MRI-Together 2021-https://mritogether.github.io/

A White Hat's Guide to P-Hacking

Dr. Xeni Deligianni- University of Basel-xeni.deligianni@unibas.ch

This tutorial is released under a CC-BY license.

We have two data distributions, one the **controls** and one a distribution that we want to compare to the control. In real scientific life this could be the quantitative values of a controlled group, let's call them **qmr** and respective values of a different group e.g. patients with a certain condition.

Let's assume for now that the distributions are **normal** Gaussian distributions. So let's assume we checked the distributions. And let' s assume, that BEFORE starting our analysis, we have a **hypothesis** that in disease presence T42 values are increased. And let's imagine we have estimated that we should measure and we measured under identical and ideal conditions **50 healthy controls** and **50 patients**.

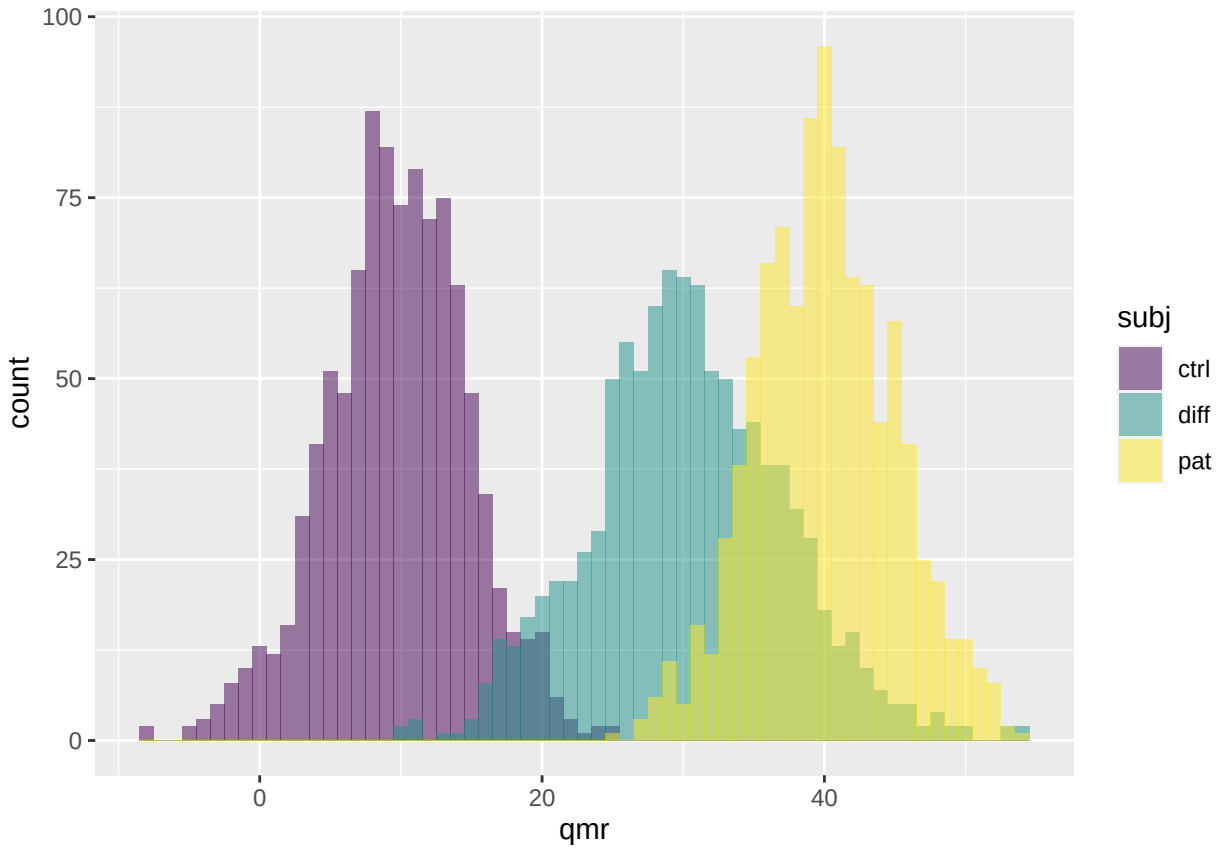
Let' s agree on some definitions first

α: Significance level.A p-value below this will lead to the null hypothesis being rejected.

Ready? Let's create some fictional data.

