Computational Biology Group

D BSSE

ETH zürich

Introduction to Bayesian Statistics with R

1: Exercise solutions

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First we load the tidyverse and set a seed.

```r
library(tidyverse); options(dplyr.summarise.inform = FALSE) # suppress summarise warnings
set.seed(42)
```

Exercise 1.1 - a statistical report

A small clinical trial on asthma patients has been run measuring the lung function of a control group on a placebo and a treatment group on a new drug.

- *Read in the trial data (`lung_data.csv`),*
- *visualize the data for each group,*
- *test whether there is a difference in function between the two groups.*

We first read in the data

```r
lung_data <- read.csv("./data/lung_data.csv")
```

Then we create a table of the descriptive statistics by *grouping* and *summarising*

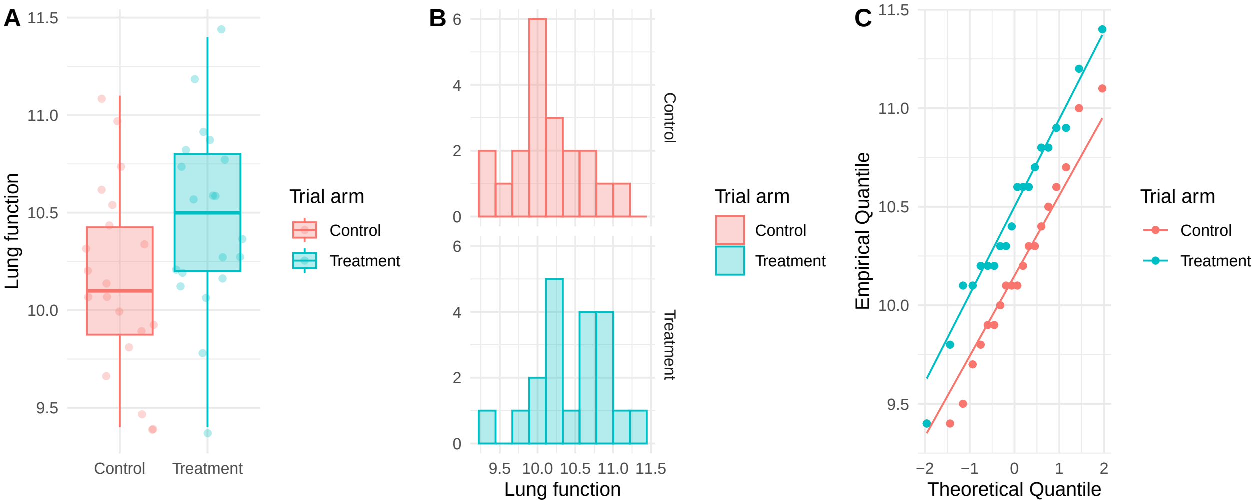
```r
lung_data %>% group_by(Trial.arm) %>%
  summarize(
    Mean =  signif(mean(Lung.function), 4),
    Sd = signif(sd(Lung.function), 2),
    Min = min(Lung.function),
    Median = median(Lung.function),
    Max = max(Lung.function),
    IQR = IQR(Lung.function),
    N = n()) %>%
  kable(caption = "Descriptive statistics of the lung data.",
        col.names = c("Trial arm", colnames(.)[-1]))
```

Table 1: Descriptive statistics of the lung data.

Trial arm	Mean	Sd	Min	Median	Max	IQR	N
Control	10.15	0.48	9.4	10.1	11.1	0.55	20
Treatment	10.48	0.47	9.4	10.5	11.4	0.60	20

