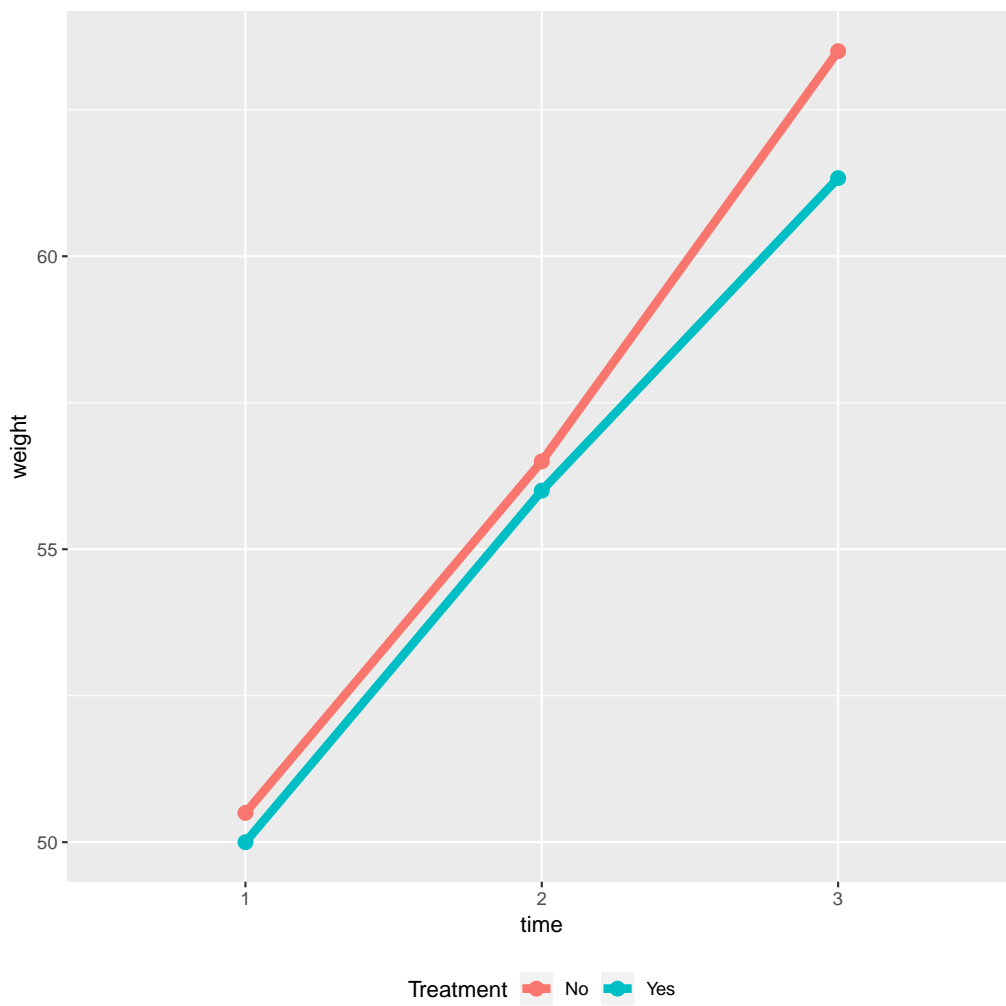
5.3.5 Increase size of the legend labels

```
gg.mean + theme(text = element_text(size=15),
  axis.line = element_line(size = 1.25),
  axis.ticks = element_line(size = 2),
  axis.ticks.length=unit(.25, "cm"),
  legend.key.size = unit(3,"line"))

gg.mean + theme(axis.title = element_text(size=10),
  axis.line = element_line(size = 1.25),
  axis.ticks = element_line(size = 2),
  axis.ticks.length=unit(.25, "cm"),
  legend.key.size = unit(3,"line"))
```

5.3.6 Put the legend at the bottom

```
gg.mean4 <- gg.mean + theme(legend.position="bottom",
  legend.direction = "horizontal")
```



5.3.7 Number of lines in the legend

```
gg.mean + guides(color = guide_legend(nrow = 2, byrow = TRUE))
```

5.3.8 Default ggplot color palette

```
gg_color_hue <- function(n) {  
  hues = seq(15, 375, length = n + 1)  
  hcl(h = hues, l = 65, c = 100)[1:n]  
}
```

5.3.9 Color blind palette

```
ggthemes::colorblind_pal()(8) ## also consider scale_color_colorblind
```

```
[1] "#000000" "#E69F00" "#56B4E9" "#009E73" "#F0E442" "#0072B2" "#D55E00" "#CC79A7"
```

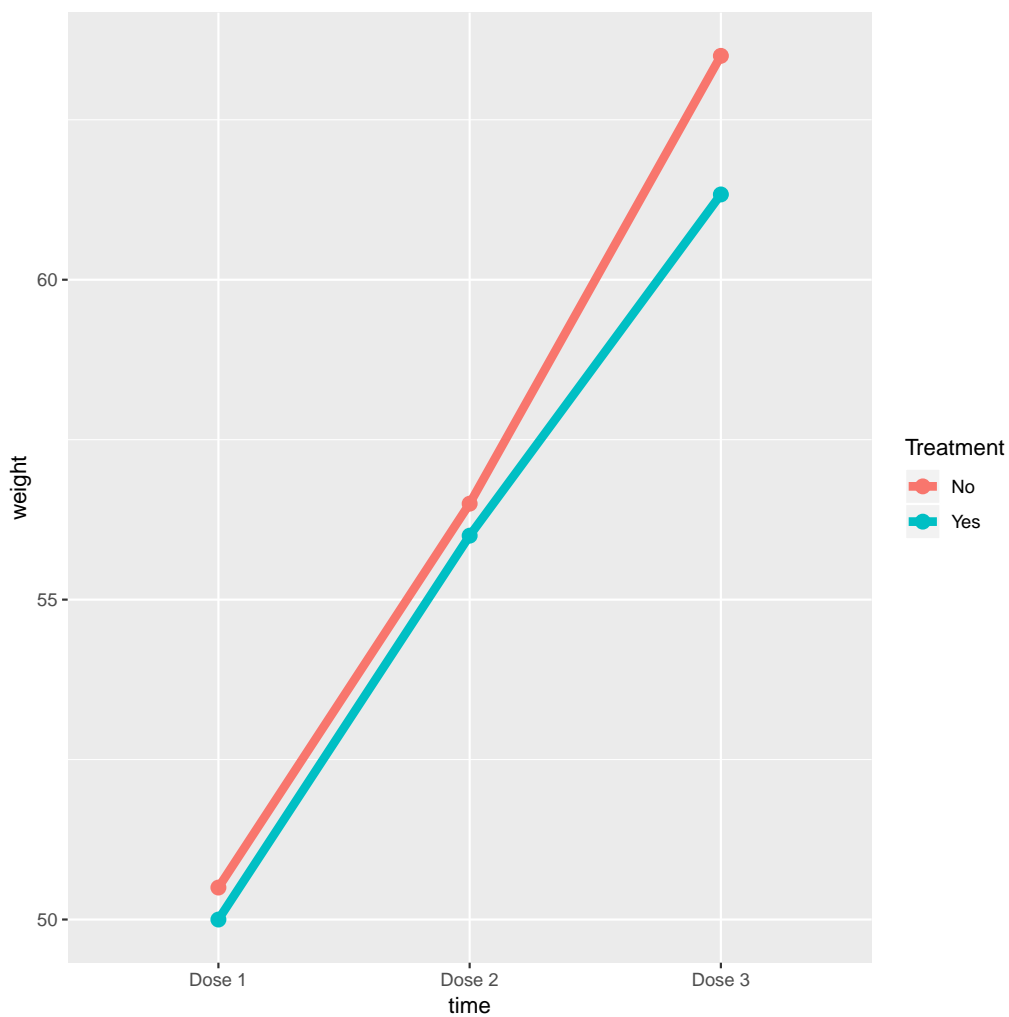
5.3.10 Rotate x-axis labels

```
theme(axis.text.x = element_text(angle = 90, hjust = 1))
```

```
List of 1  
 $ axis.text.x:List of 11  
  ..$ family      : NULL  
  ..$ face        : NULL  
  ..$ colour      : NULL  
  ..$ size        : NULL  
  ..$ hjust       : num 1  
  ..$ vjust       : NULL  
  ..$ angle       : num 90  
  ..$ lineheight  : NULL  
  ..$ margin      : NULL  
  ..$ debug       : NULL  
  ..$ inherit.blank: logi FALSE  
  ..- attr(*, "class")= chr [1:2] "element_text" "element"  
- attr(*, "class")= chr [1:2] "theme" "gg"  
- attr(*, "complete")= logi FALSE  
- attr(*, "validate")= logi TRUE
```

5.3.11 Change tick mark labels

```
gg.mean5 <- gg.mean + scale_x_discrete(breaks=c("1","2","3"),  
  labels=c("Dose 1", "Dose 2", "Dose 3"))
```



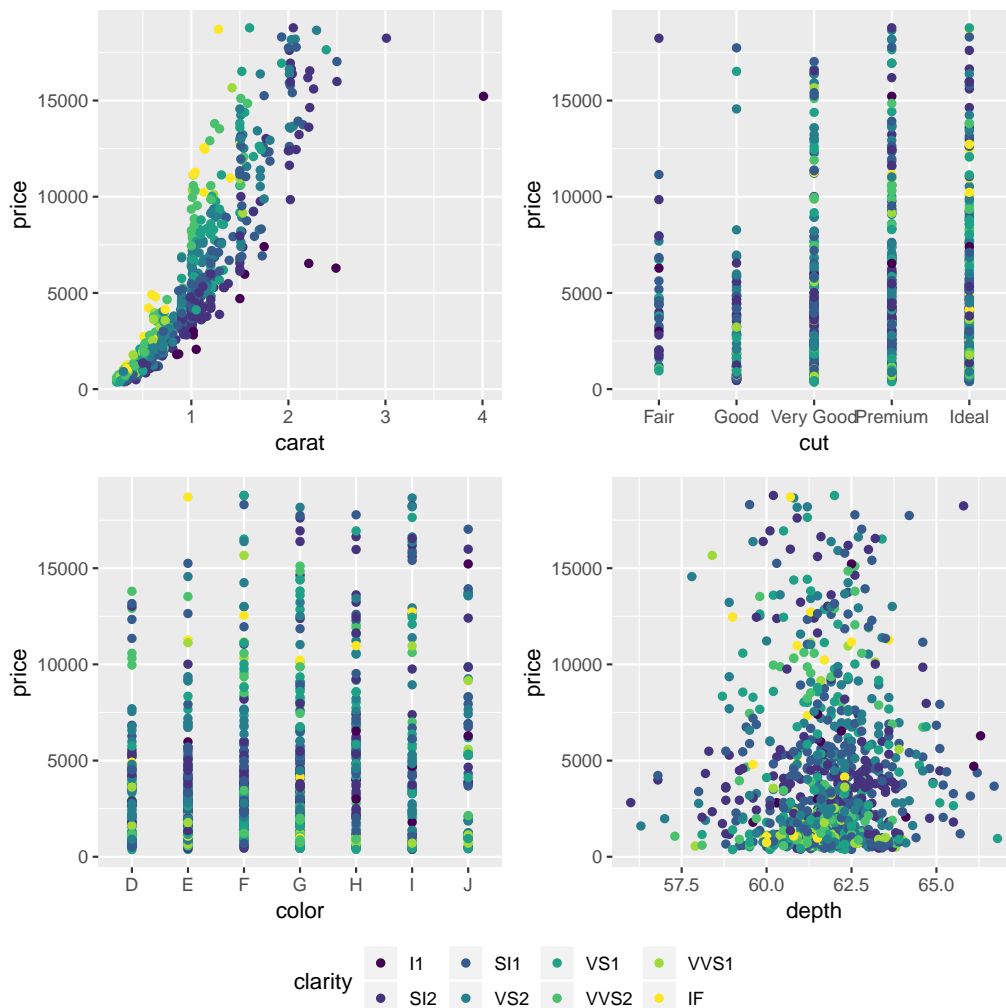
5.3.12 Combine ggplots

(from <https://stackoverflow.com/questions/13649473/add-a-common-legend-for-combined-ggplots>)

```
library(ggpubr)

dsamp <- diamonds[sample(nrow(diamonds), 1000), ]
p1 <- qplot(carat, price, data = dsamp, colour = clarity)
p2 <- qplot(cut, price, data = dsamp, colour = clarity)
p3 <- qplot(color, price, data = dsamp, colour = clarity)
p4 <- qplot(depth, price, data = dsamp, colour = clarity)

out <- ggarrange(p1, p2, p3, p4, ncol=2, nrow=2, common.legend = TRUE, legend="bottom")
```