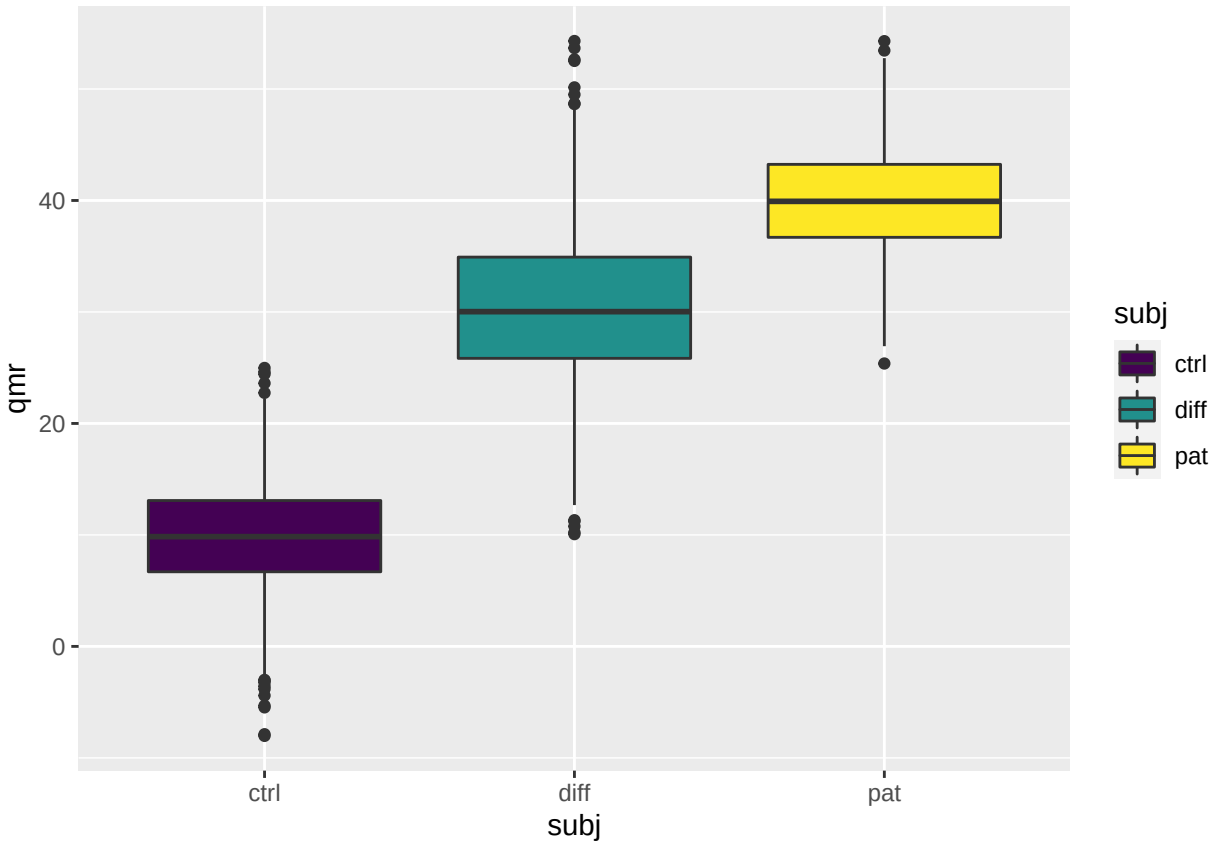
Let's create two perfectly **normal distributions**. One with **mean** 40 and **standard deviation** (sd) 5 and one with mean 10 and standard deviation 2. And let's visualize at their distributions, as well as the distribution of their difference.

```
## Loading required package: viridisLite
```



That looks clear. Doesn't it? Let's also look at the boxplot visualization.

```
library(ggplot2)# A great library for visualization
library(viridis)
load('New_Data.RData')
#qmr <-c(rnorm(1000, mean=10, sd=5),rnorm(1000, mean=40, sd=5))
#subj <- c(rep("ctrl",1000),rep("pat",1000),rep("diff",1000))
#d.exp <- data.frame(qmr,subj)
x<-d.exp[d.exp$subj=='pat',]$qmr
bw <- 2 * IQR(x) / length(x)^(1/3)#decide for the nr of bins-Friedman-Diaconis rule
ggplot(data = d.exp,mapping = aes(y = qmr,x = subj, fill=subj)) + geom_boxplot()+scale_fill_viridis_d()
```