We will also plot the data using explanatory plots. Here we store the plots as variables and use `cowplot` to create labelled figures.

```r
library(cowplot)
p <- ggplot(lung_data) + theme_minimal()

p1 <- p + geom_boxplot(aes(x = Trial.arm, y = Lung.function, color = Trial.arm,
                           fill=Trial.arm),
      outlier.shape = NA, alpha = 0.3) +
  geom_jitter(aes(x = Trial.arm, y = Lung.function, color = Trial.arm), alpha = 0.3) +
  scale_y_continuous("Lung function") + scale_x_discrete("") +
  scale_color_discrete("Trial arm") + scale_fill_discrete("Trial arm")

p2 <- p + geom_histogram(aes(x = Lung.function, color = Trial.arm, fill = Trial.arm),
      alpha = 0.3, bins = 10) +
  scale_y_continuous("") + scale_x_continuous("Lung function") +
  scale_color_discrete("Trial arm") + scale_fill_discrete("Trial arm") +
  facet_grid(Trial.arm ~ .)

p3 <- p + stat_qq(aes(sample = Lung.function, color = Trial.arm)) +
  stat_qq_line(aes(sample = Lung.function, color = Trial.arm)) +
  scale_color_discrete("Trial arm") +
  scale_x_continuous("Theoretical Quantile") + scale_y_continuous("Empirical Quantile")

plot_grid(p1, p2, p3,
  align = "vh", ncol = 3, labels = c("A", "B", "C"))
```



Finally we test for a significant difference in lung function of the two groups. Since we assume normally distributed data, we can use a two-sample (unpaired) t-test with non-equal variances between the two groups.

```r
lung_t_test <- t.test(Lung.function ~ Trial.arm, lung_data)
lung_t_test
```

```
##
##  Welch Two Sample t-test
##
## data:  Lung.function by Trial.arm
## t = -2.1569, df = 37.988, p-value = 0.0374
## alternative hypothesis: true difference in means between group Control and group Treatment is not equ
## 95 percent confidence interval:
##  -0.63003538 -0.01996462
## sample estimates:
##   mean in group Control mean in group Treatment
##                  10.150                  10.475
```

We can collate this into a statistical report:

Report

The following report summarizes the results obtained from a statistical analysis of the change in lung function of asthma patients when treated with a new drug which we assess by comparison to a control group. We are hypothesizing that treating the patients with the drug has an effect on lung function, and consequently formulate the null hypothesis

$$H_0 : \mu_T - \mu_C = 0 \;\; \text{(the treatment has no effect)},$$

where μ_T and μ_C are the population means of treated and control patients, respectively. We shall reject the null at a significance level of $\alpha = 0.05$.

The data set we are analyzing consists of a total of $n = 40$ patients of two groups consisting of $n_T = 20$ patients that have been treated with the drug and $n_C = 20$ patients that have been treated with a placebo.

Table 2: Descriptive statistics of the lung data.

Trial arm	Mean	Sd	Min	Median	Max	IQR	N
Control	10.15	0.48	9.4	10.1	11.1	0.55	20
Treatment	10.48	0.47	9.4	10.5	11.4	0.60	20

The lung function of patients treated with the new drug overall has similar descriptive statistics as the control group. A total shift in means, however, can indeed be observed (Table 2, Figure 1).