5.3.13 Symbols in facet names

5.4 Path diagram

Using lava:

```
m <- lava(Y~E+X1+X2+M,M~E,E~X2)
```

```
plot(m, plot.engine="rgraphviz")
```

Dynamic graph:

```
plot(m, plot.engine="visnetwork")
```

5.5 Lexis diagram

Simulate data

```
library(riskRegression)
library(ggplot2)
library(data.table)

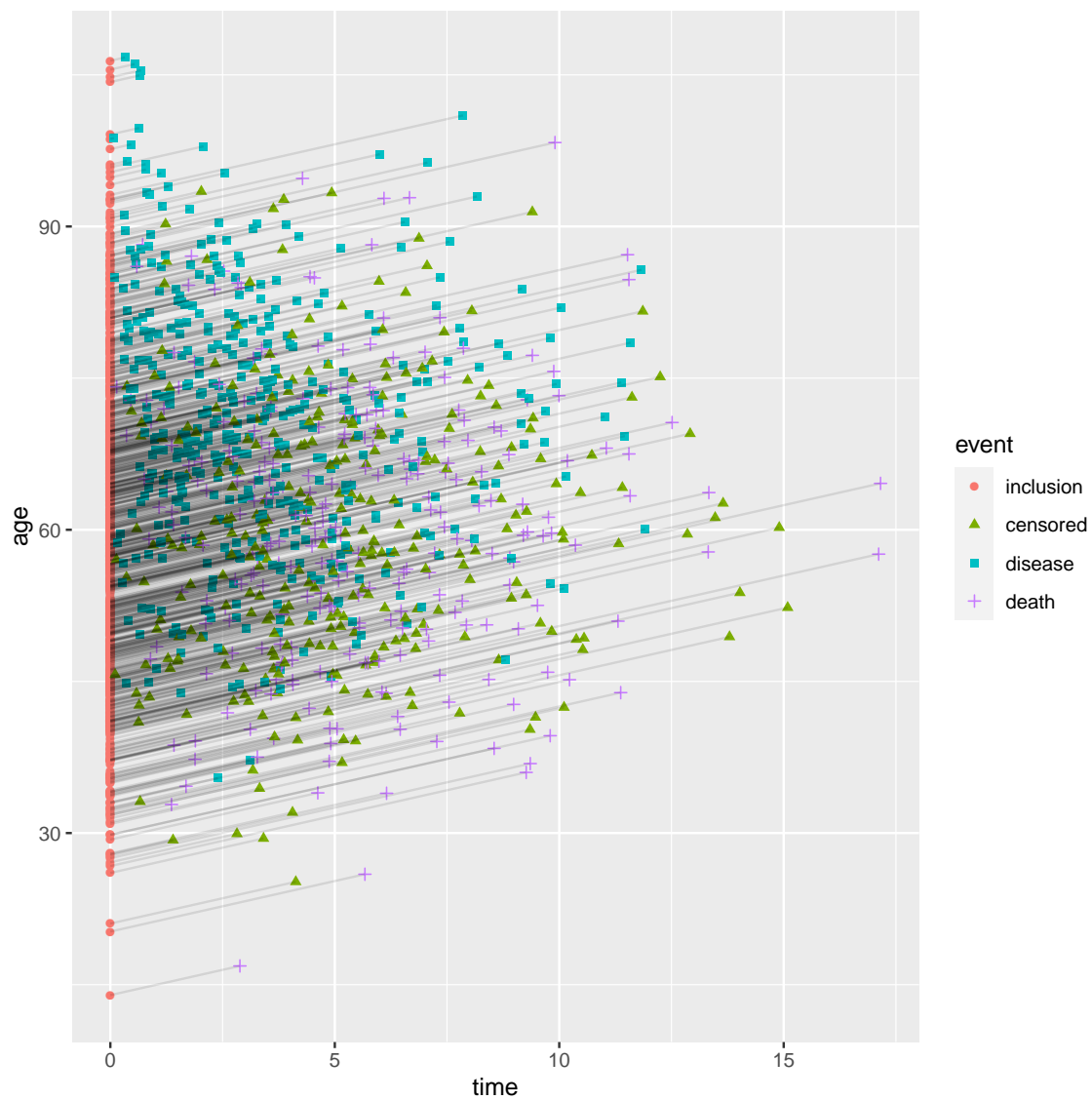
set.seed(10)
d <- sampleData(1000)
d[, id := as.character(1:.N)]
```

Reshape data

```
d$Age <- d$X6
d$age.start <- d$Age
d$age.stop <- d$Age + d$time
d$start <- 0
d$stop <- d$time
dL <- rbind(d[,.(id = id, time = start, age = age.start, status = -1)],
           d[,.(id = id, time = stop, age = age.stop, status = event)])
dL[, event := factor(status, (-1):2, c("inclusion", "censored", "disease", "death"))]
```

Display

```
gg <- ggplot(dL, aes(x = time, y = age, group = id))
gg <- gg + geom_point(aes(color=event, shape=event))
gg <- gg + geom_line(alpha = 0.1)
gg
```



6 Modeling

6.1 Test proportions

```
binom.exact(c(15,4), p = 0.5) ## 15 success, 4 failures
```

Exact two-sided binomial test (central method)

```
data: c(15, 4)
number of successes = 15, number of trials = 19, p-value = 0.01921
alternative hypothesis: true probability of success is not equal to 0.5
95 percent confidence interval:
 0.5443469 0.9394755
sample estimates:
probability of success
 0.7894737
```

6.2 Compare proportions between groups

Data:

```
tab <- rbind(c(6,12),
             c(12,5))
colnames(tab) <- c("worse","better")
rownames(tab) <- c("Dalteparin","Placebo")
tab
```

```
      worse better
Dalteparin    6    12
Placebo      12     5
```

- test conditional only on the sample sizes

```
uncondExact2x2(x1 = tab[1,2],
               x2 = tab[2,2],
               n1 = sum(tab[1,]),
               n2 = sum(tab[2,]),
               conf.int = TRUE)
```

Unconditional Exact Test on Difference in Proportions, method= FisherAdj, central

```
data:  x1/n1=(12/18) and x2/n2= (5/17)
proportion 1 = 0.66667, proportion 2 = 0.29412, p-value = 0.03488
alternative hypothesis: true p2-p1 is not equal to 0
95 percent confidence interval:
 -0.64591599 -0.02557945
sample estimates:
      p2-p1
-0.372549
```

Approximate test:

```
binomMeld.test(x1 = tab[1,2],
               x2 = tab[2,2],
               n1 = sum(tab[1,]),
               n2 = sum(tab[2,])
               )
```

melded binomial test for difference

```
data:  sample 1:(12/18), sample 2:(5/17)
proportion 1 = 0.66667, proportion 2 = 0.29412, p-value = 0.06059
```

```

alternative hypothesis: true difference is not equal to 0
95 percent confidence interval:
 -0.67110802  0.01375096
sample estimates:
difference (p2-p1)
 -0.372549

```

```

binomMeld.test(x1 = tab[1,2],
               x2 = tab[2,2],
               n1 = sum(tab[1,]),
               n2 = sum(tab[2,]),
               parmtype = "ratio"
               )

```

melded binomial test for ratio

```

data:  sample 1:(12/18), sample 2:(5/17)
proportion 1 = 0.66667, proportion 2 = 0.29412, p-value = 0.06059
alternative hypothesis: true ratio is not equal to 1
95 percent confidence interval:
 0.1465276 1.0287320
sample estimates:
ratio (p2/p1)
 0.4411765

```

- test conditional on the sample sizes and the number of events

```

fisher.exact(tab)

```

Two-sided Fisher's Exact Test (usual method using minimum likelihood)

```

data:  tab
p-value = 0.04371
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 0.0435 0.9170
sample estimates:
odds ratio
 0.2189021

```

which is better than

```

fisher.test(tab)

```


Fisher's Exact Test for Count Data

```
data: tab
p-value = 0.04371
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 0.03888003 1.05649145
sample estimates:
odds ratio
 0.2189021
```

where confidence intervals and p-values are not consistent.

- Paired: (mc-nemar test)

```
mcnemar.exact(tab)
```

Exact McNemar test (with central confidence intervals)

```
data: tab
b = 12, c = 12, p-value = 1
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 0.4109184 2.4335733
sample estimates:
odds ratio
 1
```

6.3 Estimate Mann Whitney parameter

Remove ties:

```
set.seed(10)
sleep$Y <- sleep$extra + rnorm(NROW(sleep), sd = 0.1)
```

Original p-value:

```
suppressWarnings(wilcox.test(Y ~ group, data = sleep, exact = FALSE)$p.value)
```

```
[1] 0.03763531
```

Mann-Whitney parameter (method 1)

```
library(asht)
wmwTest(Y ~ group, data = sleep, method = "asymptotic")
```

```
Wilcoxon-Mann-Whitney test with continuity correction (confidence interval requires proportional odds a
but test does not)
```

```
data: Y by group
Mann-Whitney estimate = 0.78, tie factor = 1, p-value = 0.03764
alternative hypothesis: two distributions are not equal
95 percent confidence interval:
 0.5158768 0.9172200
sample estimates:
Mann-Whitney estimate
              0.78
```

Mann-Whitney parameter (method 2)

```
library(BuyseTest)
BuyseTest.options(order.Hprojection=2)
e.BT <- BuyseTest(group ~ cont(Y), data = sleep,
  method.inference = "u-statistic")
confint(e.BT, statistic = "favorable")
```

```
      estimate      se lower.ci upper.ci   p.value
Y_1e-12    0.78 0.1049 0.5168762 0.9215649 0.03841179
attr(,"n.resampling")
Y_1e-12
      NA
```

6.4 Permutation t-test: 2 group comparison

Data:

```
set.seed(10)
X <- rlnorm(10, meanlog = 2, sdlog = 0.5)
Y <- rlnorm(10, meanlog = 1.8, sdlog = 0.5)
```

Approximation based on asymptotic result:

```
permTS(x = X, y = Y, method = "pctl")
```

Permutation Test using Asymptotic Approximation

```
data:  X and Y
Z = -1.5476, p-value = 0.1217
alternative hypothesis: true mean X - mean Y is not equal to 0
sample estimates:
mean X - mean Y
-1.533514
```

Approximation based on simulations:

```
permTS(x = X, y = Y, method = "exact.mc")
```

Exact Permutation Test Estimated by Monte Carlo

```
data:  X and Y
p-value = 0.112
alternative hypothesis: true mean X - mean Y is not equal to 0
sample estimates:
mean X - mean Y
-1.533514
```

```
p-value estimated from 999 Monte Carlo replications
99 percent confidence interval on p-value:
0.07625212 0.15272627
```

Exact:

```
permTS(x = X, y = Y, method = "exact.ce")
```

Exact Permutation Test (complete enumeration)

```
data:  X and Y
p-value = 0.1238
alternative hypothesis: true mean X - mean Y is not equal to 0
sample estimates:
mean X - mean Y
-1.533514
```

6.5 Permutation t-test: multiple group comparison

Data:

```
set.seed(10)
X <- rlnorm(10, meanlog = 2, sdlog = 0.5)
Y <- rlnorm(10, meanlog = 1.8, sdlog = 0.5)
Z <- rlnorm(10, meanlog = 1.5, sdlog = 0.5)
df <- rbind(data.frame(value = X, group = "X"),
            data.frame(value = Y, group = "Y"),
            data.frame(value = Z, group = "Z"))
```

NOT VALIDATED!!!

```
library("permuco")
lmperm(value ~ group, data = df, np = 1e4)
```

Table of marginal t-test of the betas

Permutation test using freedman_lane to handle nuisance variables and 10000 permutations.

