Diastolic Blood Pressure Analysis

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The pressure in the arteries when the heart is relaxed (diastole) is called diastolic pressure, and this is usually less than 90 mmHg in adults.

In this study Diastolic Blood Pressure (DBP) was measured (mmHg) in the supine position at baseline (i.e., DBP1) before randomization and monthly thereafter up to 4 months as indicated by DBP2, DBP3, DBP4, and DBP5.

Patients age and sex were recorded at baseline and represent potential covariates.

Patients were divided in to two groups (Drug and Placebo). Primary objective is to test whether Drug may be effective in lowering DBP as compared to placebo.

The following R packages were used for this analysis:

```r
library(tidyverse)
library(ggplot2)
library(dplyr)
library(ez)
```

We begin by importing the dataset and performing basic data checks to understand its structure and verify data integrity.

```r
# Load the dataset
data <- read.csv("dbpdata.csv")

# View the first few rows of the dataset
head(data)
```

```
##   Subject TRT DBP1 DBP2 DBP3 DBP4 DBP5 Age Sex
## 1       1   A  114  115  113  109  105  43   F
## 2       2   A  116  113  112  103  101  51   M
## 3       3   A  119  115  113  104   98  48   F
## 4       4   A  115  113  112  109  101  42   F
## 5       5   A  116  112  107  104  105  49   M
## 6       6   A  117  112  113  104  102  47   M
```

```r
# Check dataset dimensions (rows and columns)
dim(data)
```

```
## [1] 40  9
```

```r
# Check for any missing values
any(is.na(data))
```

```
## [1] FALSE
```

To improve the interpretability of the age distribution, the continuous age variable was discretized into 6 bins using 5-year intervals. The resulting AgeGroup variable is used to generate a bar plot of participant
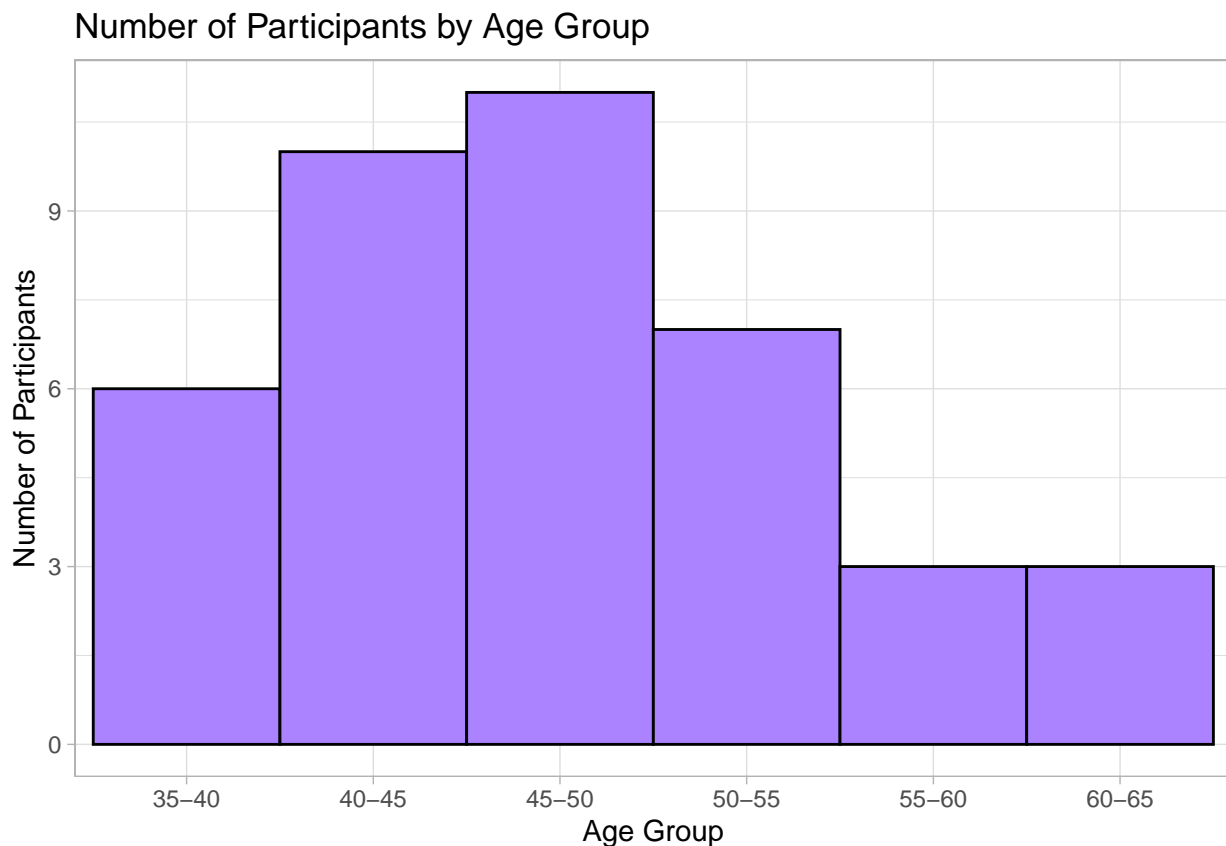
counts per group.

```r
min(data$Age)
```

```
## [1] 38
```

```r
max(data$Age)
```

```
## [1] 63
```

```r
data$AgeGroup <- cut(
  data$Age,
  breaks = c(35, 40, 45, 50, 55, 60, 65),
  labels = c("35-40", "40-45", "45-50", "50-55","55-60", "60-65"),
  right = TRUE
)

ggplot(data, aes(x = AgeGroup))+
  geom_bar(width = 1, fill = "mediumpurple1",  color = "black")+
  labs(title = "Number of Participants by Age Group",
       x = "Age Group",
       y = "Number of Participants")+
  theme_light()
```

