Code together: From messy data to insightful visualizations –part 2

R-Ladies Frankfurt Meetup #5

8th of August 2019

Artificial HIV-dataset

- Source: Github https://github.com/NFilmann/RLadiesFRA
  - Datasets basedata.csv, labdata.csv

Use `readr::read_delim` or `readr::read_csv2` for import

```
library(tidyverse)
labdata <-
read_delim("https://raw.githubusercontent.com/NFilmann/RLadies
FRA/master/labdata.csv", delim=";")
```

Which factors are associated with therapeutic success?

- Therapeutic success in HIV-positive individuals, defined as
  - Primary goal is virologic response:, i.e. reduction of the viral load to an undetectable level below <20 copies per ml) by 24 weeks after start of treatment
  - CD4 cell counts: Key measure of immune status; they should rise 50 to 100 cells per ml in the first year of therapy (a CD4 count < 200 is defined as AIDS).

Source:
https://en.wikipedia.org/wiki/Management_of_HIV/AIDS#Response_to_therapy

basedata

```
> glimpse(basedata)

Observations: 1,299

Variables: 15

$ PatientID        <dbl> 1, 2, 3,
4, 5, 6, 7, 8, 9, 10, 11,...

$ DateOfBirth      <chr>
"17.02.1944", "02.06.1966", ...

$ Start_therapy    <chr>
"09.09.2015", "24.07.2014",
"13.06.2...

$ Gender           <chr> "male",
"male", "male", "male", ...

$ StudyCenter      <dbl> 1, 1, 1,
1, 1, 1, 1, 1, 1, 1...

$ DateOfDiagnosis <chr>
"01.01.1985", "01.01.1989", ...
```

continued

```
$ DateOfDeath      <chr> NA, NA,
NA, NA, NA, NA, NA, ...

$ PreMedication    <chr> "N", "N",
"N", "N", "Y", "N",...

$ HBVpos           <chr> NA, NA,
NA, "Y", NA, NA, "...

$ HCVpos           <chr> NA, NA,
NA, NA, NA, NA, NA, NA,...

$ MedID1           <dbl> 1, 1, 2,
4, 2, 1, 2, 2, 4, 2, 2...

$ MedID2           <dbl> 3, 4, 1,
7, 1, 2, 1, 1, 2, 1, 1...
```

(MedID3, MedID4, MedID5 accordingly)

Variables in basedata

PatientID: patient ID

DateOfBirth: date of birth (dd.mm.yyyy)

Start_therapy: begin of therapy (dd.mm.yyyy)

Gender: gender

StudyCenter: study center (the hospital or medical practice) where the patient was treated

DateOfDiagnosis: date when HIV was diagnosed (dd.mm.yyyy)

DateOfDeath: if date available (dd.mm.yyyy), it depicts the date of death. NA indicates the patient is still alive.

PreMedication: Y indicates that patient has received HIV-specific treatment before, N that not.

HBVpos: Y indicates patient is infected with hepatitis B as well. NA indicates that no hepatitis B infection was diagnosed.

HCVpos: Y indicates patient is infected with hepatitis C as well. NA indicates that no hepatitis C infection was diagnosed.

MedID1, MedID2,…, MedID5: HIV specific medications coded as numbers (1-14). Note that combination treatment with three up to five medications is common.

labdata

```
> glimpse(labdata)
Observations: 7,794
Variables: 7
$ PatientID       <dbl> 1, 1, 1, 1, 1, 1, 2, 2, 2, 2, 2, 2, 3, 3, 3, 3, 3,
3, 4, 4, 4, 4...
$ Time_weeks      <dbl> 0, 4, 8, 12, 16, 24, 0, 4, 8, 12, 16, 24, 0, 4, 8,
12, 16, 24, 0...
$ Test            <chr> "CD4", "CD4", "CD4", "CD4", "CD4", "CD4", "CD4",
"CD4", "CD4", "...
$ Value           <dbl> 354, 595, 427, 699, 606, 660, 64, 102, 152, 112,
141, 172, 146, ...
$ Test_1          <chr> "HIVPCR", "HIVPCR", "HIVPCR", "HIVPCR", "HIVPCR",
"HIVPCR", "HIV...
$ TErgNumOperator <chr> NA, NA, NA, NA, NA, NA, NA, NA, "<", NA, "<", "<",
NA, NA, NA, "...
$ TErgNum         <dbl> 500, 49, 97, 31, 49, 23, 2840000, 3670, 20, 23, 20,
20, 3136, 38...
```

Variables in labdata

`PatientID`: patient ID

`Time_weeks`: measuring time (in weeks), start of therapy = 0

`Test`: Type of lab value (here `CD4`), corresponds to `Value`

`Value`: CD4 value (cells per ml)

`Test_1`: Type of lab value (here `HIVPCR`), corresponds to `TErgNumOperator` and `TErgNum`

`TErgNumOperator`: `<` indicates if corresponding viral load in `TErgNum` is below a certain value, e.g. `<20` indicates the viral load is below `20` copies per ml, the limit of quantification

`TErgNum`: viral load copies per ml (HIV)

Steps to tidy the data

1. Join both datasets
2. Make sure that each observation corresponds to one row
3. Calculate the patient age at start of therapy
4. Calculate a new variable „`virResponse`“ indicating if thrapeutic success (i.e. viral load <20 copies/ml) is reached 24 weeks after start of therapy

   (How do you deal with patients that died before end of treatment?)
5. Recode `HBVpos` and `HCVpos` in a meaningful way

See Github https://github.com/NFilmann/RLadiesFRA for the sample solution (Tidy.R) to have the dataset ready for plotting!!