	Estimate	Std. Error	t value	parametric Pr(> t)	permutation Pr(<t)	permutation Pr(>t)	permutation P
(Intercept)	6.091	0.5755	10.584	4.142e-11			
groupY	1.534	0.8139	1.884	7.035e-02	0.9631	0.0370	
groupZ	-3.095	0.8139	-3.803	7.440e-04	0.0005	0.9996	

6.6 Testing median

Data:

```
set.seed(10)
X <- rlnorm(100, meanlog = 2, sdlog = 0.5) - 6.5
```

Median test

```
quantileTest(X)
```

Exact Test/Confidence Interval for Median

```
data: X
quantile for prob = 0.5, pAG = 0.18410, pAL = 0.86437, pc = 0.36820, p-value = 0.3682
alternative hypothesis: true median is not equal to 0
95 percent confidence interval:
 -0.3701565  1.4997902
sample estimates:
      median
0.2082777
```

```
df <- data.frame(value=X)
e <- rq(value~1, tau = 0.5, data = df)
summary(e, se = "nid")
```

Warning message:

```
In rq.fit.br(x, y, tau = tau, ...) : Solution may be nonunique
```

```
Call: rq(formula = value ~ 1, tau = 0.5, data = df)
```

```
tau: [1] 0.5
```

Coefficients:

```
Value Std. Error t value Pr(>|t|)
(Intercept) 0.20213 0.49381 0.40932 0.68319
```

Other quantiles

```
e2 <- rq(value~1, tau = c(0.25,0.5,0.75), data = df)
summary(e2, se = "nid")
```

Warning messages:

```
1: In rq.fit.br(x, y, tau = tau, ...) : Solution may be nonunique
2: In rq.fit.br(x, y, tau = tau, ...) : Solution may be nonunique
3: In rq.fit.br(x, y, tau = tau, ...) : Solution may be nonunique
```

```
Call: rq(formula = value ~ 1, tau = c(0.25, 0.5, 0.75), data = df)
```

```
tau: [1] 0.25
```

```
Coefficients:
```

	Value	Std. Error	t value	Pr(> t)
(Intercept)	-1.61744	0.37283	-4.33828	0.00003

```
Call: rq(formula = value ~ 1, tau = c(0.25, 0.5, 0.75), data = df)
```

```
tau: [1] 0.5
```

```
Coefficients:
```

	Value	Std. Error	t value	Pr(> t)
(Intercept)	0.20213	0.49381	0.40932	0.68319

```
Call: rq(formula = value ~ 1, tau = c(0.25, 0.5, 0.75), data = df)
```

```
tau: [1] 0.75
```

```
Coefficients:
```

	Value	Std. Error	t value	Pr(> t)
(Intercept)	3.43848	0.68607	5.01186	0.00000

6.7 Testing linear hypotheses

Consider the linear model:

```
e.lm <- lm(weight ~ Age + Treatment + size,
  data = dtL.data)
summary(e.lm)$coef
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	13.11292977	5.84498969	2.2434479	2.559263e-02
Age	-0.05479836	0.13849481	-0.3956709	6.926272e-01
TreatmentYes	-0.65247721	0.36126020	-1.8061143	7.189597e-02
size	0.81718969	0.03513376	23.2593869	2.743182e-69

To test linear hypotheses we first need to define them using a contrast matrix:

```
name.coef <- names(coef(e.lm))
n.coef <- length(name.coef)

C <- matrix(0,nrow = 3, ncol = n.coef,
  dimnames = list (c("Age","2 Treatment","All"), name.coef))
C["Age","Age"] <- 1
C["2 Treatment","TreatmentYes"] <- 2
C["All",-1] <- 1
C
```

	(Intercept)	Age	TreatmentYes	size
Age	0	1	0	0
2 Treatment	0	0	2	0
All	0	1	1	1

6.7.1 Separate Wald tests of linear hypotheses

No adjustment for multiple comparison:

```
summary(glht(e.lm, linfct = C), test = univariate())
```

Simultaneous Tests for General Linear Hypotheses

Fit: `lm(formula = weight ~ Age + Treatment + size, data = dtL.data)`

Linear Hypotheses:

	Estimate	Std. Error	t value	Pr(> t)
Age == 0	-0.0548	0.1385	-0.396	0.6926
2 Treatment == 0	-1.3050	0.7225	-1.806	0.0719 .
All == 0	0.1099	0.3513	0.313	0.7546

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
(Univariate p values reported)

Adjustment using bonferroni:

```
summary(glht(e.lm, linfct = C), test = adjusted("bonferroni"))
```

Simultaneous Tests for General Linear Hypotheses

```
Fit: lm(formula = weight ~ Age + Treatment + size, data = dtL.data)
```

Linear Hypotheses:

	Estimate	Std. Error	t value	Pr(> t)
Age == 0	-0.0548	0.1385	-0.396	1.000
2 Treatment == 0	-1.3050	0.7225	-1.806	0.216
All == 0	0.1099	0.3513	0.313	1.000

(Adjusted p values reported -- bonferroni method)

Adjustment using the max statistic:

```
summary(glht(e.lm, linfct = C), test = adjusted("single-step"))
```

Simultaneous Tests for General Linear Hypotheses

```
Fit: lm(formula = weight ~ Age + Treatment + size, data = dtL.data)
```

Linear Hypotheses:

	Estimate	Std. Error	t value	Pr(> t)
Age == 0	-0.0548	0.1385	-0.396	0.916
2 Treatment == 0	-1.3050	0.7225	-1.806	0.157
All == 0	0.1099	0.3513	0.313	0.948

(Adjusted p values reported -- single-step method)

Alternative syntax (without contrast matrix):

```
summary(glht(e.lm,
  linfct = c("Age = 0",
    "2*TreatmentYes = 0",
    "Age + TreatmentYes + size = 0")),
  test = adjusted("single-step"))
```

Simultaneous Tests for General Linear Hypotheses

```
Fit: lm(formula = weight ~ Age + Treatment + size, data = dtL.data)
```

Linear Hypotheses:

	Estimate	Std. Error	t value	Pr(> t)
Age == 0	-0.0548	0.1385	-0.396	0.916
2 * TreatmentYes == 0	-1.3050	0.7225	-1.806	0.157
Age + TreatmentYes + size == 0	0.1099	0.3513	0.313	0.948

(Adjusted p values reported -- single-step method)

6.7.2 Confidence intervals associated with linear hypotheses

With no adjustment for multiplicity:

```
confint(glht(e.lm, linfct = C), calpha = univariate_calpha())
```

Simultaneous Confidence Intervals

```
Fit: lm(formula = weight ~ Age + Treatment + size, data = dtL.data)
```

```
Quantile = 1.9679
```

```
95% confidence level
```

Linear Hypotheses:

	Estimate	lwr	upr
Age == 0	-0.0548	-0.3273	0.2177
2 Treatment == 0	-1.3050	-2.7268	0.1169
All == 0	0.1099	-0.5815	0.8013

With adjustment for multiplicity:

```
confint(glht(e.lm, linfct = C), calpha = adjusted_calpha())
```

Simultaneous Confidence Intervals

```
Fit: lm(formula = weight ~ Age + Treatment + size, data = dtL.data)
```

```
Quantile = 2.314
```

```
95% family-wise confidence level
```

Linear Hypotheses:

	Estimate	lwr	upr
Age == 0	-0.0548	-0.3753	0.2657
2 Treatment == 0	-1.3050	-2.9769	0.3670
All == 0	0.1099	-0.7031	0.9229

6.7.3 Joint test of linear hypotheses

One can use the `Ftest()` or `Chisqtest()` to obtain a joint test:

```
summary(glht(e.lm,
  linfct = c("Age = 0",
    "2*TreatmentYes = 0",
    "Age + TreatmentYes + size = 0")),
  test = Ftest())
```

General Linear Hypotheses

Linear Hypotheses:

	Estimate
Age == 0	-0.0548
2 * TreatmentYes == 0	-1.3050
Age + TreatmentYes + size == 0	0.1099

Global Test:

	F	DF1	DF2	Pr(>F)
1	181.2	3	302	3.349e-67

The same can be obtained using the `linearHypothesis` method from the `car` package:

```
linearHypothesis(e.lm, hypothesis.matrix = C, rhs = c(0,0,0))
```

Linear hypothesis test

Hypothesis:

```
Age = 0
2 TreatmentYes = 0
Age + TreatmentYes + size = 0
```

Model 1: restricted model

Model 2: weight ~ Age + Treatment + size

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	305	7748.5				
2	302	2767.2	3	4981.3	181.21	< 2.2e-16 ***

 Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

6.8 Testing linearity assumptions in a linear model

```
e.lm <- lm(weight ~ Age + Treatment + size,  
  data = dtL.data)  
gof::cumres(e.lm)
```

```
Kolmogorov-Smirnov-test: p-value=0.022  
Cramer von Mises-test: p-value=0.004  
Based on 1000 realizations. Cumulated residuals ordered by predicted-variable.  
---  
Kolmogorov-Smirnov-test: p-value=0.555  
Cramer von Mises-test: p-value=0.348  
Based on 1000 realizations. Cumulated residuals ordered by Age-variable.  
---  
Kolmogorov-Smirnov-test: p-value=0.006  
Cramer von Mises-test: p-value=0.006  
Based on 1000 realizations. Cumulated residuals ordered by size-variable.  
---
```

6.9 Compute and display partial residuals in a linear model

For a given model:

```
e.lmm <- lmm(weight ~ Age + Treatment + size,  
             data = dtL.data)
```

Compute the partial residual (i.e. removing Treatment and size effects):

```
ePres.lmm <- residuals(e.lmm, var = c("(Intercept)","Age"), type = "partial")  
head(ePres.lmm)
```