Number of Participants by Age Group

The bar plot shows that most participants fall within 45-50 age range, followed by the 40–45 age range.

The following bar plot illustrates the distribution of baseline DBP values. The value of 114 mmHg has the highest frequency, followed by 116 mmHg.

```r
ggplot(data, aes(x = DBP1))+
  geom_bar(width = 0.5, fill = "lightpink2", color = "black")+
  scale_x_continuous(breaks = 114:121)+
  labs(title = "Number of Patients by Baseline DBP",
       x = "DBP",
       y = "Number of Patients")+
  theme_light()
```


Number of Patients by Baseline DBP
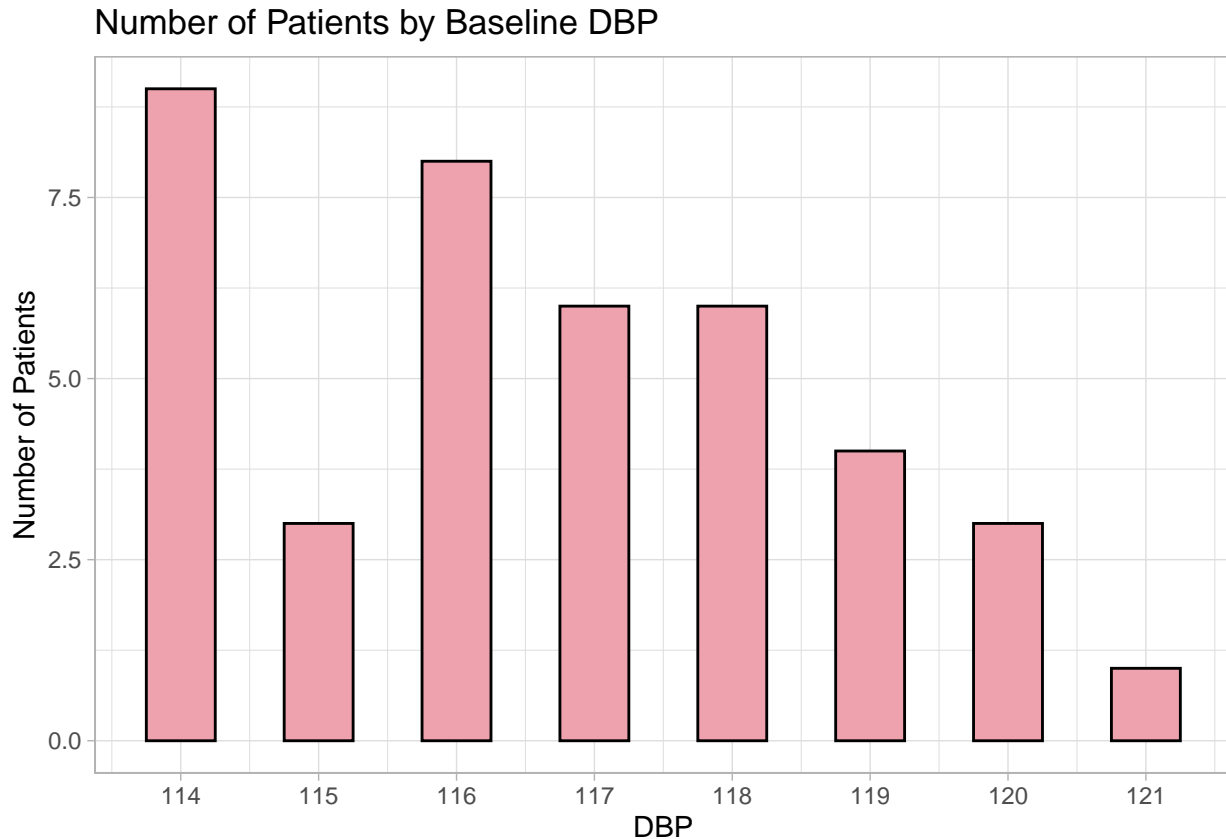
The following boxplots illustrates the DBP over time for patients under drug and placebo treatments separately. A reduction in DBP is observed in both groups; however, the decrease in the Drug group appears to be much more pronounced.

```r
df_dbp <- pivot_longer(
  data,
  cols = 3:7,
  names_to = "Time",
  values_to = "DBP"
)

ggplot(df_dbp, aes(x = Time, y = DBP, fill = TRT)) +
  geom_boxplot(position = position_dodge(0.8)) +
  labs(title = "DBP over Time by Treatment Group",
       x = "Time Point",
       y = "Diastolic Blood Pressure",
       fill = "Treatment") +
  scale_fill_manual(
    values = c("A" = "deeppink3", "B" = "aquamarine3"),
```

```r
    labels = c("A" = "Drug", "B" = "Placebo")) +
  theme_light()
```