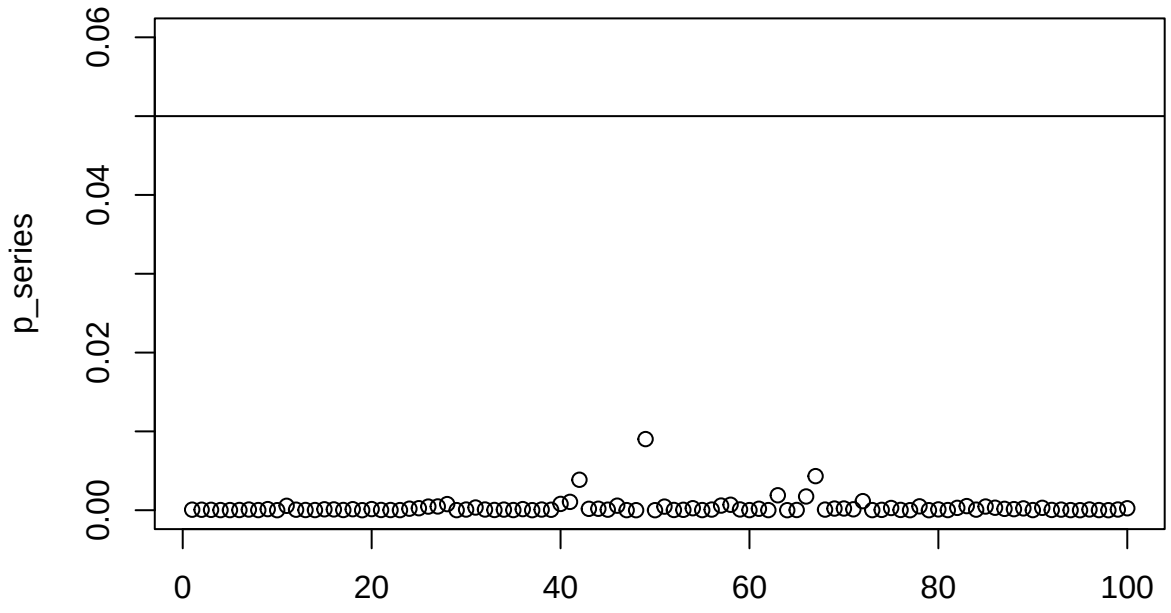

```
#colorblind accessible colors
```

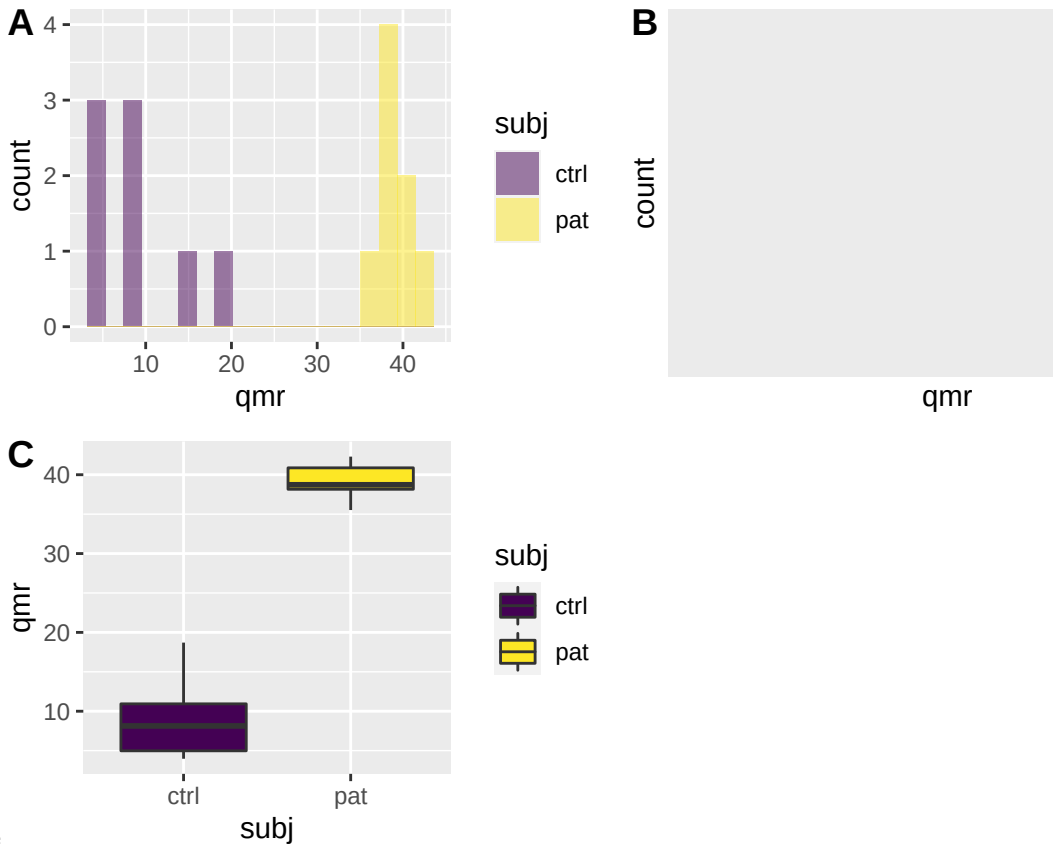
So what's next? How likely is that this difference is 0.

What would we get by testing whether there is a difference in these 2 distributions. Having all our assumptions, most of us would go for a t-test.

```
load('New_Data.RData')

#qmr <-c(rnorm(1000, mean=10, sd=5),rnorm(1000, mean=40, sd=5))
#subj <- c(rep("ctrl",1000),rep("pat",1000),rep("diff",1000))
#d.exp <- data.frame(qmr,subj)
# Randomly choose number of samples (1000/50/25/15/5)

nr_s<-4

p_series<-vector()
for (i in 1:100) {
  sample_rows_ctrl<-sample(nrow(d.exp[d.exp$subj=="ctrl",]),nr_s)
  sample_rows_pat<-1000+sample(nrow(d.exp[d.exp$subj=="pat",]),nr_s)
  d.exp_sub<-rbind(d.exp[sample_rows_ctrl,],d.exp[sample_rows_pat,])
  p_Res<-t.test(d.exp_sub[d.exp_sub$subj=="pat",]$qmr, d.exp_sub[d.exp_sub$subj=="ctrl",]$qmr, paired =
alternative = "two.sided", conf.level = 0.95,var.equal=TRUE)
  p_series [i]<-p_Res$p.value
}
```

```
plot(p_series,ylim=c(0,0.06))
abline(h=0.05)
```