Sample code for tidying the data

```
library(tidyverse)
#Import the data
labdata <-
read_delim("https://raw.githubusercontent.com/NFilmann/RLadiesFRA/master/labdata.csv", delim=";")
basedata <-
read_delim("https://raw.githubusercontent.com/NFilmann/RLadiesFRA/master/basedata.csv", delim=";")

#Have a look at the data
str(labdata)
str(basedata)


# 1. Join both datasets
# The primary key in each table is the variable PatientID

# At first we assure, that we have no missing values in PatientID
summary(unique(labdata$PatientID))
summary(basedata$PatientID)
#-> no missings, and the IDs match

HIVdata <- full_join(labdata, basedata)
str(HIVdata)

# 2. Make sure that each observation corresponds to one row

HIVdata=split(labdata, labdata$Time_weeks) %>%
  reduce(left_join, by = "PatientID") %>%
  full_join(basedata, .)
str(HIVdata)

HIVdata <- HIVdata %>% rename_all(funs(str_replace(., ".y.y.y",
".24"))) %>%
  rename_all(funs(str_replace(., ".x.x.x", ".16"))) %>%
  rename_all(funs(str_replace(., ".y.y", ".12"))) %>%
  rename_all(funs(str_replace(., ".x.x", ".8"))) %>%
  rename_all(funs(str_replace(., ".y", ".4"))) %>%
  rename_all(funs(str_replace(., ".x", ".0")))


HIVdata <- HIVdata %>% rename_all(funs(str_replace(., "Start_thera.4",
"Start_therapy"))) %>%
  rename_all(funs(str_replace(., "Stu.4Center", "StudyCenter")))

str(HIVdata)
```

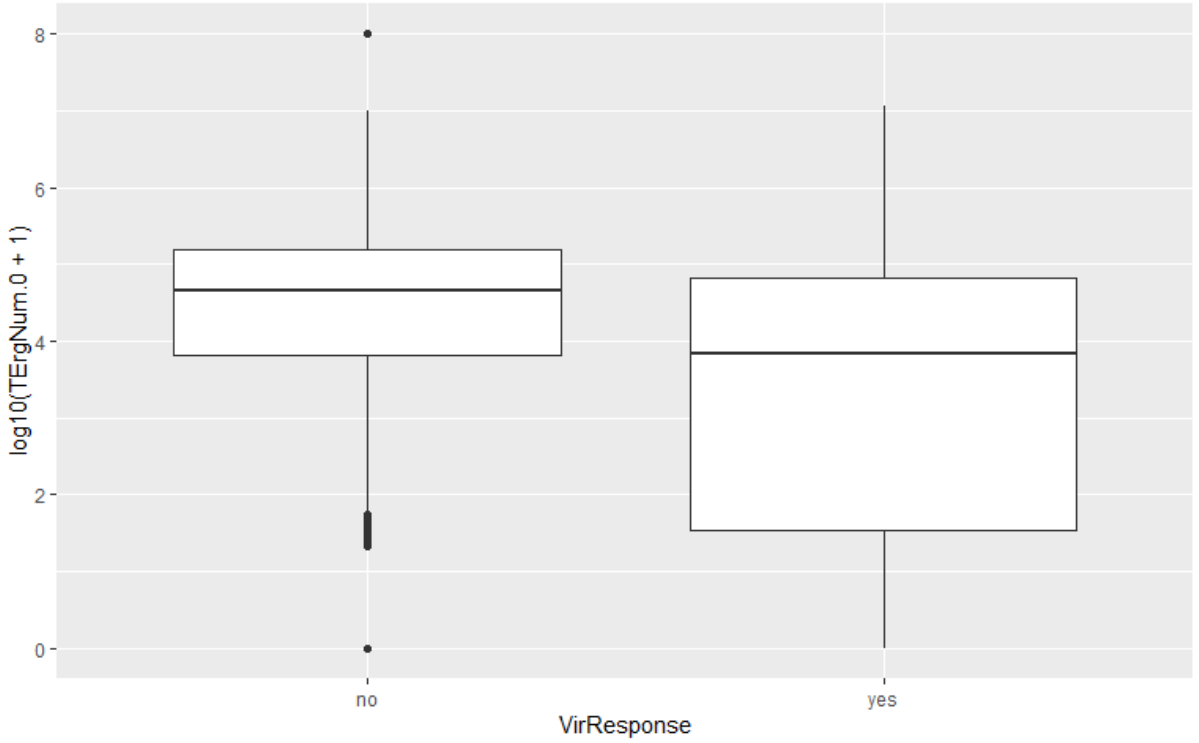
```
# 3. Calculate the patient age at start of therapy
HIVdata <-HIVdata %>% mutate(HIVdata,
Age=((difftime(as.Date(HIVdata$Start_therapy, format="%d.%m.%Y"),
as.Date(HIVdata$DateOfBirth, format="%d.%m.%Y"))))) %>%
  mutate(Age=as.numeric(round(Age/365.25,0)))
str(HIVdata)


# 4&5. Calculate a new variable „VirResponse“ indicating if thrapeutic
success (i.e. viral load <20 copies/ml) is reached 24 weeks after
start of therapy
# Recode HBVpos and HCVpos in a meaningful way

#For VirResponse you could use simply the variable
"TErgNumOperator.24", where an "<" indicates that the
#treatment was succesful
HIVdata <-HIVdata  %>% mutate(
                    VirResponse =
                    as.numeric(!is.na(TErgNumOperator.24)),
                    HBVpos = as.numeric(!is.na(HBVpos)),
                    HCVpos = as.numeric(!is.na(HCVpos)))


#labeling the variables in a meaningful way
HIVdata <-HIVdata %>%
  mutate(VirResponse = recode(VirResponse,  "0" = "no", "1" = "yes"),
         HBVpos = recode(HBVpos,  "0" = "neg", "1" = "pos"),
         HCVpos = recode(HCVpos,  "0" = "neg", "1" = "pos"))

# #Labeling the variable names
HIVdata <-HIVdata %>%
  mutate(VirResponse = structure(VirResponse, label = "Virologic
                  Response"),
  TErgNum.0 = structure(TErgNum.0, label = "Viral load at baseline"),
  Value.0 = structure(Value.0, label = "CD4 at baseline"),
  HBVpos = structure(HBVpos, label = "HBV pos"),
  HCVpos = structure(HCVpos, label = "HCV pos"))

str(HIVdata)
#(How do you deal with patients that died before end of treatment?)
#They don't have any lab values at week 24, so they are already taken
into account.


#Of course we could go on here, for example the variables, that
contain the medication are a mess,
#but we rather look at some plots now.
```