DBP over Time by Treatment Group
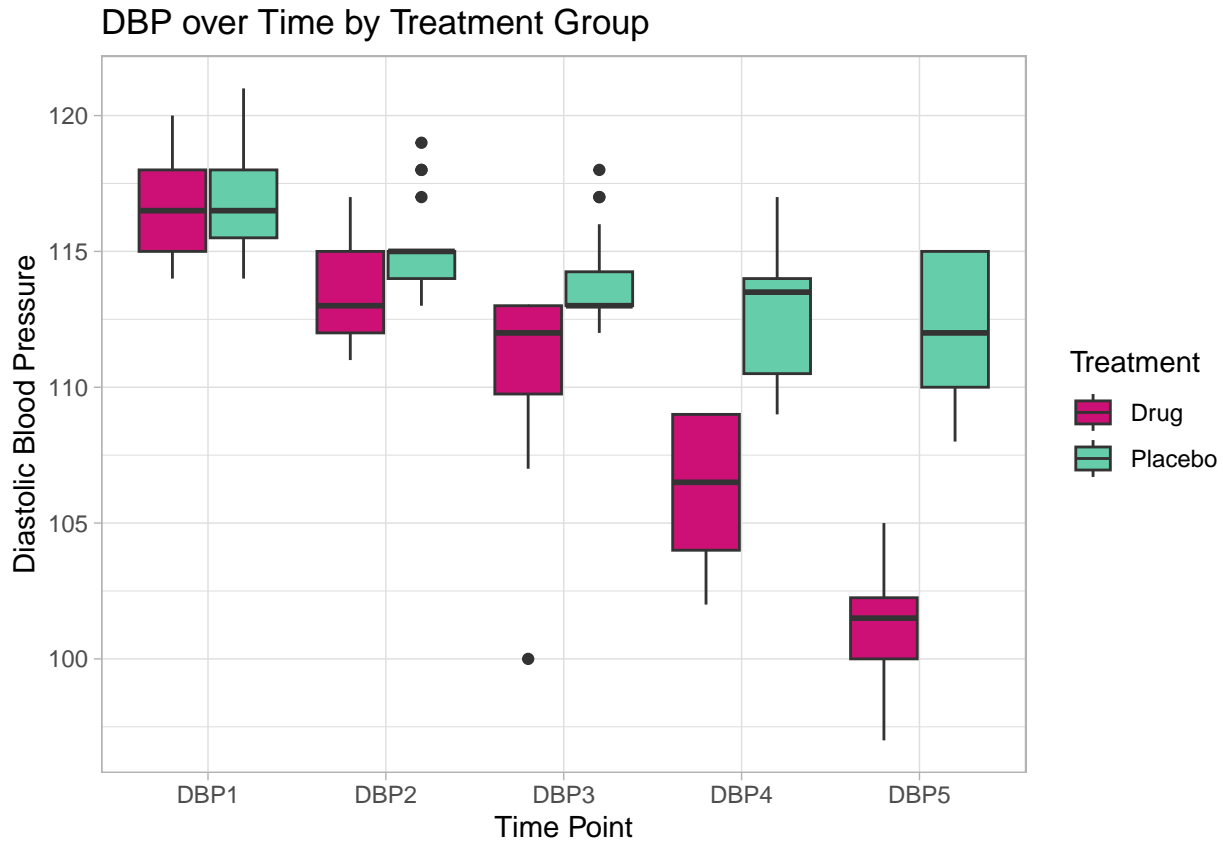
The table below summarizes the mean diastolic blood pressure (DBP) at each timepoint for both the Drug and Placebo groups. A steady decline in DBP is observed in the Drug group, while the reduction is more gradual in the Placebo group.

```r
TRT_Drug <- data[data$TRT == "A", ]
TRT_Placebo <- data[data$TRT == "B", ]
mean_Drug <- apply(TRT_Drug[,3:7], 2, mean)
mean_Placebo <- apply(TRT_Placebo[,3:7], 2, mean)

df_mean <- data.frame(
  TimePoint = c("DBP1", "DBP2", "DBP3", "DBP4", "DBP5"),
  Drug = mean_Drug,
  Placebo = mean_Placebo
)

knitr::kable(df_mean, caption = "Mean DBP at Each Timepoint by Treatment Group")
```

Table 1: Mean DBP at Each Timepoint by Treatment Group

	TimePoint	Drug	Placebo
DBP1	DBP1	116.55	116.75
DBP2	DBP2	113.50	115.20
DBP3	DBP3	110.70	114.05
DBP4	DBP4	106.25	112.45

	TimePoint	Drug	Placebo
DBP5	DBP5	101.35	111.95

Since blood pressure tends to increase with age, any observed difference in DBP between the Drug and Placebo groups could be confounded by age if the groups are not balanced. To assess group comparability before analyzing treatment effects, we test whether the mean age differs between the two groups. This involves performing an independent samples t-test. Prior to this, we check the assumptions of normality within each group and equality of variances between groups. If both assumptions are satisfied, we use the standard t-test; otherwise, we apply Welch's t-test, which does not assume equal variances.

```r
shapiro.test(data$Age[data$TRT=="A"])
```

```
##
##  Shapiro-Wilk normality test
##
## data:  data$Age[data$TRT == "A"]
## W = 0.90937, p-value = 0.062
```

```r
shapiro.test(data$Age[data$TRT=="B"])
```

```
##
##  Shapiro-Wilk normality test
##
## data:  data$Age[data$TRT == "B"]
## W = 0.91747, p-value = 0.0886
```