###So let's sum up and continue

##

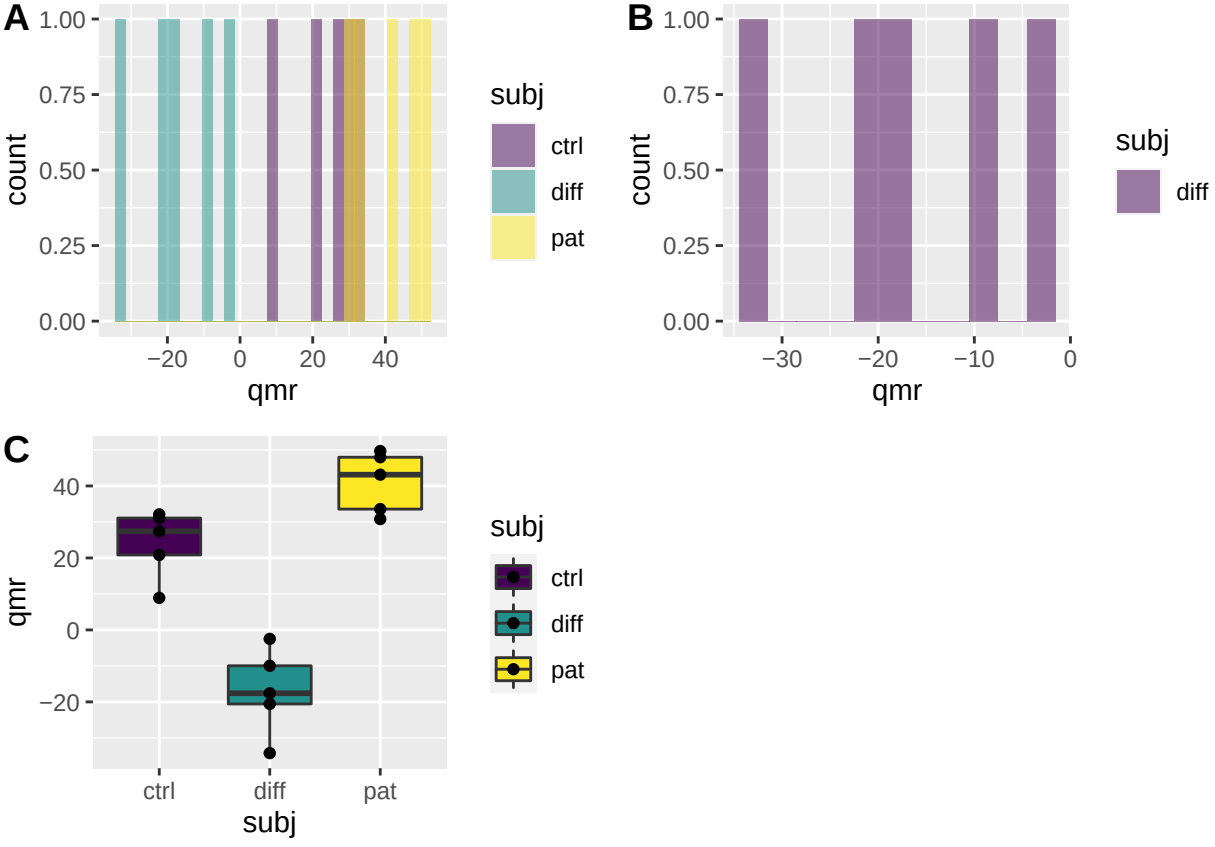
```
##  Paired t-test
##
## data:  d.exp_sub[d.exp_sub$subj == "pat", ]$qmr and d.exp_sub[d.exp_sub$subj == "ctrl", ]$qmr
## t = 14.295, df = 7, p-value = 1.949e-06
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  25.00649 34.91887
## sample estimates:
## mean of the differences
##                29.96268
```

But what if we don't have 1000 samples or 1000 representative samples?

Trap Nr. 1: Be real! 5 data points is not 5000

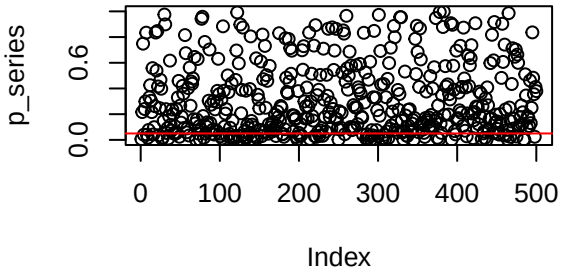
Topic 1: The number of samples is important What if we have 15 samples of some less different data. Let's get them & repeat the steps

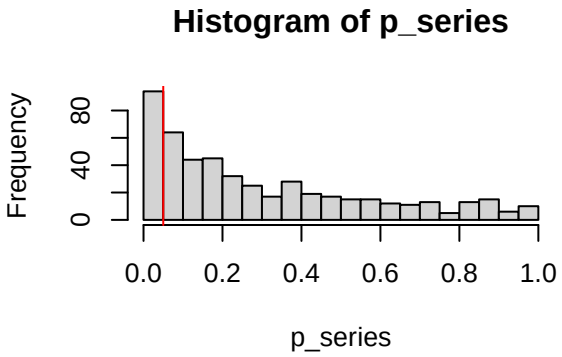
p-values change but our difference is still constantly higher than 0. ## But what if things are not so clear? Let's modify bring the mean values closer and increase the standard deviation. Keeping the assumptions for t-test we keep standard deviation the same.

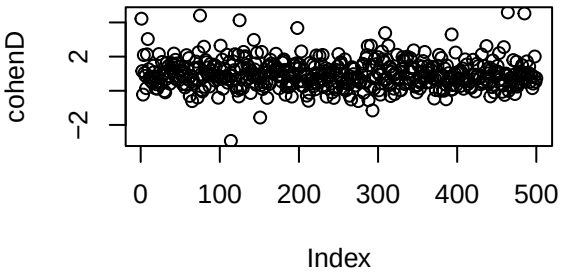



```
##
##  Paired t-test
##
## data:  d.exp[d.exp$subj == "pat", ]$qmr and d.exp[d.exp$subj == "ctrl", ]$qmr
```

```
## t = 3.1788, df = 4, p-value = 0.03357
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##   2.147982 31.792787
## sample estimates:
## mean of the differences
##                16.97038

##
## Cohen's d
##
## d estimate: 1.877434 (large)
## 95 percent confidence interval:
##     lower     upper
## 0.1269388 3.6279300
```







What can we do?