Now it‘s your turn – plot the data

- 1. Make a boxplot between baseline viral load and Virologic response,
  - b) stratify also for gender

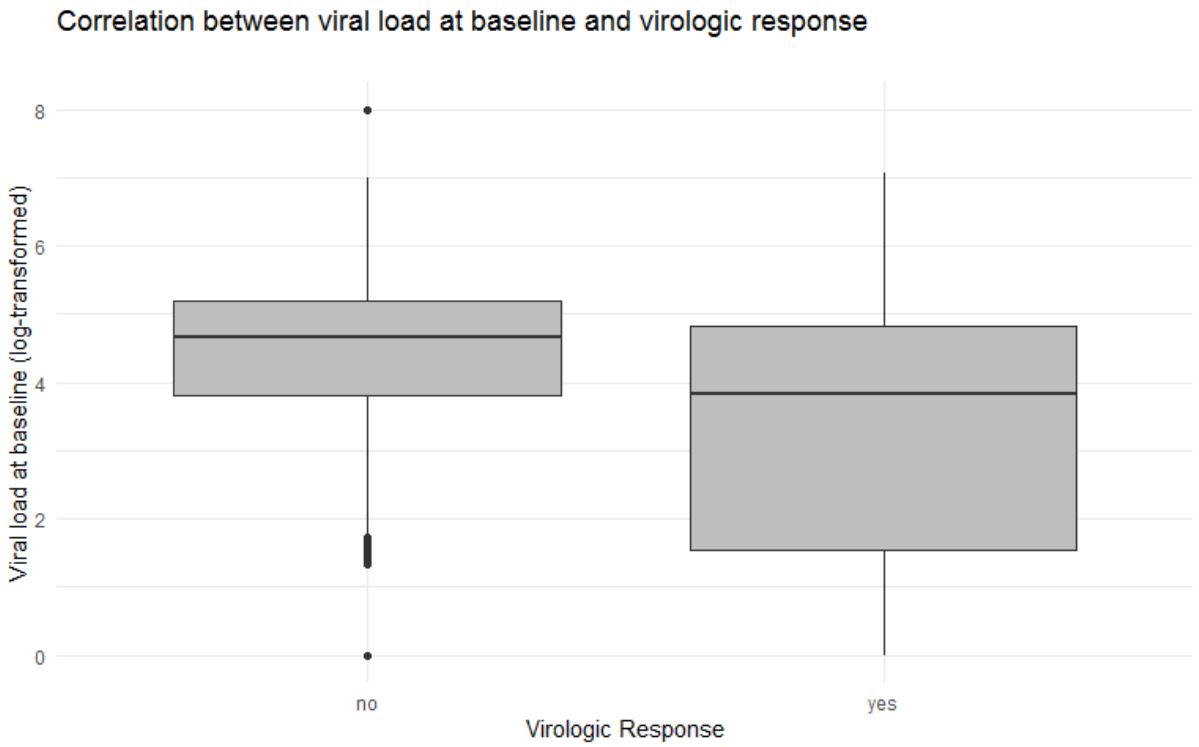
Basic boxplot

```
ggplot( data = HIVdata ) +
  aes(x = VirResponse, y = log10(TErgNum.0+1))+
  geom_boxplot()
```