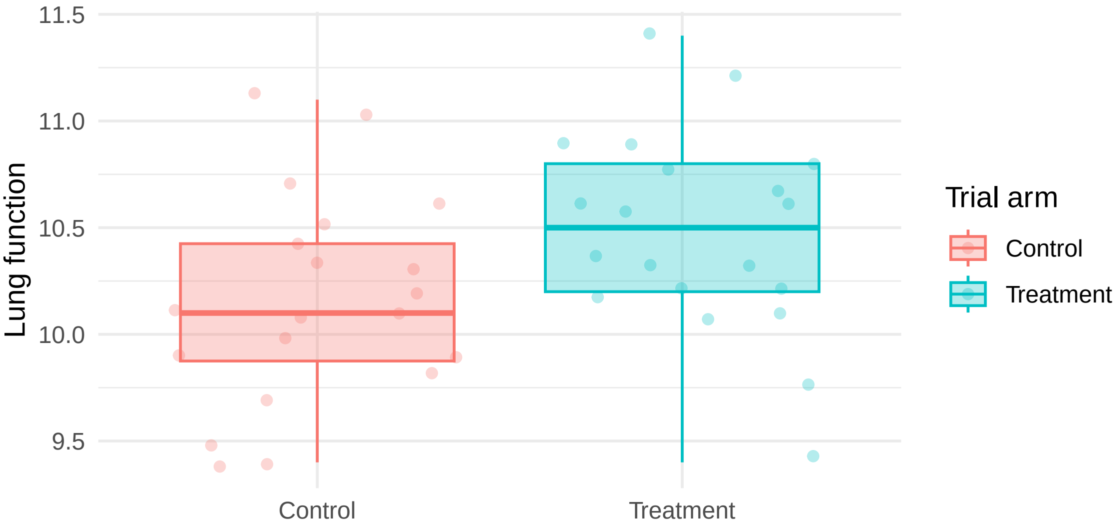


Figure 1: Boxplots of the two groups do not indicate any outliers.

Furthermore, the data do not reveal any outliers in either of the groups and both groups seem to follow a normal distribution (Figure 2). For normally distributed data with no outliers the most appropriate test is the t-test.

Thus, we conduct a two-sample t-test for independent means yielding a test statistic t = -2.16 with $\nu = 38$ degrees of freedom and p-value $p = 0.037$. Since $p < \alpha$ we reject the null hypothesis that the two groups share the same lung function on average.

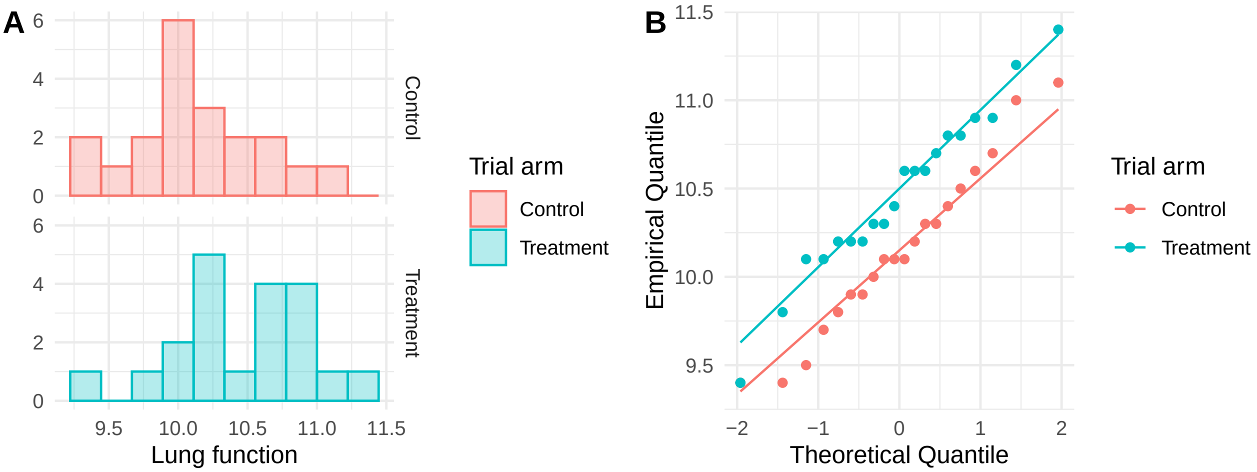


Figure 2: The two groups are approximately normally distributed.

Bonus Exercise 1.2 - normality and outliers

The t-test assumes normality and no outliers. To get a feel for how important those assumptions are, we can break them and check with simulated data.

- *What happens to the power if we use a different distribution (with the same mean and sd) instead of a normal?*
- *What happens if we add an outlier (for example, shift one of the treatment group by a large negative value)?*

Let's first use the code from the Exercises and replace the Gaussian distribution with a uniform one. To have a variance of 1, the uniform distribution should span a range of $2\sqrt{3}$. We again shift the mean for the treatment group by -0.25.

```
n_reps <- 4e3 # how many repetitions
p_vals <- rep(NA, n_reps) # to store the p-values
for (ii in 1:n_reps) {
  test_samples <- runif(50, min = -sqrt(3), max = sqrt(3)) - 0.25 # treatment group
  control_samples <- runif(50, min = -sqrt(3), max = sqrt(3)) # control group
  p_vals[ii] <- t.test(test_samples, control_samples)$p.value # t-test
}
mean(p_vals < 0.05) # the power given by the fraction of significant tests
```

```
## [1] 0.233
```

The power is almost identical to the Gaussian case!