```
[1]  9.245476 10.928046  8.910788 11.102611  9.455830 12.307822
```

Graphical display:

```
residuals(e.lmm, var = c("(Intercept)","Age"), type = "partial", plot = "scatterplot")
```

`'geom_smooth()'` using method = `'loess'` and formula `'y ~ x'`

To get the regression line on top:

```
e.lm <- lm(weight ~ Age + Treatment + size, data = dtL.data)  
autoplot(butils::partialResiduals(e.lm, var = "Age"))
```

Note that the default partial residuals:

```
GS <- residuals(e.lm, type = "partial")[,"Age"]
```

also remove the overall average (i.e. intercept) and are computed for a average covariate value:

```
table(round(GS - ePres.lmm,5))
```

```
-10.90649  
      306
```

This is what is obtained with `"partial-center"`:

```
range(GS - residuals(e.lmm, var = c("(Intercept)","Age"), type = "partial-center"))
```

6.10 Equivalence Poisson and Cox model

Load veteran dataset and subset it to ease visualization:

```
library(survival)
veteranR <- veteran[veteran$celltype=="large" & veteran$status == 1,]
```

Make sure there is not ties:

```
any(duplicated(veteranR$time))
```

```
[1] FALSE
```

For reference here is the treatment effect estimated by a Cox model:

```
e.coxph <- coxph(Surv(time,status)~trt, data = veteranR, x = TRUE)
eBeta.coxph <- summary(e.coxph)$coef
eBeta.coxph
```

```
      coef exp(coef) se(coef)      z Pr(>|z|)
trt 0.3673965  1.44397 0.4061045  0.9046847 0.3656324
```

and the baseline hazards:

```
ePred.coxph <- predictCox(e.coxph, centered = FALSE,
  type = c("hazard", "cumhazard", "survival"))
eLambda.coxph <- as.data.table(ePred.coxph)[1:3,]
eLambda.coxph
```

```
  observation times      hazard cumhazard survival
1:           1    12 0.02210619 0.02210619 0.9781364
2:           2    15 0.02283511 0.04494130 0.9560536
3:           3    19 0.02397669 0.06891800 0.9334032
```

We can emulate a Cox model using a Poisson model. This can be achieved by using fine enough time intervals:

```
timeInterval <- sort(unique(veteranR$time))
n.interval <- length(timeInterval)
```

First we split the data per interval:

```
veteranRexpanded <- survSplit(Surv(time,status)~id+trt, data = veteranR, cut =
  timeInterval, episode = "interval")
```

We note that we can retrieve the previous Cox model with this data format:

```
e.coxph2 <- coxph(Surv(tstart,time,status) ~ trt, data = veteranRexpanded)
summary(e.coxph2)$coef
```

```
      coef exp(coef) se(coef)      z Pr(>|z|)
trt 0.3673965  1.44397 0.4061045 0.9046847 0.3656324
```

We can now compute the at risk time as:

```
veteranRexpanded$atrisk <- veteranRexpanded$time - veteranRexpanded$tstart
```

And fit the Poisson model:

```
e.pois <- glm(status ~ trt + factor(interval), family = poisson(link="log"), offset = log(
  atrisk), data = veteranRexpanded)
logLik(e.pois)
summary(e.pois)$coef["trt",,drop=FALSE]
```

```
'log Lik.' -86.85672 (df=27)
      Estimate Std. Error z value Pr(>|z|)
trt 0.3673965  0.4061043 0.904685 0.3656323
```

We note that all subjects have the same at risk time within each interval so the offset is in fact optional to estimate the treatment effect:

```
e.pois2 <- glm(status ~ trt + factor(interval), family = poisson(link="log"), data =
  veteranRexpanded)
logLik(e.pois2)
summary(e.pois2)$coef["trt",,drop=FALSE]
```

```
'log Lik.' -86.85672 (df=27)
      Estimate Std. Error z value Pr(>|z|)
trt 0.3673965  0.4061043 0.904685 0.3656323
```

The additional benefit is that the hazard can be more easily deduced from this parametrisation:

```
elambda.pois <- c(exp(coef(e.pois2)["(Intercept)"]),
  exp(coef(e.pois2)["(Intercept)"] + coef(e.pois2)["factor(interval)2"]),
  exp(coef(e.pois2)["(Intercept)"] + coef(e.pois2)["factor(interval)3"]))
cbind(times = timeInterval[1:3],
  hazard = unname(elambda.pois),
  cumhazard = unname(cumsum(elambda.pois)),
  survival = unname(exp(-cumsum(elambda.pois))))
```

```
      times      hazard cumhazard survival
[1,]    12 0.02210619 0.02210619 0.9781364
[2,]    15 0.02283511 0.04494130 0.9560536
[3,]    19 0.02397669 0.06891800 0.9334032
```

than when specifying the time at risk:

```
elambda.pois2 <- c(exp(coef(e.pois)["(Intercept)"])*timeInterval[1],  
  exp(coef(e.pois)["(Intercept)"] + coef(e.pois)["factor(interval)2"]) * diff(  
    timeInterval)[1],  
  exp(coef(e.pois)["(Intercept)"] + coef(e.pois)["factor(interval)3"]) * diff(  
    timeInterval)[2])  
cbind(times = timeInterval[1:3],  
  hazard = unname(elambda.pois2),  
  cumhazard = unname(cumsum(elambda.pois2)),  
  survival = unname(exp(-cumsum(elambda.pois2))))
```

	times	hazard	cumhazard	survival
[1,]	12	0.02210619	0.02210619	0.9781364
[2,]	15	0.02283511	0.04494130	0.9560536
[3,]	19	0.02397669	0.06891800	0.9334032

6.11 Displaying incidence rates with confidence intervals

Load veteran dataset and split the dataset into 3 time periods:

```
library(survival)
timeInterval <- c(50,200)
veteranE <- survSplit(Surv(time,status)~id+trt, data = veteran, cut = timeInterval,
  episode = "interval")
head(veteranE)
```

	id	trt	tstart	time	status	interval
1	1	1	0	50	0	1
2	1	1	50	72	1	2
3	2	1	0	50	0	1
4	2	1	50	200	0	2
5	2	1	200	411	1	3
6	3	1	0	50	0	1

Introducing the time spent in each interval:

```
veteranE$atrisk <- veteranE$time - veteranE$tstart
head(veteranE)
```

	id	trt	tstart	time	status	interval	atrisk
1	1	1	0	50	0	1	50
2	1	1	50	72	1	2	22
3	2	1	0	50	0	1	50
4	2	1	50	200	0	2	150
5	2	1	200	411	1	3	211
6	3	1	0	50	0	1	50

We can compute the incidence rate by counting the number of events divided the total time spent in each interval:

```
veteranE$interval.trt <- interaction(veteranE$interval,veteranE$trt)
by(veteranE,veteranE$interval.trt,
  function(iData){sum(iData$status)/sum(iData$atrisk)}
)
```

```
veteranE$interval.trt: 1.1
[1] 0.008139105
```

```
-----
veteranE$interval.trt: 2.1
[1] 0.008012406
```

```
-----
veteranE$interval.trt: 3.1
[1] 0.008011653
```

```
-----
veteranE$interval.trt: 1.2
[1] 0.01160542
```



```
-----
veteranE$interval.trt: 2.2
[1] 0.007243991
-----
```

```
veteranE$interval.trt: 3.2
[1] 0.003875969
```

Alternatively we can fit a Poisson model:

```
veteranE$trt.f <- as.factor(veteranE$trt)
veteranE$interval.f <- as.factor(veteranE$interval)

e.pois <- glm(status ~ 0+interval.f:trt.f, family = poisson(link="log"),
  offset = log(atrisk), data = veteranE)
logLik(e.pois)
summary(e.pois)$coef
```

```
'log Lik.' -316.1628 (df=6)
              Estimate Std. Error   z value    Pr(>|z|)
interval.f1:trt.f1 -4.811075   0.2131883 -22.56726 9.090518e-113
interval.f2:trt.f1 -4.826764   0.1796051 -26.87431 4.385988e-159
interval.f3:trt.f1 -4.826858   0.3015113 -16.00888 1.107909e-57
interval.f1:trt.f2 -4.456283   0.1825727 -24.40827 1.397279e-131
interval.f2:trt.f2 -4.927583   0.2131745 -23.11526 3.252023e-118
interval.f3:trt.f2 -5.552960   0.2886751 -19.23602 1.848808e-82
```

and exponentiate the coefficient and confidence intervals to get the incidence rates:

```
exp(cbind(coef(e.pois), confint(e.pois)))
```

```
Waiting for profiling to be done...
              2.5 %      97.5 %
interval.f1:trt.f1 0.008139105 0.005194146 0.012029059
interval.f2:trt.f1 0.008012406 0.005512570 0.011172997
interval.f3:trt.f1 0.008011653 0.004159865 0.013719853
interval.f1:trt.f2 0.011605416 0.007932257 0.016267460
interval.f2:trt.f2 0.007243991 0.004622910 0.010706140
interval.f3:trt.f2 0.003875969 0.002075417 0.006500046
```

Note that here because treatment is coded 1 and 2 (and not 0 and 1), using treatment as numeric does not (directly) lead to the log incidence rates:

```
e.pois2 <- glm(status ~ 0+interval.f+interval.f:trt, family = poisson(link="log"),
  offset = log(atrisk), data = veteranE)
logLik(e.pois2)
summary(e.pois2)$coef
```

```
'log Lik.' -316.1628 (df=6)
              Estimate Std. Error   z value    Pr(>|z|)
interval.f1      -5.1658668   0.4638208 -11.1376351 8.227506e-29
```

interval.f2	-4.7259453	0.4177025	-11.3141421	1.116895e-29
interval.f3	-4.1007567	0.6685579	-6.1337344	8.583980e-10
interval.f1:trt	0.3547917	0.2806814	1.2640372	2.062167e-01
interval.f2:trt	-0.1008188	0.2787496	-0.3616824	7.175894e-01
interval.f3:trt	-0.7261015	0.4174235	-1.7394837	8.194972e-02

6.12 Twin study

6.12.1 Data

```
head(mydf)
```

```
   grp pair nr    y
1    1    1  1 17.2
2    1    1  2 16.5
3    1    2  1 18.7
4    1    2  2 18.2
5    1    3  1 17.5
6    1    3  2 16.5
```

Move to wide format

```
library(reshape2)
mydfW <- dcast(mydf, id.vars = c("pair"), formula = pair+grp ~ nr, value.var = "y")
colnames(mydfW)[3:4] <- paste0("y", colnames(mydfW)[3:4])
head(mydfW)
```

```
   pair grp  y1  y2
1     1   1 17.2 16.5
2    10   1 18.6 20.0
3   100   2 23.9 21.6
4    11   1 19.4 20.1
5    12   1 18.3 19.5
6    13   1 19.3 20.5
```

6.12.2 REML solution

Estimation using a different residual correlation and variable for each group:

```
library(nlme)
e.lme <- lme(y ~ grp,
  random = list(pair = pdDiag(~grp-1)),
  weight = varIdent(form =~ 1|grp),
  data = mydf)
2*logLik(e.lme)
```

```
'log Lik.' -681.5524 (df=6)
```

Variance-covariance structure:

```
list(getVarCov(e.lme, indiv = 1, type = "marginal"),
     getVarCov(e.lme, indiv = 51, type = "marginal"))
```