In both groups, p-value > 0.05. Therefore, normality is satisfied in both groups.

```r
var.test(Age ~ TRT, data = data)
```

```
##
##  F test to compare two variances
##
## data:  Age by TRT
## F = 0.64747, num df = 19, denom df = 19, p-value = 0.3516
## alternative hypothesis: true ratio of variances is not equal to 1
## 95 percent confidence interval:
##  0.2562749 1.6357911
## sample estimates:
## ratio of variances
##           0.647466
```

Equal variance test shows that p-value > 0.05. Therefore, equal variance assumption is satisfied.

Since the assumptions of normality and equal variances were both satisfied, we performed an independent two-sample t-test assuming equal variances to compare the mean age between the Drug and Placebo groups.

```r
t.test(Age ~ TRT, data = data, var.equal = TRUE)
```

```
##
##  Two Sample t-test
##
## data:  Age by TRT
## t = 0.73245, df = 38, p-value = 0.4684
## alternative hypothesis: true difference in means between group A and group B is not equal to 0
## 95 percent confidence interval:
##  -2.734017  5.834017
```

```
## sample estimates:
## mean in group A mean in group B
##          48.60           47.05
```

The independent two-sample t-test shows that the mean age do not significantly differ between the two treatment groups, indicating that age is comparable across groups at baseline.

Men and women have biologically different cardiovascular profiles. On average, men tend to have higher DBP than women until women reach menopause. Sex hormones, vascular resistance, and cardiac output differ by sex.Hence, sex is associated with the DBP.

The following plot shows the distribution of sex in the Drug and Placebo groups. It can be observed that both sexes are equally represented in each group.

```
data$Treatment <- factor(data$TRT, levels = c("A", "B"),
                         labels = c("Drug", "Placebo"))
ggplot(data, aes(x = Treatment, fill = Sex))+
  geom_bar(position = "fill", color = "black",
           width = 0.5)+
  coord_flip()+
  scale_fill_manual(values = c("F" = "orchid1", "M" = "steelblue3"),
                    labels = c("F" = "Female", "M" = "Male"))+
  scale_y_continuous(labels = scales::percent)+
  labs(title = "Proportion of Sex Whithin Treatment Groups",
       x = "Treatment Group",
       y = "Proportion of Patients",
       fill = "Sex")+
  theme_light()
```