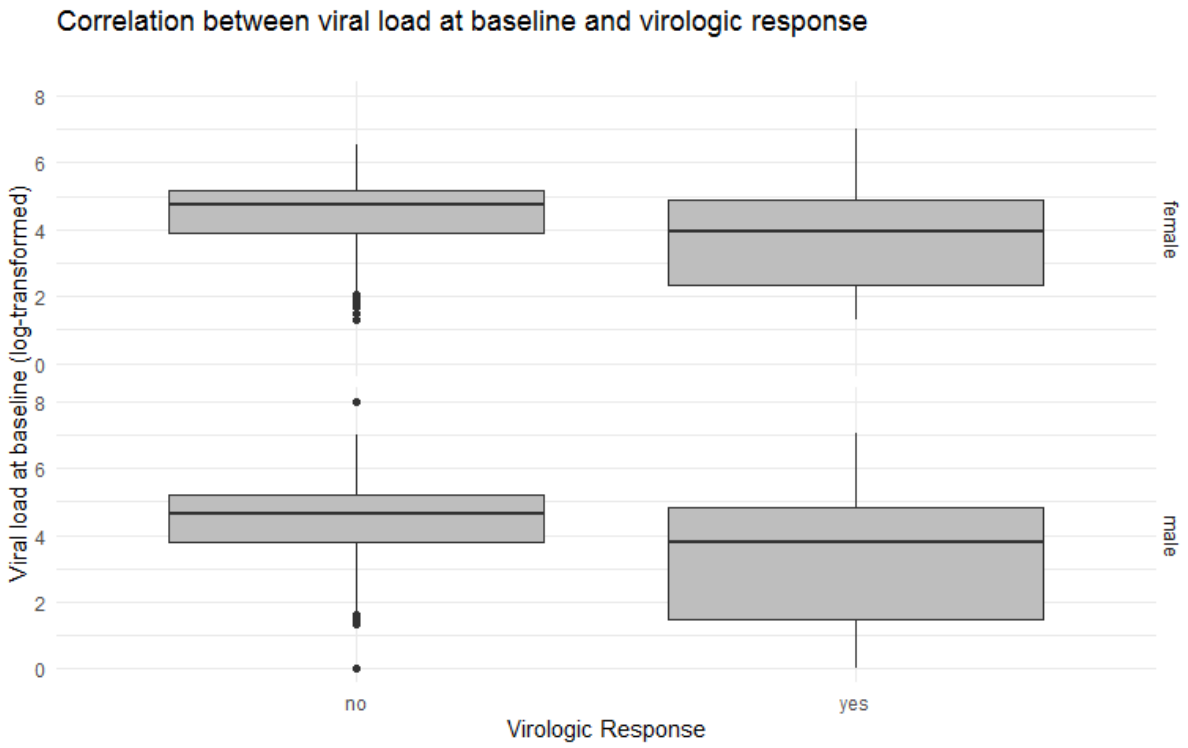
Boxplot with more features

```
ggplot( data = HIVdata ) +
  aes(x = VirResponse, y = log10(TErgNum.0+1))+
  geom_boxplot(fill = "grey")+
  theme_minimal()+
  ggtitle("Correlation between viral load at baseline and virologic response") +
  xlab(attributes(HIVdata$VirResponse)$label) +
  ylab(paste(attributes(HIVdata$TErgNum.0)$label, "(log-transformed)"))
```



Boxplot – stratified for gender

```
ggplot( data = HIVdata ) +
  aes(x = VirResponse, y = log10(TErgNum.0+1))+
  facet_grid(rows = vars(Gender))+
  geom_boxplot(fill = "grey")+
  theme_minimal()+
  ggtitle("Correlation between viral load at baseline and virologic response") +
  xlab(attributes(HIVdata$VirResponse)$label) +
  ylab(paste(attributes(HIVdata$TErgNum.0)$label, "(log-transformed)"))
```