Decide in advance the sample size we need! If we don' t know maybe it is an exploratory analysis after all

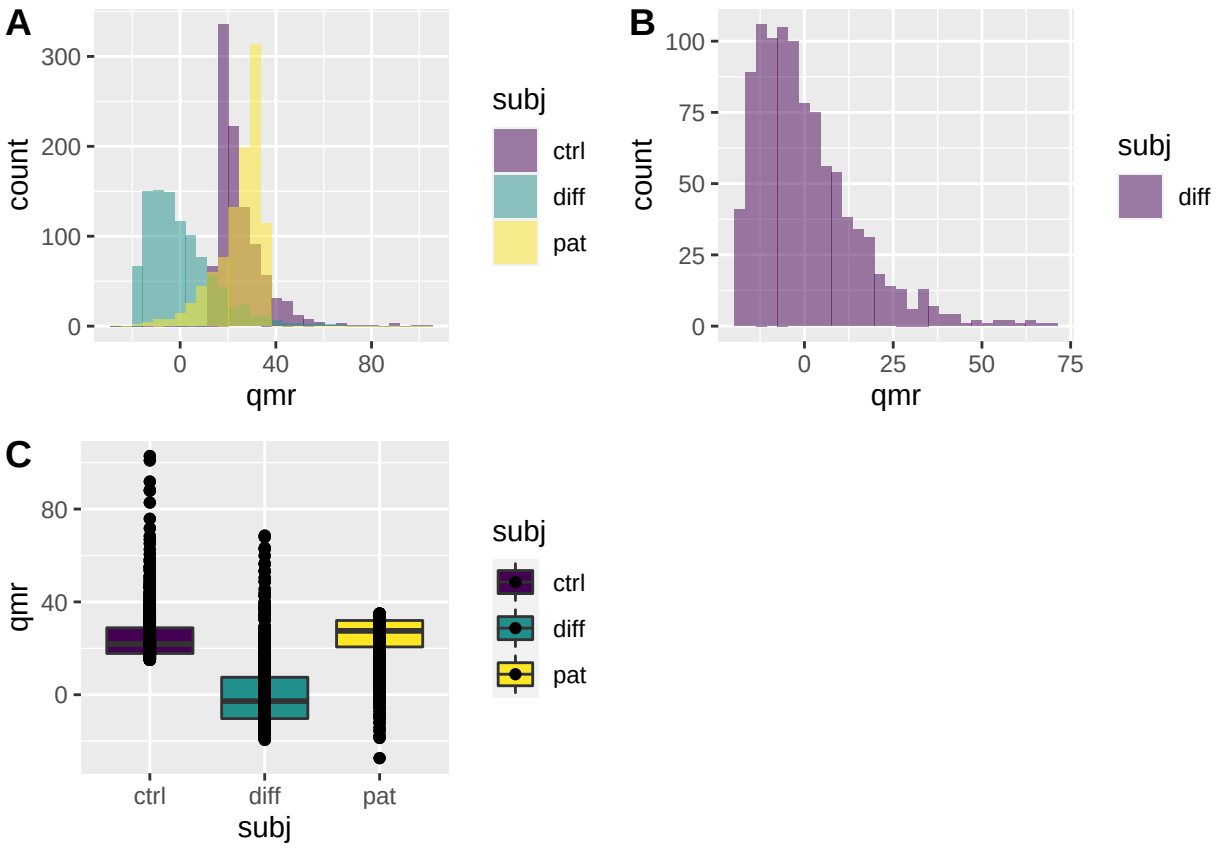
###Clinical vs statistical significance (to the slides and back)

Trap Nr. 2: Step 1: Look at your data

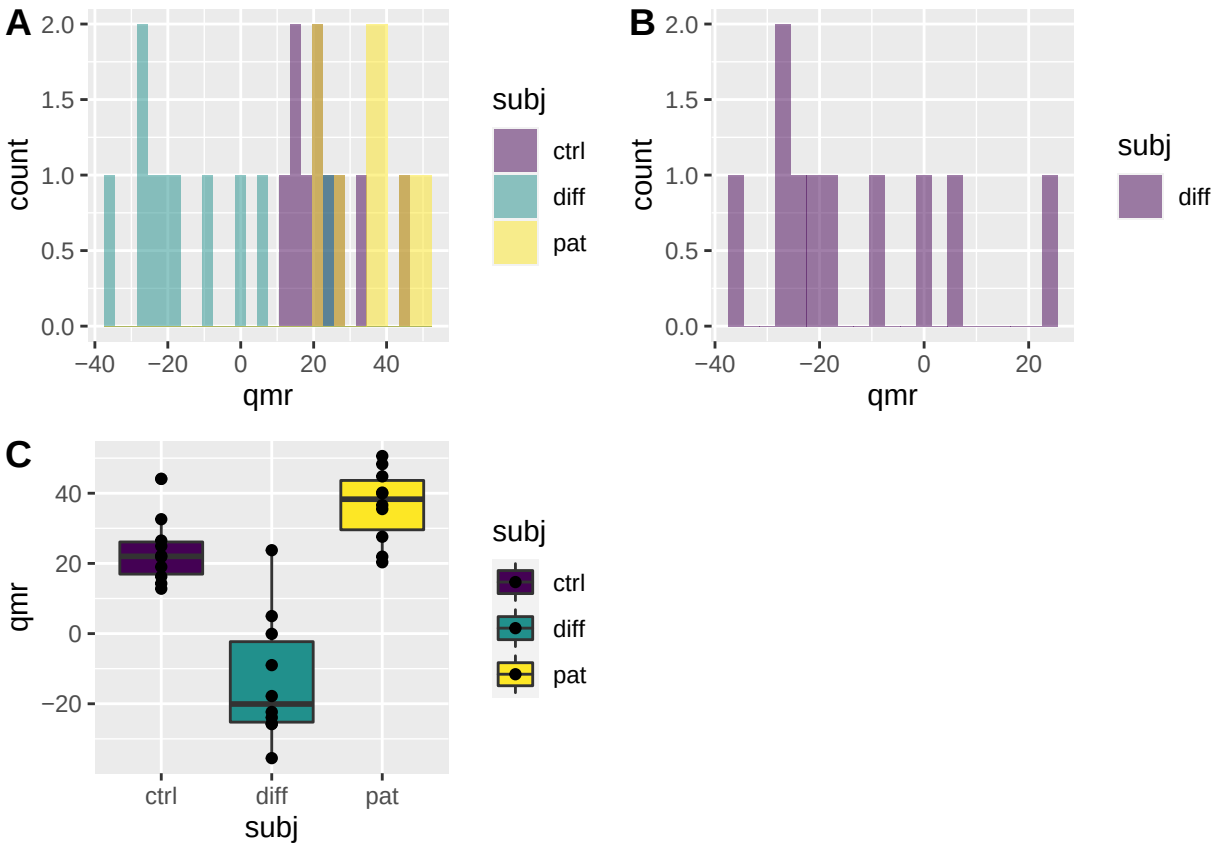
Not all datasets are normal, t-test is not for everything!