Let's look at the outlier instead

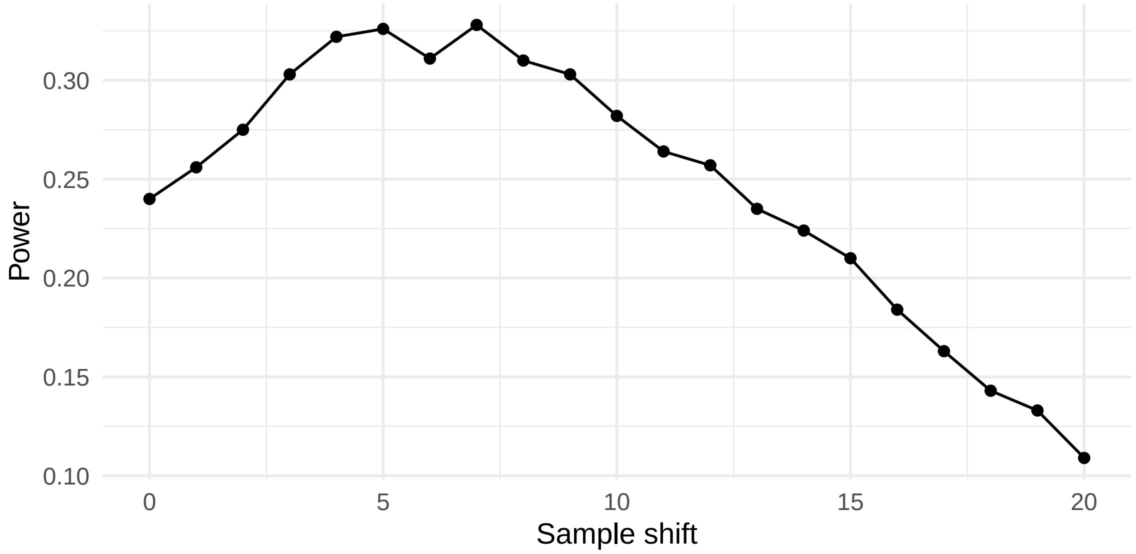
```
n_reps <- 4e3 # the number of repetitions
sample_shifts <- 0:20 # the possible shifts
p_vals_df <- data.frame() # start with an empty dataframe

for (s_shift in sample_shifts) { # loop over possible shifts
  p_vals <- rep(NA, n_reps) # to store the p-values
  for (ii in 1:n_reps) {
    test_samples <- rnorm(50, mean = -0.25, sd = 1) # treatment group
    test_samples[1] <- test_samples[1] - s_shift # shift one to make it an outlier
    control_samples <- rnorm(50, mean = 0, sd = 1) # control group
    p_vals[ii] <- t.test(test_samples, control_samples)$p.value # t-test
  }
  # build a local data frame for the repetitions with a given shift
  local_df <- data.frame(sample_shift = s_shift, p_vals = p_vals)
  p_vals_df <- rbind(p_vals_df, local_df) # append to the full data frame
} # end sample shift loop
```

We can then extract the empirical power

```
p_vals_df %>% group_by(sample_shift) %>%
  summarize(power = mean(p_vals < 0.05) %>% signif(3)) -> power_df
```

And plot it

```
power_df %>%
  ggplot() +
  geom_point(aes(x = sample_shift, y = power)) +
  geom_line(aes(x = sample_shift, y = power)) +
  scale_x_continuous("Sample shift") +
  scale_y_continuous("Power") +
  theme_minimal()
```



So after slightly increasing the power, having a large outlier actually ends up decreasing it!