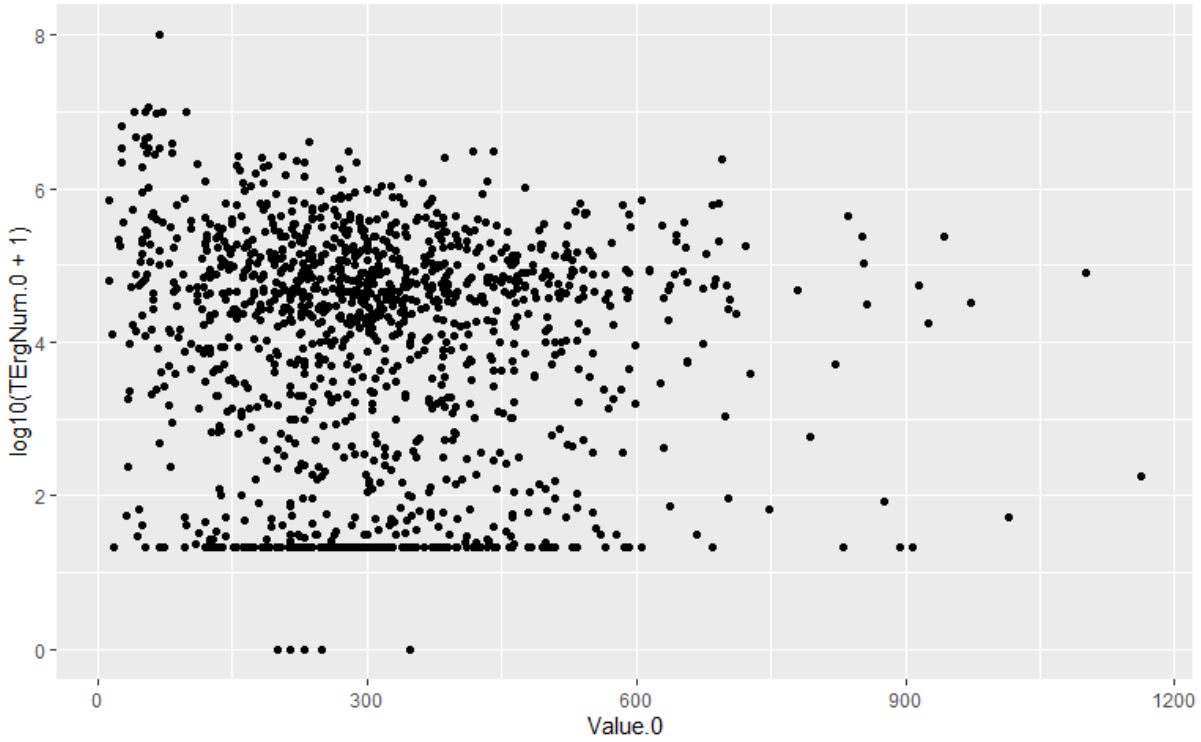


Plot the data

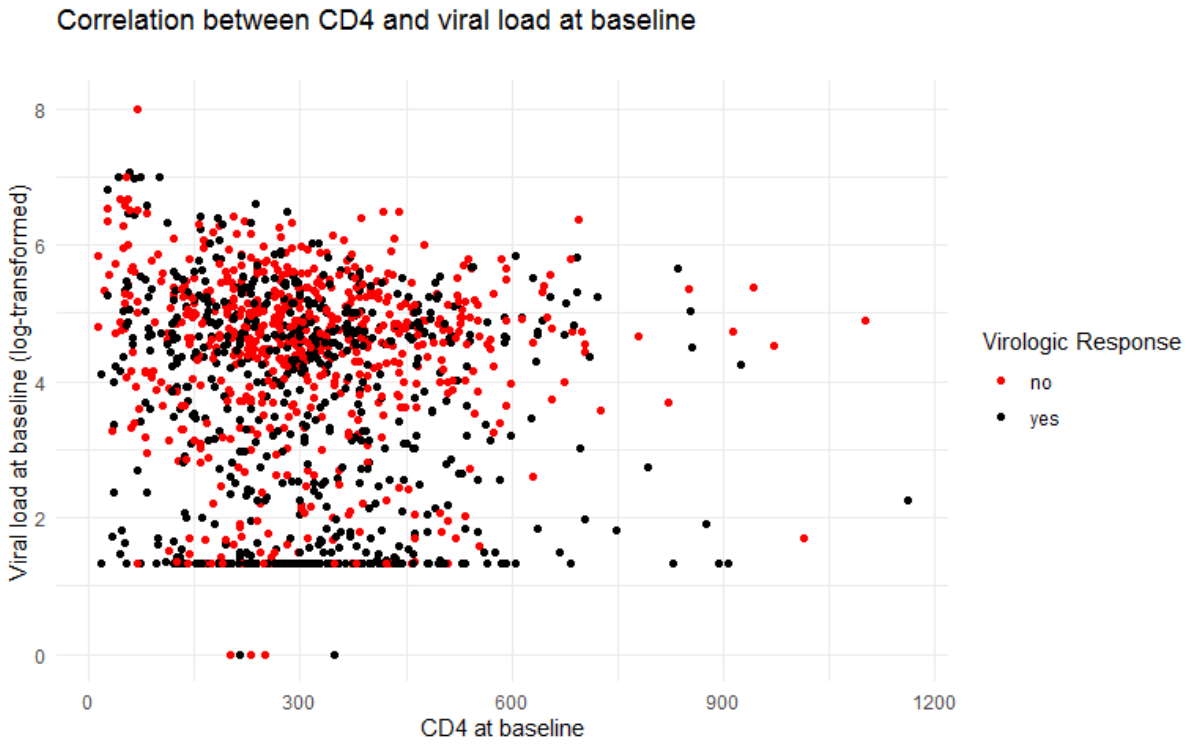
- 2. Use a scatterplot to visualize the correlation between baseline CD4 and baseline viral load

Basic scatterplot

```
ggplot( data = HIVdata ) +
  aes(x = Value.0, y = log10(TErgNum.0+1))+
  geom_point()
```



```
ggplot( data = HIVdata ) +
  aes(x = Value.0, y = log10(TErgNum.0+1), color=VirResponse)+
  geom_point()+
  theme_minimal()+
  ggtitle("Correlation between CD4 and viral load at baseline", subtitle = " ") +
  xlab(attributes(HIVdata$Value.0)$label) +
  ylab(paste(attributes(HIVdata$TErgNum.0)$label, "(log-transformed)"))+
  scale_color_manual(values=c("red", "black"))+
  labs(color=  xlab(attributes(HIVdata$VirResponse)$label))
  #geom_smooth(span = 1.5)
```