The same way as mean is not always the proper statistic.

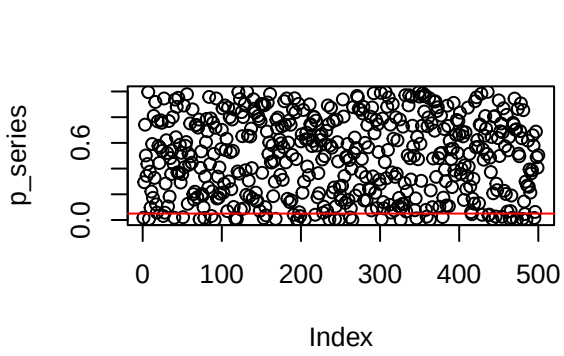
```
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```

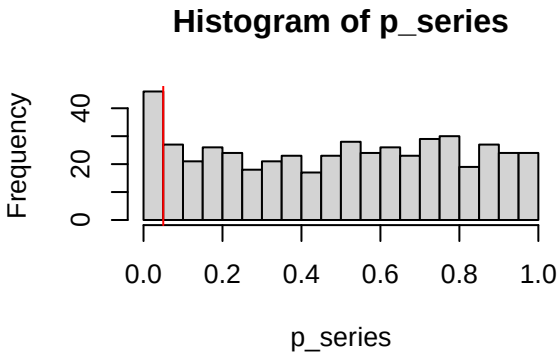


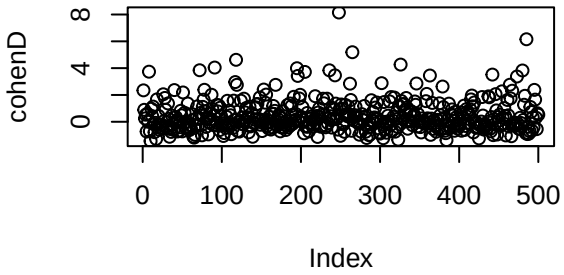

```
##
##  Paired t-test
##
## data:  d.exp[d.exp$subj == "pat", ]$qmr and d.exp[d.exp$subj == "ctrl", ]$qmr
## t = -0.76922, df = 999, p-value = 0.4419
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -1.2379758  0.5407345
## sample estimates:
## mean of the differences
##              -0.3486206

##
##  Wilcoxon signed rank test with continuity correction
##
## data:  d.exp[d.exp$subj == "pat", ]$qmr and d.exp[d.exp$subj == "ctrl", ]$qmr
## V = 276158, p-value = 0.00457
## alternative hypothesis: true location shift is not equal to 0
```



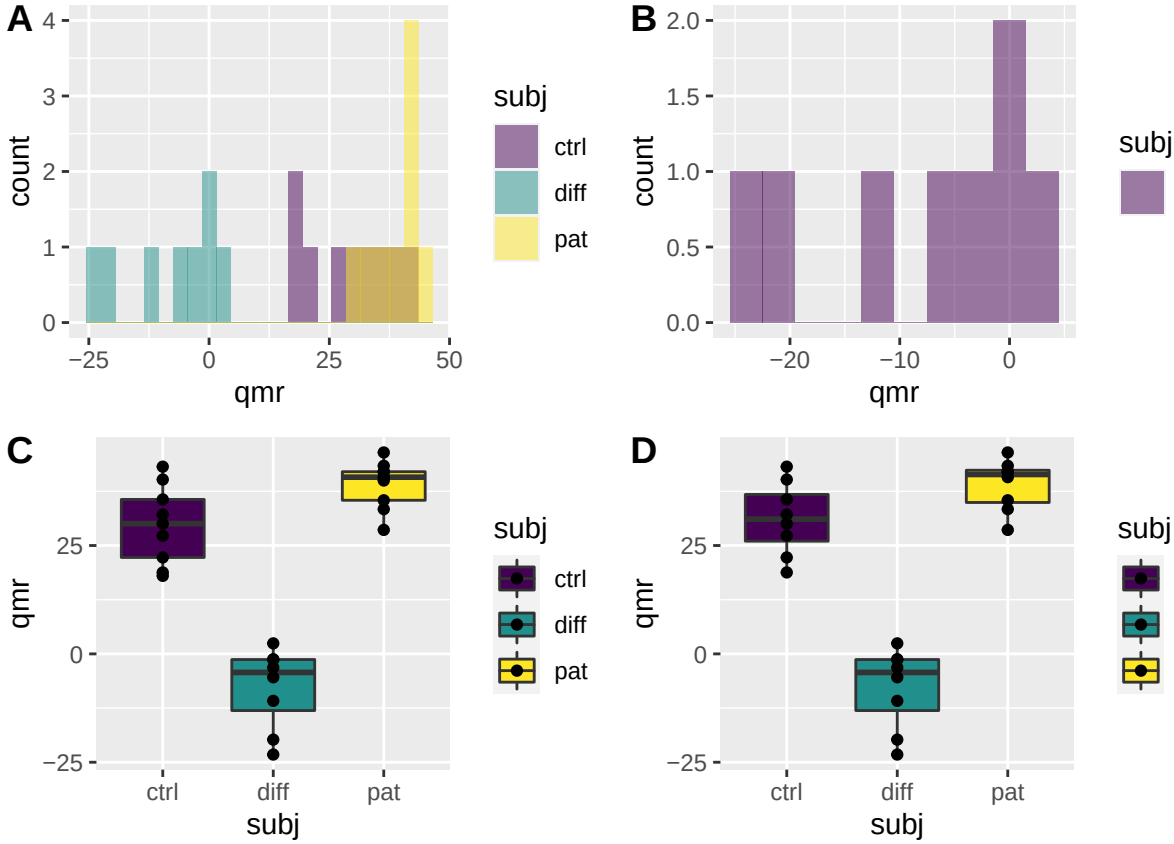