Proportion of Sex Whithin Treatment Groups
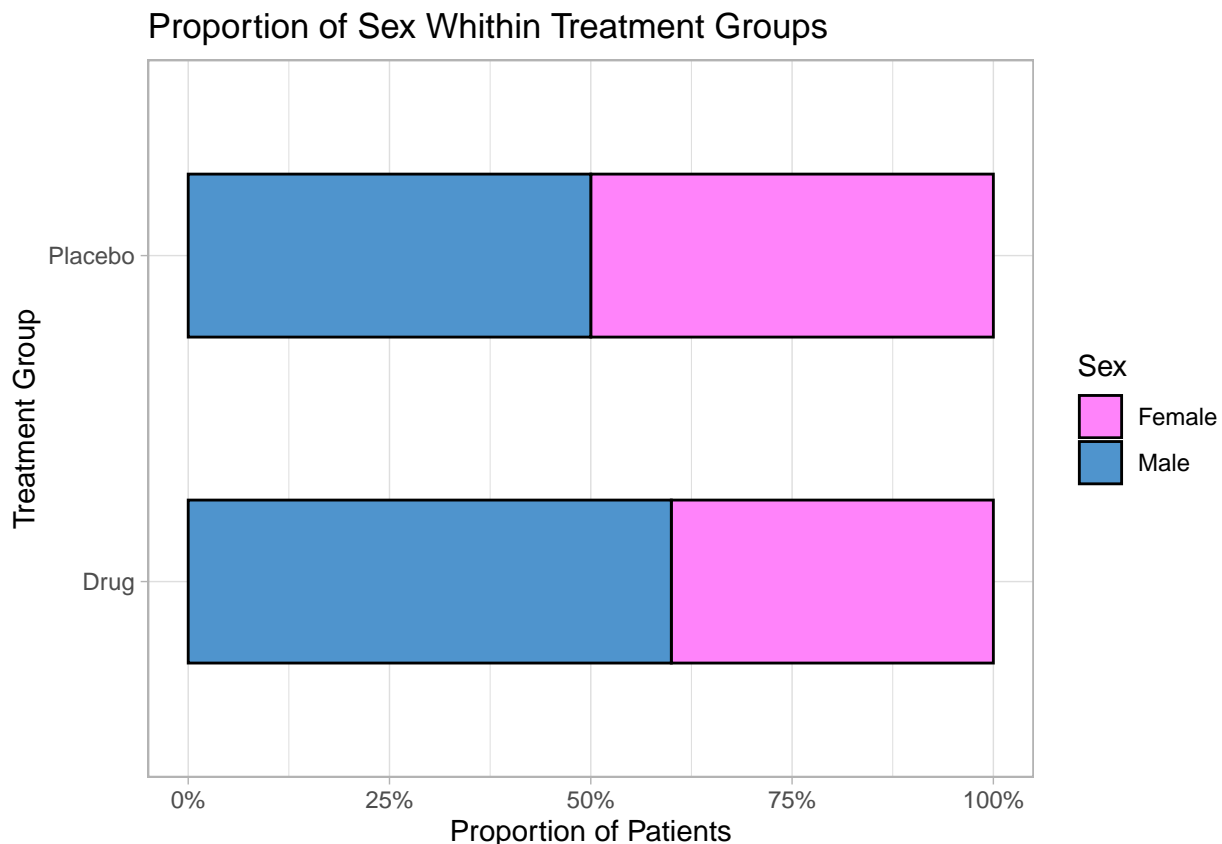
To determine whether there is a statistically significant association between sex of patients and Treatment group (Drug vs Placebo) a Chi-squared test of independence is conducted.

```
chisq.test(table(data$TRT, data$Sex))
```

```
##
##  Pearson's Chi-squared test with Yates' continuity correction
##
## data:  table(data$TRT, data$Sex)
## X-squared = 0.10101, df = 1, p-value = 0.7506
```

The test shows that there is no significant association between treatment group and sex, indicating that the distribution of sex was similar across the Drug and Placebo groups.

To evaluate whether the Drug treatment had a statistically significant effect over time within that group, a paired t-test for DBP1 vs DBP5 within each group (e.g., Drug or Placebo group) is performed. To do so first the normality of the differences are verified.

```
group_drug <- data %>% filter(TRT == "A")

group_placebo <- data %>% filter(TRT == "B")

group_drug$diff <- group_drug$DBP1-group_drug$DBP5

ggplot(group_drug, aes(sample = diff)) +
  stat_qq(color = "steelblue", size = 2)+
  stat_qq_line(color = "darkred", linetype = "dashed")+
  labs(
    title = "Q-Q plot for DBP1 - DBP5 differences (Drug Treatment)",
    x = "Theoretical Quantiles",
    y = "Sample Quantiles"
  ) +
  theme_light()
```