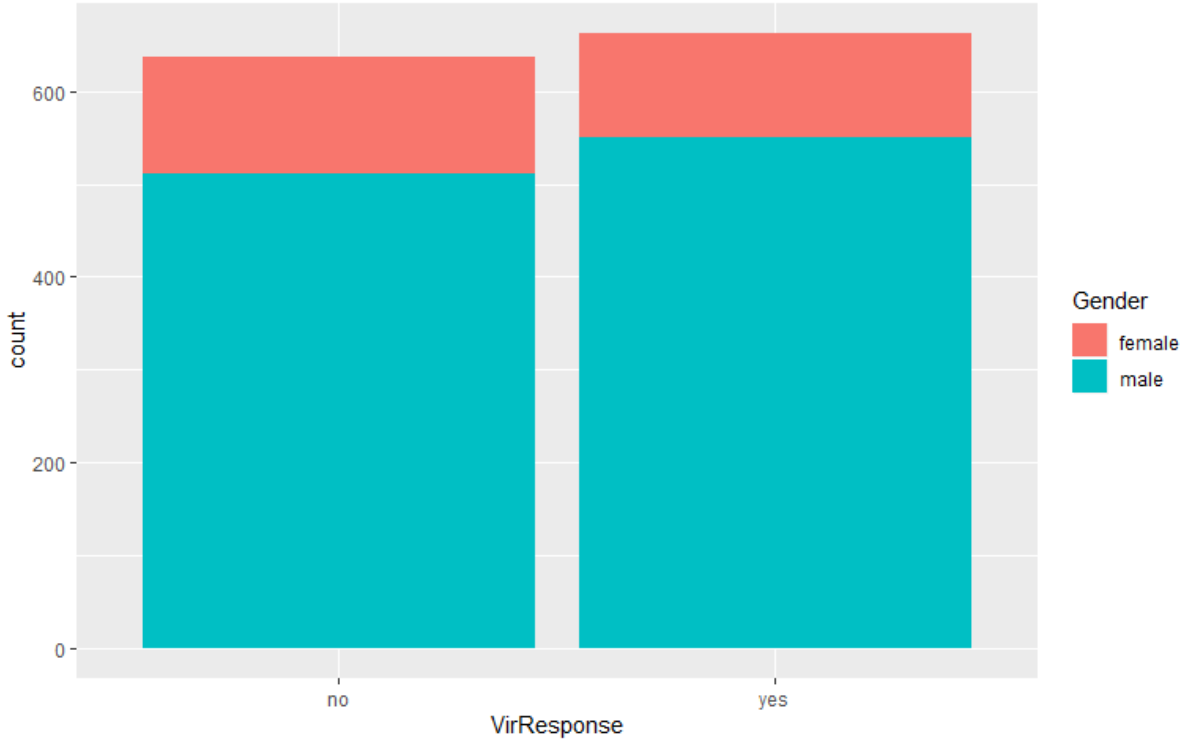


Plot the data

- 3. Visualize with barplots the association between gender and therapeutic response,
  - b) and between HCV- + HBV-status and therapeutic response

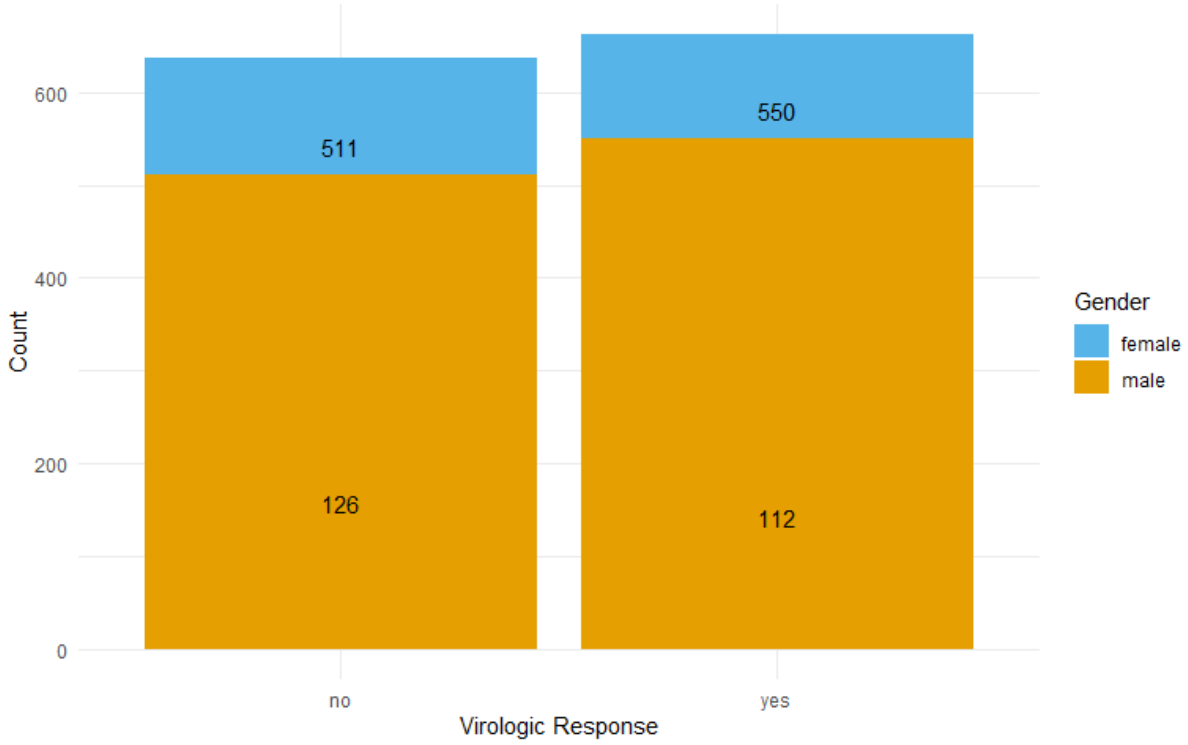
Basic barplot

```
ggplot( data = HIVdata ) +
  aes(  x = VirResponse, fill = Gender)+
  geom_bar()
```