```
##
##  Paired t-test
##
## data:  d.exp[d.exp$subj == "pat", ]$qmr and d.exp[d.exp$subj == "ctrl", ]$qmr
## t = 2.306, df = 9, p-value = 0.04654
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##   0.249618 26.007024
## sample estimates:
## mean of the differences
##                13.12832

##
## Cohen's d
##
## d estimate: 1.320048 (large)
## 95 percent confidence interval:
##     lower     upper
## 0.2831986 2.3568978
```







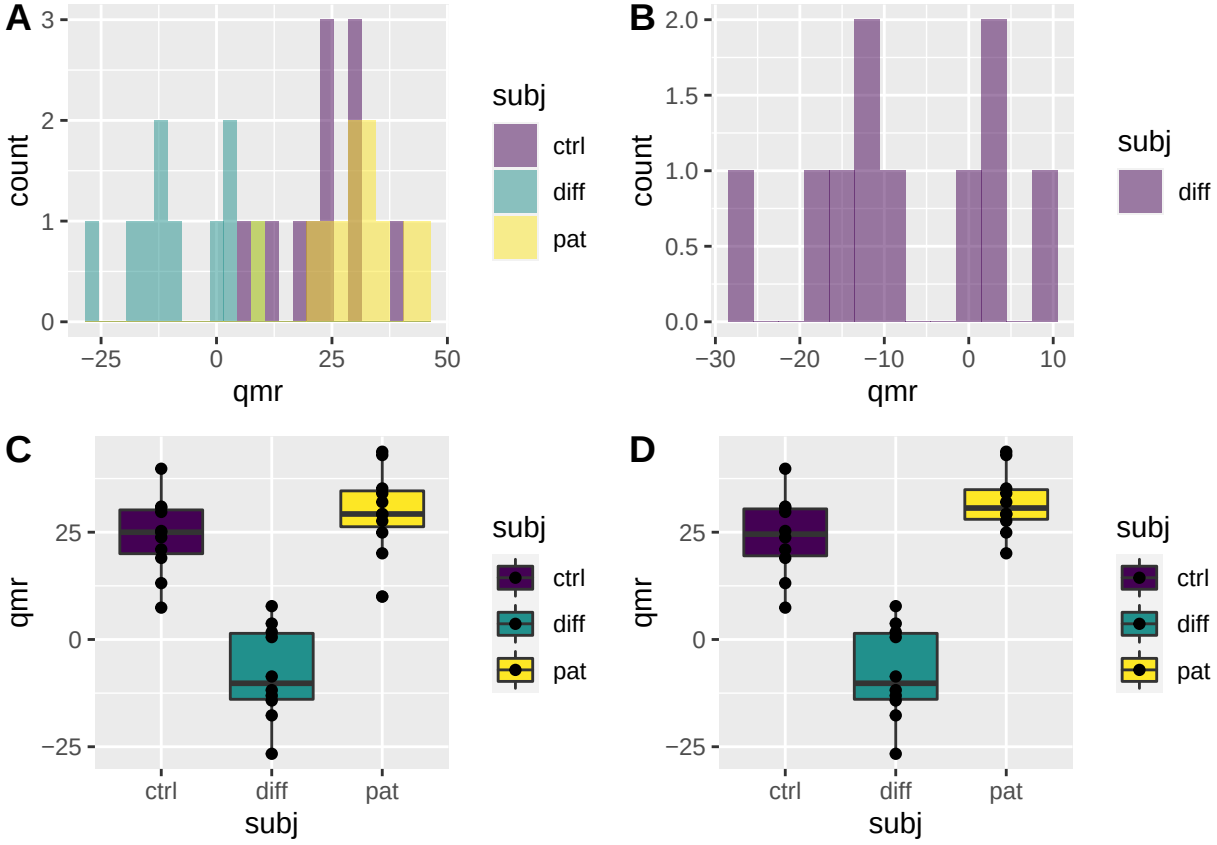
Trap 3: Just one more experiment then!It almost looks good. Let's repeat it. Trap of adding data on



marginal distributions.

Trap Nr. 3: This one looks wrong. Let's remove it

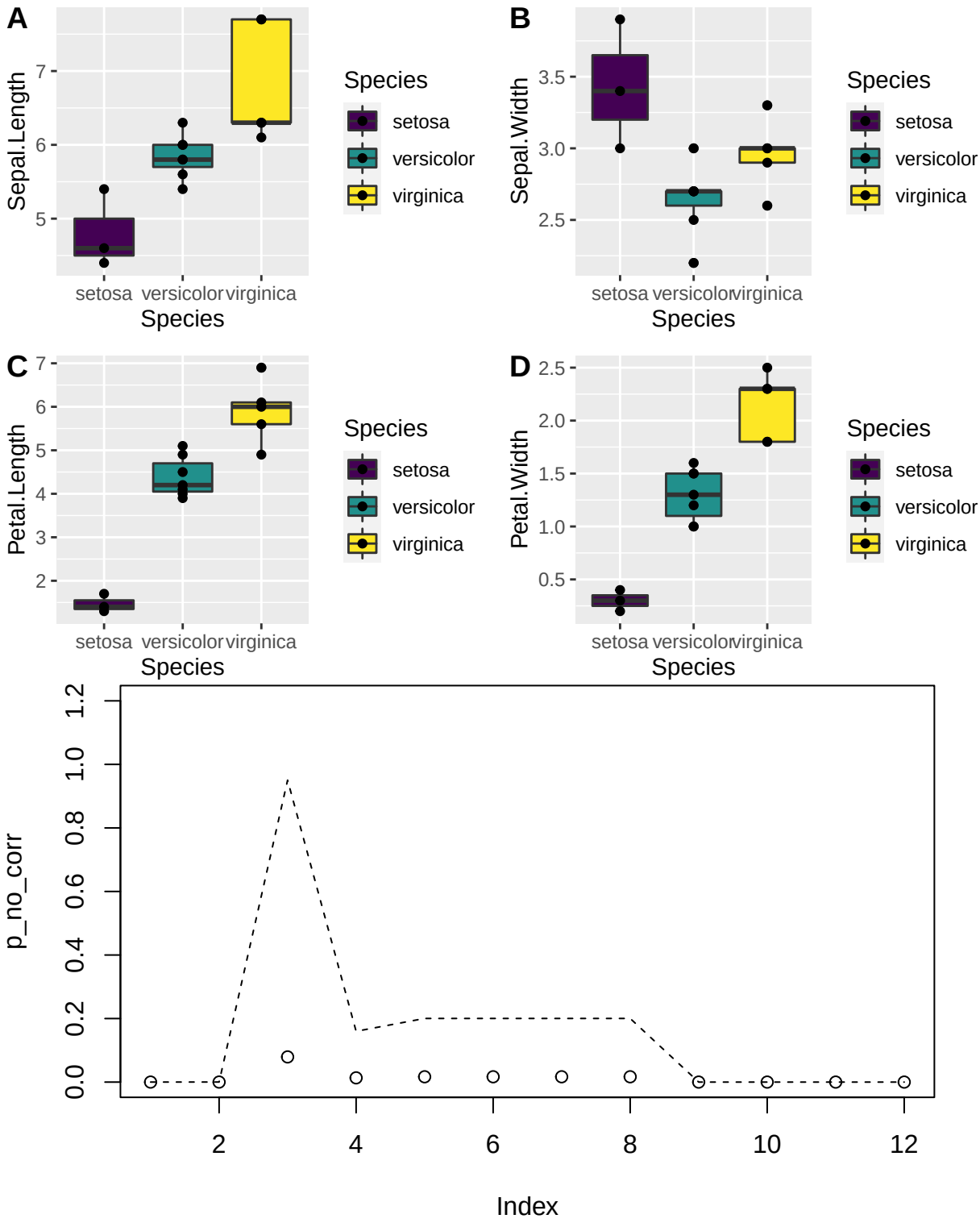
##TO DO:post-hoc data selection, Keep adjusting the data collection removing outliers, 1) use different threshold, 2) remove outliers and test till you get you result



Trap Nr. 4: Problem of repeated sequential testing

Bonferroni and other corrections

```