```
[[1]]
pair 1
Marginal variance covariance matrix
      1      2
1 2.6521 1.7993
2 1.7993 2.6521
Standard Deviations: 1.6285 1.6285
```

```
[[2]]
pair 51
Marginal variance covariance matrix
      1      2
1 1.66730 0.51944
2 0.51944 1.66730
Standard Deviations: 1.2913 1.2913
```

Inference mean structure

```
## difference in mean between the two groups (H0: est.=0 i.e. equal means)
intervals(e.lme)$fixed["grp2",]
## better calculation of the degree of freedom for the mean comparison
library(emmeans)
summary(pairs(emmeans(e.lme, specs = ~grp), reverse = TRUE), infer = TRUE)
```

```
      lower      est.      upper
0.3937073 0.9050000 1.4162927
contrast estimate    SE df lower.CL upper.CL t.ratio p.value
2 - 1          0.905 0.258 98   0.394    1.42 3.513   0.0007
```

Degrees-of-freedom method: containment

Confidence level used: 0.95

Inference variance structure (WARNING: residual variance)

```
## ratio between the variances (H0: est.=1 i.e. equal variance)
as.data.frame(intervals(e.lme)$varStruct)
```

```
      lower      est.      upper
2 0.879652 1.160188 1.530192
```

Inference covariance/correlation structure

```
## standard deviation of the random effects
as.data.frame(intervals(e.lme)$reStruct)
## correlation
getCor <- function(x){
  tau <- intervals(x)$reStruct$pair[, "est." ]^2
  sigma2 <- c(1, intervals(x)$varStruct[, "est." ]^2)*sigma(x)^2
  c(tau/(sigma2+tau),
    diff(tau/(sigma2+tau)))
}
getCor(e.lme)
```

```
      pair.lower pair.est. pair.upper
sd(grp1) 1.0463670 1.3413858 1.719584
sd(grp2) 0.4505184 0.7207221 1.152984
[1] 0.6784453 0.3115382 -0.3669071
```

No straightforward solution for testing. Resampling is an option:

```
library(lmeresampler)
set.seed(10)
lmeresampler::bootstrap(e.lme, fn=getCor, type="parametric", B=100)
```

PARAMETRIC BOOTSTRAP

Call:

```
parametric_bootstrap.lme(model = model, fn = fn, B = B)
```

Bootstrap Statistics :

```
      original      bias      std. error
t1* 0.6784453 -0.04854023 0.08868033
t2* 0.3115382 0.05187772 0.12314478
t3* -0.3669071 0.10041795 0.11675326
```

6.12.3 ML solution

Estimation using a different residual correlation and variable for each group:

```
library(lava)
m1 <- lvm(y1[muGRP1:sigmaGRP1] ~ 1, y2[muGRP1:sigmaGRP1] ~ 1)
covariance(m1) <- y1~y2
m2 <- lvm(y1[muGRP2:sigmaGRP2] ~ 1, y2[muGRP2:sigmaGRP2] ~ 1)
covariance(m2) <- y1~y2

e.lvm <- estimate(list(m1,m2), data = split(mydfW, mydfW$grp))
2*logLik(e.lvm)
```

'log Lik.' -678.2732 (df=6)

Variance-covariance structure:

```
rbind(c(variance = coef(e.lvm)["y1~~y1@1"], covariance = coef(e.lvm)["y1~~y2@1"]),
      c(variance = coef(e.lvm)["y1~~y1@2"], covariance = coef(e.lvm)["y1~~y2@2"]))
```

```
      variance.y1~~y1@1 covariance.y1~~y2@1
[1,]          2.607600          1.754800
[2,]          1.645475          0.497575
```

Inference using delta-method:

```
estimate(e.lvm, robust = FALSE, f = function(x){
  c("mu1" = as.double(x["y1@1"]),
    "mu2" = as.double(x["y1@2"]),
    "mu2-mu1" = as.double(x["y1@2"]-x["y1@1"]),
    "sd1" = as.double(sqrt(x["y1~~y1@1"]-x["y1~~y2@1"])),
    "sd2" = as.double(sqrt(x["y1~~y1@2"]-x["y1~~y2@2"])),
    "sd2/sd1" = as.double(sqrt((x["y1~~y1@2"]-x["y1~~y2@2"])/(x["y1~~y1@1"]-x["y1~~y2@1"]))),
    "rho1" = as.double(x["y1~~y2@1"]/x["y1~~y1@1"]),
    "rho2" = as.double(x["y1~~y2@2"]/x["y1~~y1@2"]),
    "rho2-rho1" = as.double(x["y1~~y2@2"]/x["y1~~y1@2"]-x["y1~~y2@1"]/x["y1~~y1@1"])
  )
})
```

	Estimate	Std.Err	2.5%	97.5%	P-value
mu1	20.0600	0.20886	19.65063	20.46937	0.000e+00
mu2	20.9650	0.14639	20.67808	21.25192	0.000e+00
mu2-mu1	0.9050	0.25506	0.40510	1.40490	3.879e-04
sd1	0.9235	0.09235	0.74247	1.10447	1.524e-23
sd2	1.0714	0.10714	0.86141	1.28139	1.524e-23
sd2/sd1	1.1602	0.16408	0.83861	1.48177	1.537e-12
rho1	0.6730	0.07738	0.52130	0.82461	3.401e-18
rho2	0.3024	0.12849	0.05055	0.55423	1.860e-02
rho2-rho1	-0.3706	0.14999	-0.66454	-0.07659	1.349e-02

By hand:

```
library(numDeriv)
fn <- function(x){ c("mu1" = as.double(x["y1@1"]),
  "mu2" = as.double(x["y1@2"]),
  "mu2-mu1" = as.double(x["y1@2"]-x["y1@1"]),
  "var1" = as.double(x["y1~~y1@1"]),
  "sd1" = as.double(sqrt(x["y1~~y1@1"]-x["y1~~y2@1"])),
  "sd2" = as.double(sqrt(x["y1~~y1@2"]-x["y1~~y2@2"])),
  "sd2/sd1" = as.double(sqrt((x["y1~~y1@2"]-x["y1~~y2@2"])/(x["y1~~y1@1"]-x["y1~~y2@1"]))),
  "rho1" = as.double(x["y1~~y2@1"]/x["y1~~y1@1"]),
  "rho2" = as.double(x["y1~~y2@2"]/x["y1~~y1@2"]),
  "rho2-rho1" = as.double(x["y1~~y2@2"]/x["y1~~y1@2"]-x["y1~~y2@1"]/x["y1~~y1@1"]
  )
  ) }
dfn <- jacobian(fn, coef(e.lvm), method="Richardson")
cbind(fn(coef(e.lvm)),sqrt(diag(dfn %*% vcov(e.lvm) %*% t(dfn))))
```

	[,1]	[,2]
mu1	20.0600000	0.20886359
mu2	20.9650000	0.14639160
mu2-mu1	0.9050000	0.25505784
var1	2.6076000	0.44449749
sd1	0.9234717	0.09234717
sd2	1.0714010	0.10714010
sd2/sd1	1.1601882	0.16407538
rho1	0.6729560	0.07737590
rho2	0.3023899	0.12848984
rho2-rho1	-0.3705661	0.14998890

7 Loops and parallel computations

7.1 Apply with progress bar

```
ls.res <- pbapply::pblapply(1:5, FUN = rnorm)
```

```
| 0 % ~calculating  
|+++++++| 20% ~00s  
|+++++++| 40% ~00s  
|+++++++| 60% ~00s  
|+++++++| 80% ~00s  
|+++++++| 100% elapsed = 00s
```


7.2 Parallel computation

7.2.1 Detect the number of cores

```
cores <- parallel::detectCores()
cores
```

```
[1] 4
```

7.2.2 Start a cluster

```
cpus <- 2

cl <- snow::makeSOCKcluster(cpus)
doSNOW::registerDoSNOW(cl)
```

7.2.3 Get the name of each core

```
cpus.name <- unlist(parallel::clusterCall(cl = cl, function(x){
  myName <- paste(Sys.info()[['nodename']], Sys.getpid(), sep='-')
  return(myName)
})))
cpus.name
```

```
[1] "SUND31034-5800" "SUND31034-5992"
```

7.2.4 Export element to cluster

```
parallel::clusterExport(cl, varlist = "cpus.name")

parallel::clusterCall(cl = cl, function(x){
  indexCPU <- which(cpus.name == paste(Sys.info()[['nodename']], Sys.getpid(), sep='-'))
  indexCPU
})
```

```
[[1]]
```

```
[1] 1
```

```
[[2]]
```

```
[1] 2
```

7.2.5 Show progress bar (in console)

```
n.sim <- 20

pb <- txtProgressBar(max = n.sim, style=3)
opts <- list(progress = function(n) setTxtProgressBar(pb, n))

ls.res <- foreach::"%dpar%“(
  foreach::foreach(i=1:n.sim, .options.snow=opts), {
    Sys.sleep(0.1)
  })
```

7.2.6 Show progress bar (external)

```
n.sim <- 20
parallel::clusterExport(cl, varlist = "n.sim")

ls.res <- foreach::"%dpar%“(
  foreach::foreach(iCpus=1:cpus), {
    pb <- tcltk::tkProgressBar(paste0("CPU ",iCpus), min = 0, max = n.sim, initial = 0)

    for(iSim in 1:n.sim){
      Sys.sleep(0.1)
      tcltk::setTkProgressBar(pb = pb, value = iSim,
        label = paste(iSim, " over ",n.sim," iterations done") )
    }

    close(pb)
  })
```

7.2.7 Stop a cluster

```
parallel::stopCluster(cl)
```

7.2.8 Parallel computation in C++

<https://github.com/boennecd/pedmod/blob/main/src/r-api.cpp>

Header:

```
#ifdef _OPENMP
#include <omp.h>
#endif
```

```
#ifdef _OPENMP
#pragma omp parallel num_threads(n_threads)
{
```

```
#endif

#ifdef _OPENMP
#pragma omp for schedule(static) reduction(+:n_fails)
#endif

for(int i = 0; i < all_idx.size(); ++i){
    n_fails += did_fail;
}

#ifdef _OPENMP
}
#endif
```

8 *lava* package

8.1 Generate repeated measurements

Model: Simulation:

```
set.seed(10)
dfW.data <- sim(m, n = 102, latent = FALSE)
```

Display simulated data:

```
head(dfW.data)
```

	weight_t1	Gender	Treatment	weight_t2	weight_t3	size_t1	size_t2	size_t3	Age	Id
1	49.59633	Male	Yes	56.62904	55.58780	50.66805	55.88362	61.69410	39.54546	1
2	52.35484	Female	No	56.68563	63.21026	50.26003	55.72930	60.36953	37.70748	2
3	46.53011	Male	No	54.36636	62.05018	46.61315	50.89281	56.52237	40.80342	3
4	48.48417	Female	Yes	54.79413	59.72995	45.95248	53.09941	59.82107	40.94933	4
5	52.17022	Female	Yes	55.71550	64.21010	52.86341	58.40516	63.79082	42.06512	5
6	52.18837	Male	Yes	58.86797	64.51316	49.36853	57.90530	64.45437	37.68392	6

Modify simulated data