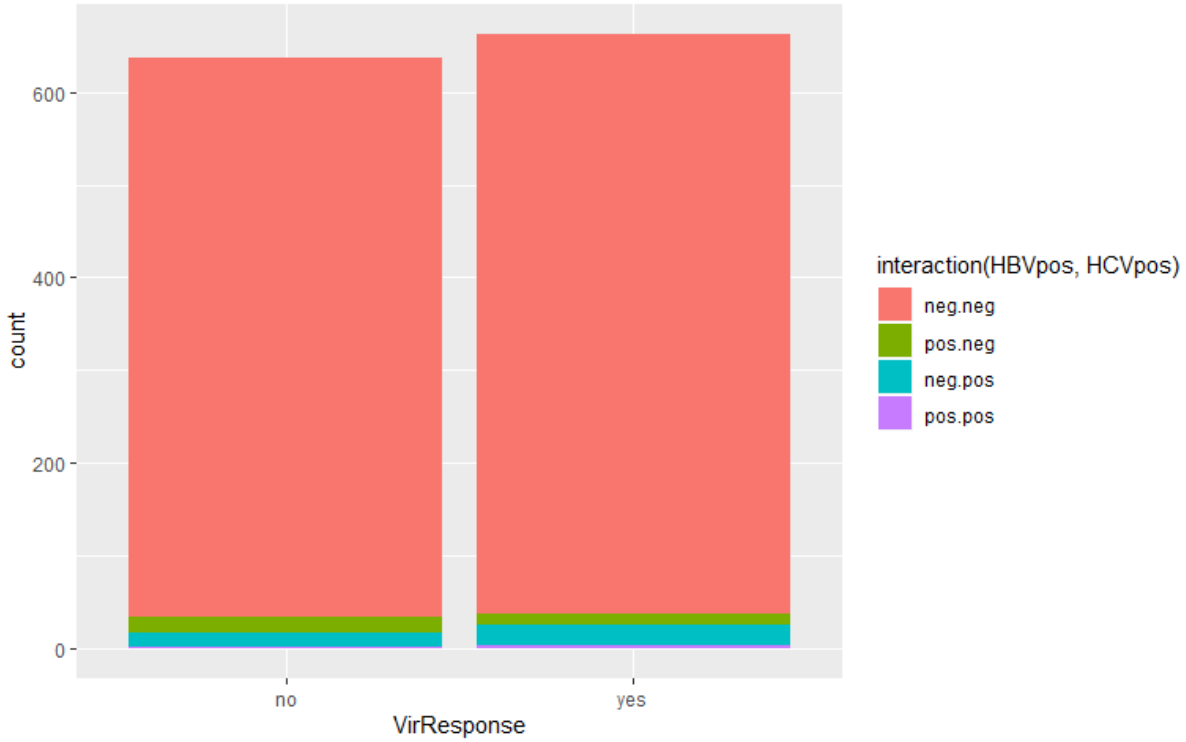
Barplot with more features

```
ggplot( data = HIVdata ) +
  aes(  x = VirResponse, fill = Gender)+
  geom_bar(show.legend = TRUE)+
  theme_minimal()+
  scale_fill_manual(values=c("#56B4E9", "#E69F00"))+
  geom_text(stat='count', aes(label=..count..), vjust=-1)+
  xlab(attributes(HIVdata$VirResponse)$label) +
  ylab("Count")
```