##   Sepal.Length    Sepal.Width     Petal.Length    Petal.Width
##  Min.   :4.300   Min.   :2.000   Min.   :1.000   Min.   :0.100
##  1st Qu.:5.100   1st Qu.:2.800   1st Qu.:1.600   1st Qu.:0.300
##  Median :5.800   Median :3.000   Median :4.350   Median :1.300
##  Mean   :5.843   Mean   :3.057   Mean   :3.758   Mean   :1.199
##  3rd Qu.:6.400   3rd Qu.:3.300   3rd Qu.:5.100   3rd Qu.:1.800
##  Max.   :7.900   Max.   :4.400   Max.   :6.900   Max.   :2.500
##        Species
##  setosa    :50
##  versicolor:50
##  virginica :50
##
##
##
```



Trap Nr. 5: TODO POST HOC hypothesis

Be ware of one-sided tests,

###Check the assumptions: (different variation, reaching normality)

```
## [1] 0.04930856 0.97534572 0.02465428
```

##References https://www.youtube.com/watch?v=HDCOUXE3HMM Cambell book
##how to hack tutorial nicolas

```
## set global chunk options: all images will be 7x5 inches
knitr::opts_chunk$set(fig.width = 7, fig.height = 5)
options(digits = 4)
```

I encourage you to watch: The dance of p-values: https://www.youtube.com/watch?v=5OL1RqHrZQ8 by Geoff Cumming who is also a presenter