```
dtW.data <- as.data.table(dfW.data)
dtW.data[,paste0("weight_t",1:3)] := lapply(.SD,round),
  .SDcols = paste0("weight_t",1:3)]
dtW.data[,paste0("size_t",1:3)] := lapply(.SD,round, digit = 2),
  .SDcols = paste0("size_t",1:3)]
dtW.data[,Age := round(Age)]

setcolorder(dtW.data, c("Id","Age","Gender","Treatment",
  paste0("weight_t",1:3),paste0("size_t",1:3)))
head(dtW.data)
```

	Id	Age	Gender	Treatment	weight_t1	weight_t2	weight_t3	size_t1	size_t2	size_t3
1:	1	40	Male	Yes	50	57	56	50.67	55.88	61.69
2:	2	38	Female	No	52	57	63	50.26	55.73	60.37
3:	3	41	Male	No	47	54	62	46.61	50.89	56.52
4:	4	41	Female	Yes	48	55	60	45.95	53.10	59.82
5:	5	42	Female	Yes	52	56	64	52.86	58.41	63.79
6:	6	38	Male	Yes	52	59	65	49.37	57.91	64.45

Export data:

```
fwrite(dtW.data, file = "./mydata.csv", sep = ";", dec = ",")
fwrite(dtW.data, file = "./mydata.txt", sep = " ", dec = ".")
```

8.2 Generate data with heteroschadasticity

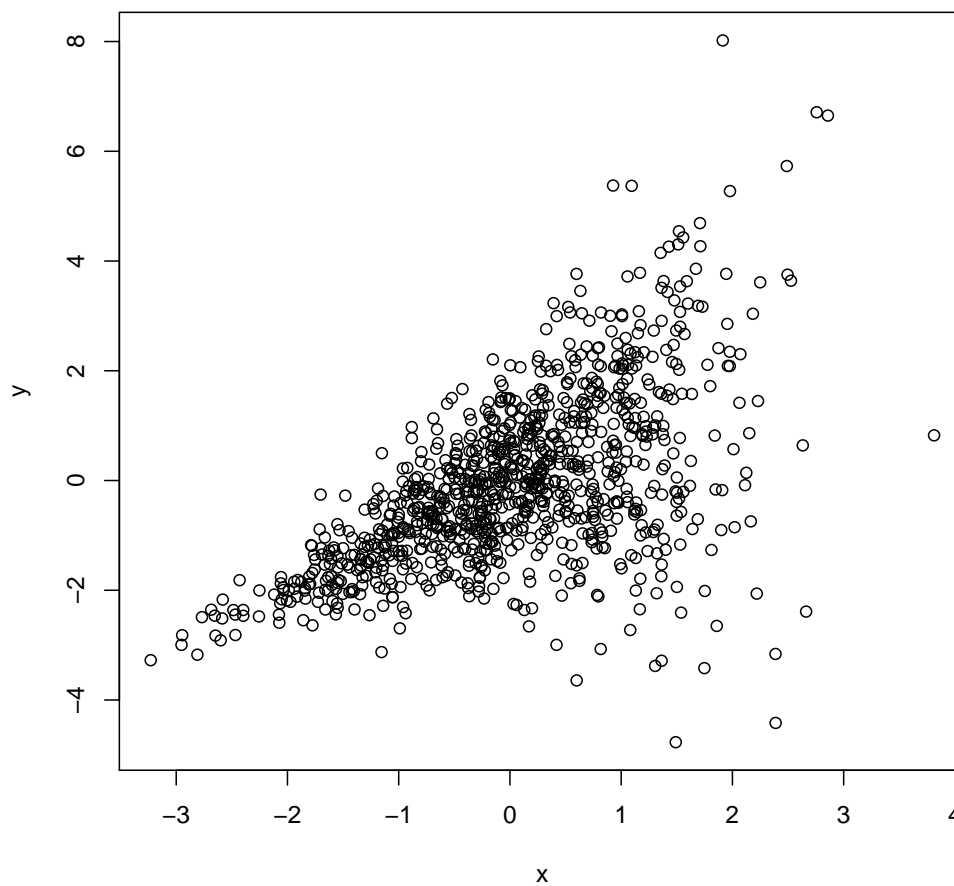
Model:

```
mSim <- lvm(y[m:v]~x)
constrain(mSim, v ~ x + a + b) <- function(x){ x[,2] + x[,3] * exp(x[,1]) }
parameter(mSim, start = c(0,1)) <- ~ a + b
```

Simulation:

```
set.seed(10)
n <- 1e3
df.tempo <- sim(mSim, n = n)
```

Display:



8.3 Generate survival time under non proportional hazard (non-PH)

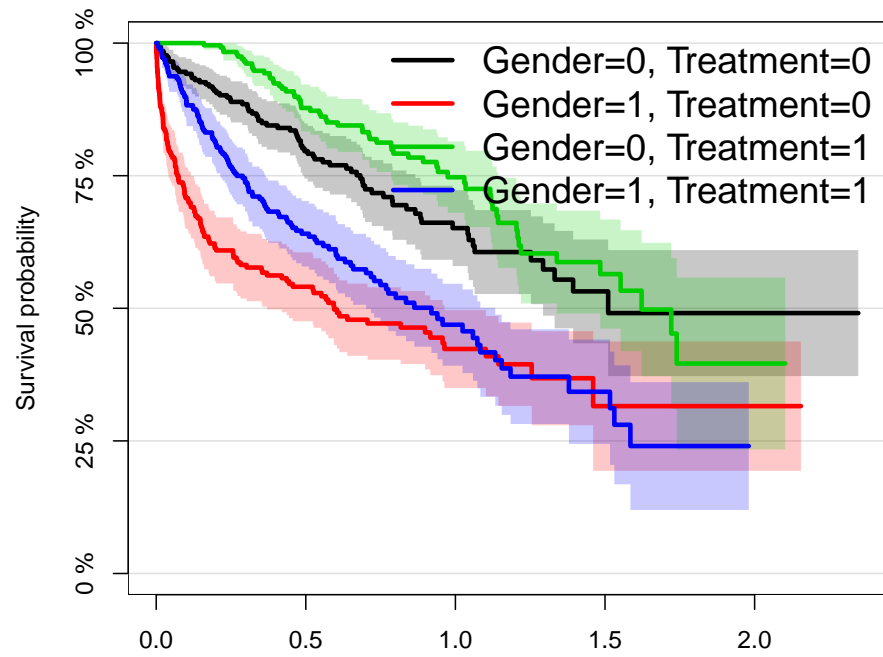
Model:

```
mSim <- lvm()
regression(mSim) <- eventtime ~ Gender + Age
regression(mSim) <- s ~ exp(0.6 * Treatment - 0.5 * Gender)
distribution(mSim, ~ Treatment + Gender) <- binomial.lvm()
distribution(mSim, ~ cens) <- coxWeibull.lvm(scale = 1)
distribution(mSim, ~ eventtime) <- coxWeibull.lvm(scale = 0.3, shape = ~ s)
eventTime(mSim) <- time ~ min(eventtime = 1, cens = 0)
```

Simulation:

```
set.seed(10)
n <- 1e3
df.tempo <- sim(mSim, n = n)
```

Display:



Gender	Time										
0, Treatment:	259	216	173	107	73	45	24	10	7	2	1
1, Treatment:	236	139	99	68	43	21	8	5	1	1	0
0, Treatment:	249	234	174	128	81	49	31	14	5	0	0
1, Treatment:	256	190	120	79	46	25	12	5	1	0	0

8.4 Generate survival time with delayed treatment effect

Generative model with non-PH group effect but no Age effect:

```
rates1 <- c(0.25,0.5,0.1); cuts <- c(0,3,5)
rates2 <- c(0.25,0.1,0.1); cuts <- c(0,3,5)
lasttime <- 20

m1 <- lvm(Age[50:5]~1)
m2 <- lvm(Age[50:5]~1)
distribution(m1,~eventtime) <- coxExponential.lvm(rate=rates1,timecut=cuts)
distribution(m2,~eventtime) <- coxExponential.lvm(rate=rates2,timecut=cuts)
transform(m1,status~eventtime) <- function(x){as.numeric(x[,1]<= lasttime)}
transform(m2,status~eventtime) <- function(x){as.numeric(x[,1]<= lasttime)}
transform(m1,time~eventtime) <- function(x){pmin(lasttime,x[,1])}
transform(m2,time~eventtime) <- function(x){pmin(lasttime,x[,1])}
latent(m1) <- ~eventtime
latent(m2) <- ~eventtime
```

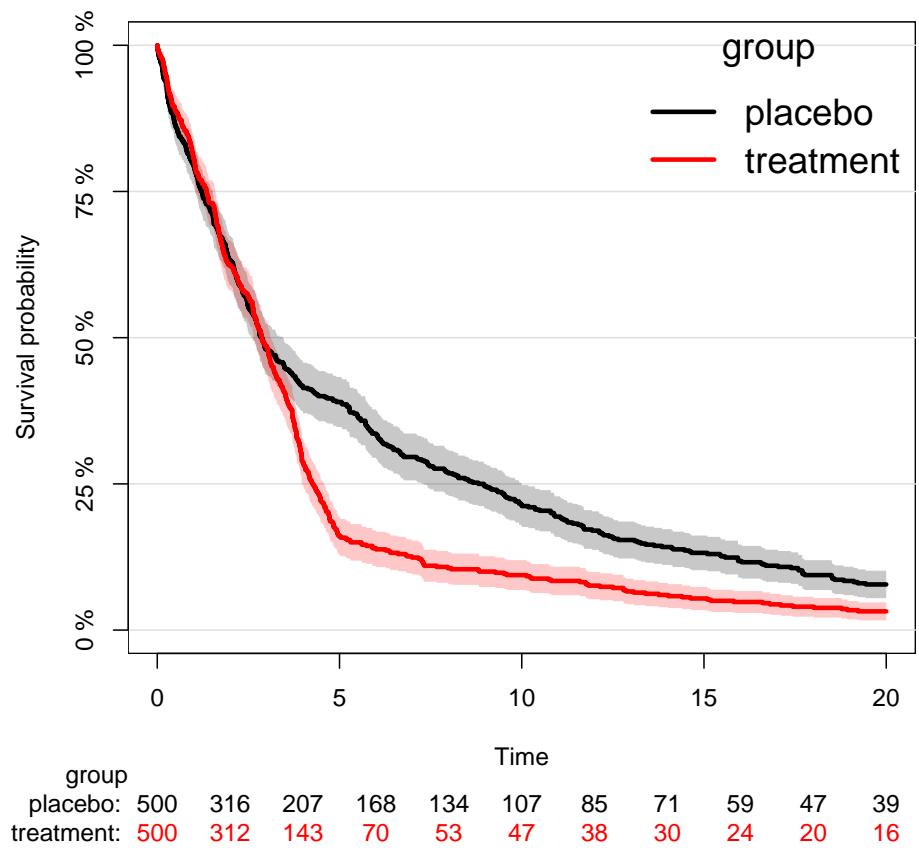
Simulate data:

```
set.seed(12)
n <- 500
d1 <- as.data.table(sim(m1,n,latent=FALSE))
d2 <- as.data.table(sim(m2,n,latent=FALSE))
dt.data <- rbind(cbind(d1,group="treatment"),cbind(d2,group="placebo"))
dt.data
```

	Age	status	time	group
1:	46.68935	1	3.8755119	treatment
2:	53.52666	1	3.2816799	treatment
3:	47.86065	1	0.8515517	treatment
4:	47.94281	1	10.1313180	treatment
5:	45.53314	1	2.6198951	treatment

996:	46.47948	1	2.1560011	placebo
997:	52.78256	1	6.6831242	placebo
998:	45.10627	1	6.0589065	placebo
999:	49.24545	1	12.5248064	placebo
1000:	49.08839	1	1.9096902	placebo

Display survival curves by group:



8.5 Tune optimization parameters