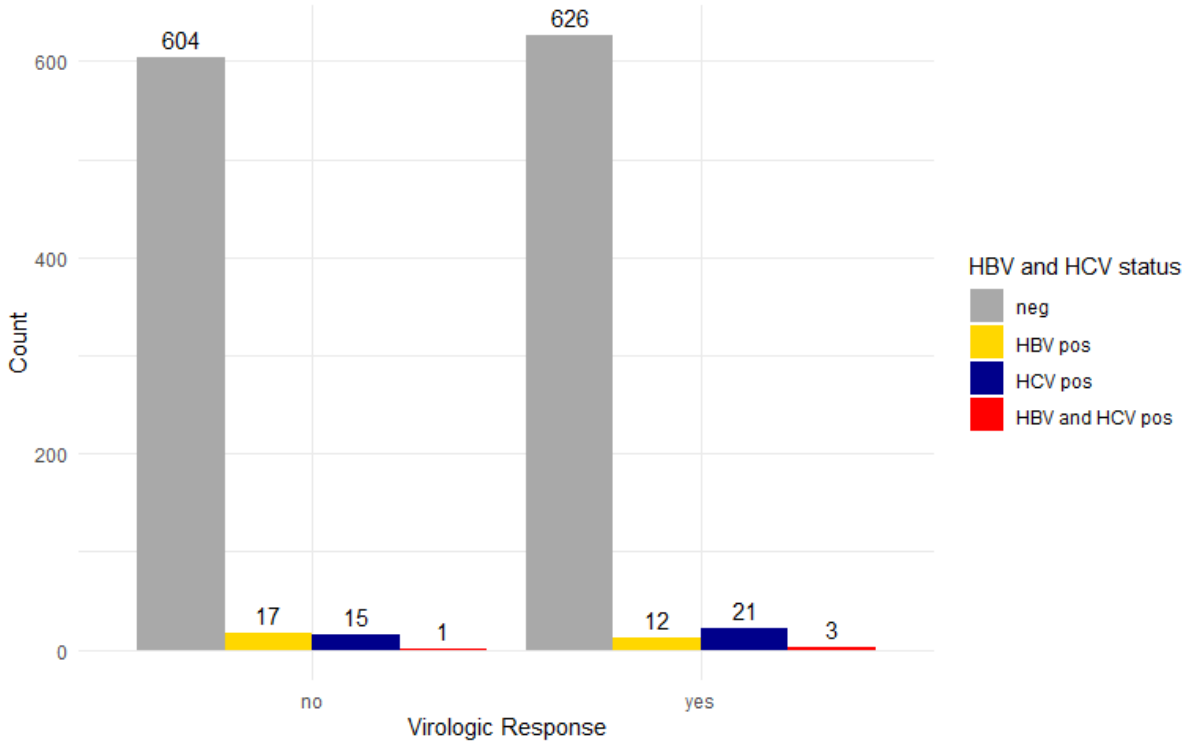


Barplot – association between HBV-HCV-status and treatment success

```
ggplot(data = HIVdata) +
  aes(  x = VirResponse, fill = interaction(HBVpos, HCVpos))+
  geom_bar(show.legend = TRUE)
```



```
ggplot(data = HIVdata) +
  aes(  x = VirResponse, fill = interaction(HBVpos, HCVpos))+
  geom_bar(show.legend = TRUE, position ="dodge")+
  labs(fill="HBV and HCV status")+
  scale_fill_manual(labels = c("neg", "HBV pos", "HCV pos", "HBV and HCV pos"), values
= c("darkgrey", "gold","darkblue", "red"))+
  theme_minimal()+
  geom_text(stat = 'count', aes(label=..count..),
            position = position_dodge(.9),
            vjust = -0.5) +
  xlab(attributes(HIVdata$VirResponse)$label) +
  ylab("Count")
```



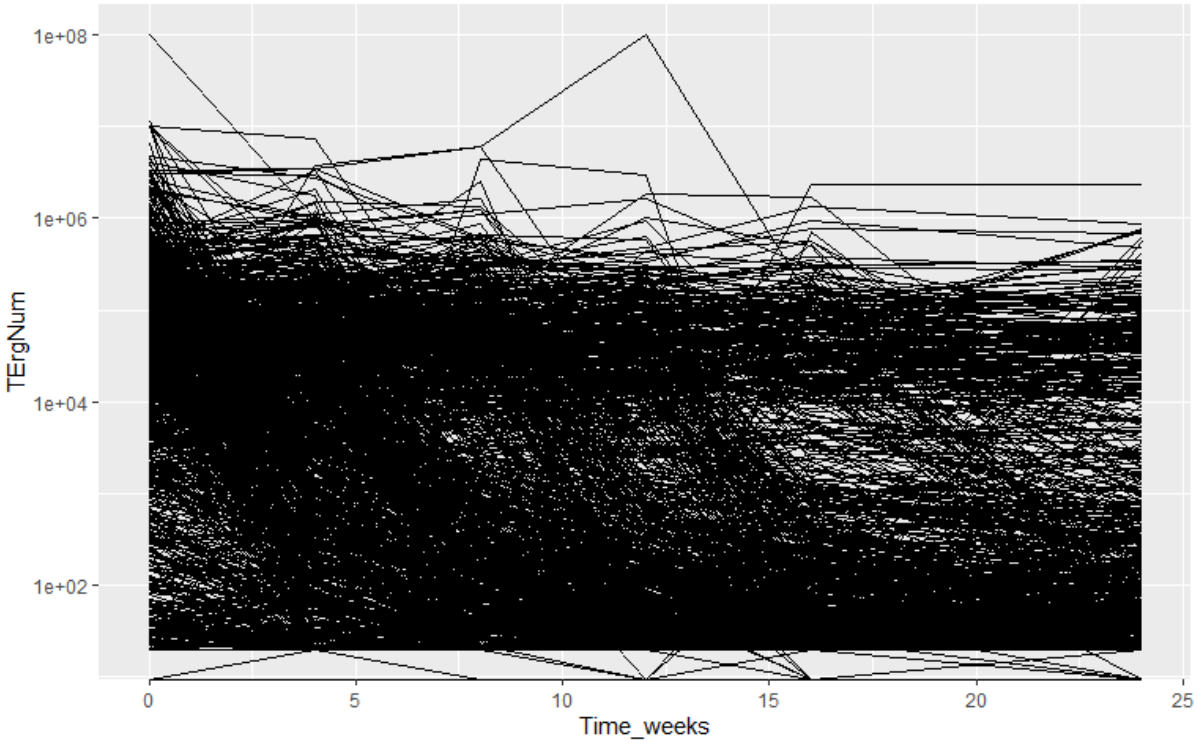
Plot the data

- 4. Depict the viral kinetics with a spaghetti plot

```
# here the original data formate is more appropiate
HIVdata_long <- full_join(labdata, basedata) %>%
  mutate(Time_weeks = structure(Time_weeks, label = "Time (weeks)"),
  TErgNum = structure(TErgNum, label = "Viral load"))
```

Basic spaghetti

```
ggplot(data = HIVdata_long)+
  aes(x = Time_weeks, y = TErgNum, group = PatientID)+
  scale_y_log10()+
  geom_line()
```



```
ggplot(data = HIVdata_long, aes(x = Time_weeks, y = TErgNum+1, group = PatientID))+
  geom_line(col="grey")+
  theme_minimal()+
  #facet_grid(. ~ Gender)+
  scale_y_log10()+
  stat_summary(aes(group = 1), geom = "line", fun.y = median,col="red",size = 2) +
  xlab(attributes(HIVdata_long$Time_weeks)$label) +
  ylab(attributes(HIVdata_long$TErgNum)$label)+
  geom_hline(yintercept = 20) +
  annotate("text", 5, 40, label = "Limit of detection", size=3)
```