```
library(lava)
set.seed(10)
dd <- sim(lvm(Y~X1+X2+X3), 100)
ee <- estimate(lvm(Y~X1+X2+X3+eta), data = dd, control = list(trace = 1, iter.max = 200))
```

```
0:      260.69531: -0.00392152  0.00000  0.00000  0.00000  0.00000  1.89517  1.19723  0.900000
1:      232.00124: -0.0200212 -0.0305115  0.473562  0.497905  0.592152  1.80796  1.17166  0.808180
2:      202.02739: -0.0397653 -0.0662080  0.941194  0.998447  1.03587  1.47069  1.05604  0.430261
3:      189.85429: -0.0476622 -0.0778219  0.942488  0.999840  1.03679  1.27746  0.902950  0.0991273
4:      188.92755: -0.0488980 -0.0794005  0.942488  0.999840  1.03679  1.26451  0.851417  0.0150308
5:      188.92730: -0.0489067 -0.0794116  0.942488  0.999840  1.03679  1.26448  0.850633  0.0137765
6:      188.92730: -0.0489067 -0.0794116  0.942488  0.999840  1.03679  1.26448  0.850633  0.0137765
Warning messages:
1: In estimate.lvm(lvm(Y ~ X1 + X2 + X3 + eta), data = dd, control = list(trace = 1)) :
  Lack of convergence. Increase number of iteration or change starting values.
2: In sqrt(diag(asVar)) : NaNs produced
```

8.6 Output correlation between two endogenous variables

Simulate some data:

```
library(lava)
mSim <-lvm(c(gene1,gene2,gene3,gene4,gene5)~expression,
  expression~score)
covariance(mSim) <- gene2 ~ gene3
latent(mSim) <- ~expression

set.seed(10)
d <- lava::sim(mSim, n = 400, latent = FALSE)
```

Fit the lvm:

```
m <- mSim
e <- lava::estimate(m, data = d)
```

Estimate correlation via *lava*:

```
cov2cor(attr(predict(e), "cond.var"))
```

```
      gene1    gene2    gene3    gene4    gene5
gene1 1.0000000 0.5236249 0.5204666 0.4945280 0.5354561
gene2 0.5236249 1.0000000 0.7623392 0.4711268 0.5101182
gene3 0.5204666 0.7623392 1.0000000 0.4682851 0.5070414
gene4 0.4945280 0.4711268 0.4682851 1.0000000 0.4817718
gene5 0.5354561 0.5101182 0.5070414 0.4817718 1.0000000
```

Estimate correlation via `lvmCov2Cor` (only correlation through the latent variable):

```
lvmCov2Cor(e, var1 = "gene1", var2 = "gene2")
```

	variable	estimate	se	lower	upper	null	p.value
variance 1	gene1	2.0942854	0.13667200	1.8264133	2.3621576	NA	NA
variance 2	gene2	2.2976185	0.14862591	2.0063171	2.5889200	NA	NA
direct covariance	(gene1,gene2)	0.0000000	0.00000000	0.0000000	0.0000000	0	NaN
total covariance	(gene1,gene2)	1.1486221	0.10851604	0.9359345	1.3613096	0	0
direct correlation	(gene1,gene2)	0.0000000	0.00000000	0.0000000	0.0000000	0	NaN
total correlation	(gene1,gene2)	0.5236249	0.03010923	0.4646119	0.5826379	0	0

Estimate correlation via `lvmCov2Cor` (direct and indirect correlation):

```
lvmCov2Cor(e, var1 = "gene2", var2 = "gene3")
```

	variable	estimate	se	lower	upper	null	p.value
variance 1	gene2	2.2976185	0.14862591	2.0063171	2.5889200	NA	NA
variance 2	gene3	1.9920357	0.12875100	1.7396884	2.2443830	NA	NA
direct covariance	(gene2,gene3)	0.5701469	0.08197808	0.4094728	0.7308210	0	3.528955e-12
total covariance	(gene2,gene3)	1.6309317	0.12469211	1.3865396	1.8753237	0	0.000000e+00
direct correlation	(gene2,gene3)	0.2665012	0.03458231	0.1987212	0.3342813	0	1.287859e-14
total correlation	(gene2,gene3)	0.7623392	0.02017803	0.7227910	0.8018874	0	0.000000e+00

Estimate the correlation via *lava* (manual version):

```
estimate(e, function(x){
  var.gene1 <- x["gene1~~gene1"] + x["expression~~expression"]
  var.gene2 <- x["gene2~~gene2"] + x["gene2~expression"]^2 * x["expression~~expression"]
  cov.gene12 <- x["gene2~expression"] * x["expression~~expression"]
  c(var.gene1 = var.gene1,
    var.gene2 = var.gene2,
    cov = cov.gene12,
    cor = cov.gene12/sqrt(var.gene1 * var.gene2))
})
```

	Estimate	Std.Err	2.5%	97.5%	P-value
var.gene1.gene1~~gene1	2.0943	0.13327	1.8331	2.3555	1.191e-55
var.gene2.gene2~~gene2	2.2976	0.14104	2.0212	2.5741	1.163e-59
cov.gene2~expression	1.1486	0.10913	0.9347	1.3625	6.600e-26
cor.gene2~expression	0.5236	0.03115	0.4626	0.5847	2.024e-63

8.7 Output correlation between two latent variables

Simulate some data:

```
library(lava)
mSim <- lvm(c(PEQ_poslife, PEQ_posself, PEQ_posmood, PEQ_possoc, PEQ_posbehav) ~ lv.peq,
  c(MEQ_mystical, MEQ_mood) ~ 1*lv.meq,
  c(MEQ_timespace, MEQ_ineffability) ~ lv.meq,
  lv.meq[0:2] ~ 1,
  lv.peq[0:0.25] ~ 1)
covariance(mSim) <- lv.peq ~ lv.meq
covariance(mSim) <- MEQ_timespace ~ MEQ_ineffability
latent(mSim) <- ~lv.peq + lv.meq

set.seed(10)
d <- sim(mSim, n = 40, latent = FALSE)
```

Fit the lvm:

```
m1 <- lvm(c(PEQ_poslife, PEQ_posself, PEQ_posmood, PEQ_possoc, PEQ_posbehav) ~ lv.peq,
  c(MEQ_mystical, MEQ_mood) ~ 1*lv.meq,
  c(MEQ_timespace, MEQ_ineffability) ~ lv.meq)
covariance(m1) <- lv.peq ~ lv.meq
covariance(m1) <- MEQ_timespace ~ MEQ_ineffability
latent(m1) <- ~lv.peq
latent(m1) <- ~lv.meq
e <- estimate(m1, d)
```

Estimate the correlation via *lava*:

```
estimate(e, function(x){
  c(var.meq = x["lv.meq~~lv.meq"],
    var.peq = x["lv.peq~~lv.peq"],
    cov = x["lv.peq~~lv.meq"],
    cor = x["lv.peq~~lv.meq"]/sqrt(x["lv.peq~~lv.peq"]*x["lv.meq~~lv.meq"]))
})
```

	Estimate	Std.Err	2.5%	97.5%	P-value
var.meq.lv.meq~~lv.meq	2.4150	0.6270	1.18606	3.6439	0.0001174
var.peq.lv.peq~~lv.peq	0.1808	0.1133	-0.04126	0.4030	0.1105233
cov.lv.peq~~lv.meq	0.4022	0.1885	0.03268	0.7717	0.0329009
cor.lv.peq~~lv.meq	0.6086	0.1638	0.28748	0.9296	0.0002034

Estimate the correlation via *lvmCov2Cor*:

```
lvmCov2Cor(e, var1 = "lv.meq", var2 = "lv.peq", robust = TRUE)
```

	variable	estimate	se	lower	upper
variance 1	lv.meq	2.4149694	0.6270062	1.18605985	3.6438789
variance 2	lv.peq	0.1808441	0.1133218	-0.04126259	0.4029509
direct covariance	(lv.meq,lv.peq)	0.4021716	0.1885216	0.03267591	0.7716672

total covariance	(lv.meq,lv.peq)	0.4021716	0.1885216	0.03267591	0.7716672
direct correlation	(lv.meq,lv.peq)	0.6085599	0.1638215	0.28747555	0.9296442
total correlation	(lv.meq,lv.peq)	0.6085599	0.1638215	0.28747555	0.9296442
	null		p.value		
variance 1	NA		NA		
variance 2	NA		NA		
direct covariance	0	0.032900854			
total covariance	0	0.032900854			
direct correlation	0	0.000203386			
total correlation	0	0.000203386			

8.8 Handling left, right, and interval censored data

Simulate data:

```
n <- 10000
tau <- c(left = -2, right = 2)

set.seed(10)
X <- rnorm(n)
Y <- rnorm(n, mean = X)
df <- data.frame(Y=Y,X=X)
```

Right censoring:

```
df$YobsR <- pmin(Y,tau["right"])
df$censR <- Y>tau["right"]

df$SurvR <- Surv(df$YobsR,df$censR==FALSE, type = "right")

rbind(naive = coef(lm(YobsR ~ X, data = df)),
      corrected = coef(estimate(lvm(SurvR ~ X), df))[1:2])
```

```
              (Intercept)              X
naive         -0.07039338  0.9290829
corrected -0.02081243  1.0065446
```

Left censoring:

```
df$YobsL <- pmax(Y,tau["left"])
df$censL <- Y< (tau["left"])

df$SurvL <- Surv(df$YobsL,df$censL==FALSE, type = "left")

rbind(naive = coef(lm(YobsL ~ X, data = df)),
      corrected = coef(estimate(lvm(SurvL ~ X), df))[1:2])
```

```
              (Intercept)              X
naive          0.03314233  0.9150299
corrected -0.02171591  0.9991420
```

Interval censoring:

```
df$Yobs <- pmax(pmin(Y,tau["right"]),tau["left"])
df$Surv <- Surv(time = ifelse(df$censL,-Inf,df$YobsR),
  time2 = ifelse(df$censR,+Inf,df$YobsL),
  type = "interval2")

rbind(naive = coef(lm(Yobs ~ X, data = df)),
      corrected = coef(estimate(lvm(Surv ~ X), df))[1:2]) ## FAILS
```

8.9 LVM as a weighted mean

Simulate some data:

```
library(lava)

mSim <- lvm(coldPain ~ 0.1*age + 1*etaPain,
           heatPain ~ 0.1*age + 2*etaPain,
           musclePain ~ 0.1*age + 0.5*etaPain,
           tolerancePain ~ 0.1*age + 2*etaPain,
           etaPain ~ status)
latent(mSim) <- ~etaPain
distribution(mSim, ~status) <- binomial.lvm()
## distribution(mSim, ~coldPain+heatPain+musclePain+tolerantcePain) <- Gamma.lvm(rate = 2,
##                                         shape = 10)
distribution(mSim, ~age) <- gaussian.lvm(mean = 30, sd = 5)

set.seed(10)
d <- sim(mSim, 1e3, latent = FALSE)
```

Estimate LVM with constraints on the latent variable:

```
m <- lvm(coldPain ~ age + etaPain,
        heatPain ~ age + etaPain,
        musclePain ~ age + etaPain,
        tolerancePain ~ age + etaPain,
        etaPain ~ status)
latent(m) <- ~etaPain
e <- estimate(m, data = d)
```

Extract fitted latent variable values:

```
LV.predict <- predict(e, x = manifest(e), y = latent(e))
c(tapply(LV.predict, d$status, mean), coef(e)["etaPain~status"])
```

0	1	etaPain~status
0.01286411	0.92152131	0.90865707

Manually compute weights:

```
## residuals
epsilon <- residuals(e)
## all coef
e.allCoef <- summary(e)$coef[, "Estimate"]
## variance-covariance matrices matrices
lambda <- e.allCoef[paste0(endogenous(e), "~", latent(e))]
mu <- e.allCoef[endogenous(e)]
tau <- e.allCoef[paste0(latent(e), "~", latent(e))]
sigma <- e.allCoef[paste0(endogenous(e), "~", endogenous(e))]

Sigma22 <- tcrossprod(lambda)*tau + diag(sigma)
Sigma12 <- rbind(lambda*tau)
weight <- Sigma12 %*% solve(Sigma22)
weight
```

```
      [,1]      [,2]      [,3]      [,4]
[1,] 0.1108541 0.2186568 0.04547272 0.1854233
```

and values of the latent variable:

```
nu <- e.allCoef[latent(e)]
Gamma <- as.double(e.allCoef[paste0(latent(e), "~status")]) %*% d$status)

LV.manual <- nu + Gamma + as.double(weight %*% t(epsilon))
range(LV.manual - LV.predict)
```

```
[1] -1.332268e-15  6.217249e-15
```

8.10 Standardized coefficients

"The standardized coefficients in the last column are interpreted as the change in standard deviation of the outcome when increasing the predictor one standard deviation" (Holst 2013).

Simulate some data:

```
library(data.table);library(lava)
mSim <- lvm(Y1~X+1*eta,Y2~X+2*eta,Y3~X+3*eta)
latent(mSim) <- ~eta
n <- 2500
set.seed(10)
d <- sim(mSim, n=n, latent = FALSE)
```

Linear regression:

```
## by hand
e <- estimate(lvm(Y1~Y2+Y3), data = d)
coef(e)["Y1~Y2"]*sd(d$Y2)/sd(d$Y1)
## via the dataset
eS <- estimate(lvm(Y1~Y2+Y3), data = scale(d))
as.data.frame(coef(eS, std = "xy", type = 9))[1,,drop=FALSE]
```

```
      Y1~Y2
0.4167574
      Estimate Std. Error Z-value    P-value    std.xy
Y1~Y2 0.4167574 0.02738807 15.21675 2.73795e-52 0.4167574
```

LVM with saturated variance model:

```
m <- lvm(Y1~X+eta,Y2~X+eta,Y3~X+eta)
latent(m) <- ~eta

## by hand
e <- estimate(m, data = d)
coef(e)["Y1~X"]*sd(d$X)/sd(d$Y1)

## via the dataset
eS <- estimate(m, data = scale(d))
as.data.frame(coef(eS, std = "xy", type = 9))[1,,drop=FALSE]

## in that case the marginal variance equals the modelled one
c(model=coef(e)["Y1~~Y1"]+coef(e)["eta~~eta"]+var(d$X)*coef(e)["Y1~X"]^2,
  marginal=var(d$Y1))
## minor difference due to /(n-1) instead of /n in var
```

```
      Y1~X
0.5858683
      Estimate Std. Error Z-value    P-value    std.xy
Y1~X 0.5858683 0.01620812 36.14658 4.209965e-286 0.5858683
model.Y1~~Y1      marginal
      3.033911      3.034709
```

Non-saturated LVM:

```
m <- lvm(Y1~X+1*eta,Y2~X+1*eta,Y3~X+1*eta)
latent(m) <- ~eta

## by hand
e <- estimate(m, data = d)
coef(e)["Y1~X"]*sd(d$X)/sd(d$Y1)
coef(e)["Y1~X"]*sd(d$X)/sqrt(coef(e)["Y1~~Y1"]+coef(e)["eta~~eta"]+var(d$X)*coef(e)["Y1
~X"]^2)
as.data.frame(coef(e, std = "xy", type = 9))[1,,drop=FALSE]

## real difference between modeled and marginal variance
c(model=coef(e)["Y1~~Y1"]+coef(e)["eta~~eta"]+var(d$X)*coef(e)["Y1~X"]^2,
  marginal=var(d$Y1))
```

```
      Y1~X
0.5858683
      Y1~X
0.5645535
      Estimate Std. Error  Z-value      P-value    std.xy
Y1~X 0.9977775 0.02918153 34.19209 3.169765e-256 0.5644766
model.Y1~~Y1      marginal
      3.268187      3.034709
```

After re-scaling the data, not sure what the std.xy:

```
eS <- estimate(m, data = scale(d))
as.data.frame(coef(eS, std = "xy", type = 9))[1,,drop=FALSE]
```

```
      Estimate Std. Error  Z-value      P-value    std.xy
Y1~X 0.5858683 0.02003958 29.23556 6.852072e-188 0.5047583
```

is though.

9 Miscellaneous

9.1 Profile code R

```
library(lava)
m <- lvm(Y ~ X + G)
FUN <- function(n){
  d <- lava::sim(m, n = n)
  estimate(m,d)
}
```

`#+RESULTS[<2019-06-27 to 09:37> a0d5077301cabedce939985d9ce7fb7eb9072578]:`

```
profvis::profvis(FUN(n = 500))
profvis::profvis(FUN(n = 5000))
profvis::profvis(FUN(n = 50000))
```

`[1] 14.9 16.4 31.4 81.2`

```
Rprof(tf <- "rprof.log", memory.profiling=TRUE)
xx <- FUN(n=500000)
Rprof(NULL)
max(summaryRprof(tf, memory = "both")$by.total$mem.total)
```

`[1] 129.8`

9.2 Profile code C

`R -d "valgrind --tool=cachegrind" -f myfile.R` `R -d "valgrind --tool=callgrind" -f myfile.R` <https://kcachegrind.github.io/html/Home.html>

9.3 Debug

To not show too many lines before debug:

```
options(deparse.max.lines = 200)
```

To show at which line in the program an error occurred:

```
options(error = function() revTraceback(max.lines = 5))
```

9.4 Find all function names from a package

```
r <- unclass(lsf.str(envir = asNamespace("lava"), all = T))  
r[grepl("coef", r)]
```

```
[1] "coef.CrossValidated"  "coef.effects"        "coef.estimate"       "coef.estimate.list"  
[5] "coef.lvm"             "coef.lvm.mixture"    "coef.lvmfit"         "coef.multigroup"  
[9] "coef.multigroupfit"   "coef.multinomial"    "coef.ordreg"         "coef.pcor"  
[13] "coef.summary.estimate" "coef.summary.lvmfit"  "coef.twostageCV"     "coef.zibreg"  
[17] "describecoef"         "excoef"              "stdcoef"
```

9.5 Install development version of R

<https://cran.r-project.org/bin/windows/base/rdevel.html>

9.6 Install suggested packages

```
char.package <- utils::packageDescription("butils", fields = "Suggests")
vec.package <- unlist(strsplit(gsub("[[:blank:]]", "", charPackage), split = ","))
install.packages(vec.package)
```

9.7 R version

```
sessionInfo()
```

```
R version 3.5.1 (2018-07-02)
```

```
Platform: x86_64-w64-mingw32/x64 (64-bit)
```

```
Running under: Windows 7 x64 (build 7601) Service Pack 1
```

```
Matrix products: default
```

```
locale:
```

```
[1] LC_COLLATE=Danish_Denmark.1252 LC_CTYPE=Danish_Denmark.1252 LC_MONETARY=Danish_Denmark.1252  
[4] LC_NUMERIC=C LC_TIME=Danish_Denmark.1252
```

```
attached base packages:
```

```
[1] parallel stats graphics grDevices utils datasets methods base
```

```
other attached packages:
```

```
[1] ggpubr_0.2 magrittr_1.5 officer_0.3.2 Publish_2018.04.17 lava_1.6.5  
[6] doSNOW_1.0.16 snow_0.4-3 iterators_1.0.10 foreach_1.4.4 pbapply_1.3-4  
[11] multcomp_1.4-8 TH.data_1.0-9 MASS_7.3-50 mvtnorm_1.0-8 survival_2.44-1.1  
[16] prodlim_2018.04.18 car_3.0-2 carData_3.0-2 ggplot2_3.1.0 data.table_1.12.0
```

```
loaded via a namespace (and not attached):
```

```
[1] Rcpp_1.0.1 lattice_0.20-35 visNetwork_2.0.4 zoo_1.8-4 assertthat_0.2.0  
[6] digest_0.6.17 R6_2.3.0 cellranger_1.1.0 plyr_1.8.4 pillar_1.3.1  
[11] rlang_0.3.1 lazyeval_0.2.1 curl_3.2 readxl_1.1.0 uuid_0.1-2  
[16] Matrix_1.2-14 labeling_0.3 splines_3.5.1 stringr_1.3.1 foreign_0.8-70  
[21] htmlwidgets_1.3 munsell_0.5.0 compiler_3.5.1 pkgconfig_2.0.2 base64enc_0.1-3  
[26] htmltools_0.3.6 tidyselect_0.2.5 gridExtra_2.3 tibble_2.0.1 rio_0.5.10  
[31] codetools_0.2-15 viridisLite_0.3.0 crayon_1.3.4 dplyr_0.7.8 withr_2.1.2  
[36] grid_3.5.1 jsonlite_1.5 gtable_0.2.0 scales_1.0.0 zip_1.0.0  
[41] stringi_1.2.4 ggthemes_4.0.1 bindrcpp_0.2.2 xml2_1.2.0 sandwich_2.5-0  
[46] cowplot_0.9.3 openxlsx_4.1.0 tools_3.5.1 forcats_0.3.0 glue_1.3.0  
[51] purrr_0.3.0 hms_0.4.2 yaml_2.2.0 abind_1.4-5 colorspace_1.3-2  
[56] bindr_0.1.1 haven_1.1.2
```

9.8 Install a package from a zip file (windows)

```
install.packages("package_version.zip", repos = NULL, type = "win.binary")
```

9.9 Install and load two version of the same package

Install

```
devtools::install_github("bozenne/BuyseTest") ## v1
install.packages("http://cran.r-project.org/src/contrib/Archive/BuyseTest/BuyseTest_1.0.tar.gz",
  lib = "C:/Users/hpl802/Downloads/LIBRTEMPO", type = "source", repos = NULL)
```

Load

```
library(BuyseTest) ## v1
detach("package:BuyseTest", unload = TRUE)
library(BuyseTest, lib.loc="C:/Users/hpl802/Downloads/LIBRTEMPO") ## v2
detach("package:BuyseTest", unload = TRUE)
```

9.10 CRAN check rocker

<https://www.brodieg.com/2018/04/06/adventures-in-r-and-compiled-code/>

```
docker run -rm -ti -v $(pwd):/mydir wch1/r-debug RDvalgrind -e "install.packages('/mydir/fansi0.2.1.tar.gz')"  
RDvalgrind -d valgrind # and run tests  
RDcsan  
wget -O - https://github.com/bozenne/BuyseTest/tarball/master | tar xz
```