Q–Q plot for DBP1 – DBP5 differences (Drug Treatment)
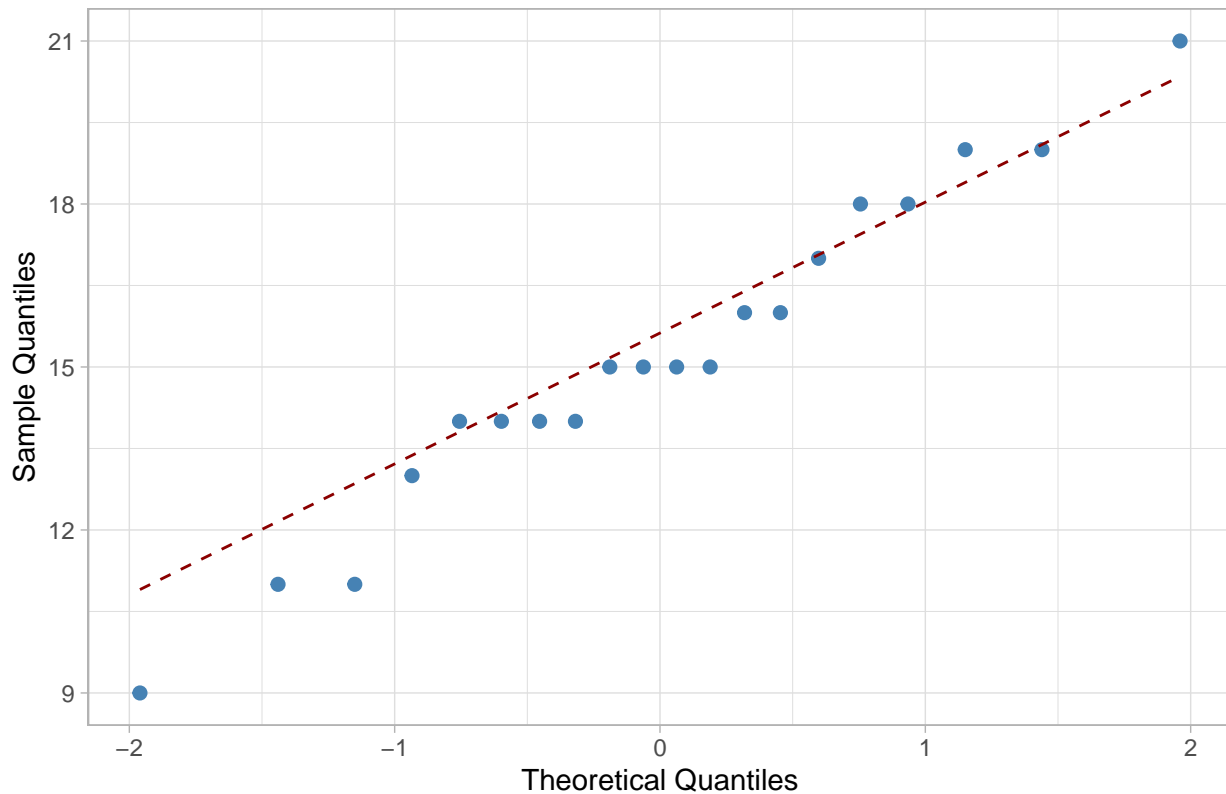
The Q-Q plot of the differences in diastolic blood pressure (DBP1 − DBP5) in the Drug group shows that the points closely followed the reference line, indicating that the distribution of the differences is approximately normal.

```
shapiro.test(group_drug$diff)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  group_drug$diff
## W = 0.9741, p-value = 0.8379
```

A Shapiro-Wilk test indicated that the differences between baseline and final diastolic blood pressure (DBP1 − DBP5) in the Drug group are approximately normally distributed (W = 0.974, $p = 0.838$), supporting the assumption of normality required for the paired t-test.

```
t.test(group_drug$DBP1, group_drug$DBP5, paired = TRUE)
```

```
##
##  Paired t-test
##
## data:  group_drug$DBP1 and group_drug$DBP5
## t = 22.915, df = 19, p-value = 2.649e-15
## alternative hypothesis: true mean difference is not equal to 0
## 95 percent confidence interval:
##  13.81164 16.58836
## sample estimates:
## mean difference
##            15.2
```

A paired t-test shows that the mean diastolic blood pressure significantly decreases from baseline (DBP1) to the final time point (DBP5) in the Drug group, with a mean reduction of 15.2 mmHg.

```
t.test(group_placebo$DBP1, group_placebo$DBP5, paired = TRUE)
```

```
##
##  Paired t-test
##
## data:  group_placebo$DBP1 and group_placebo$DBP5
## t = 8.8732, df = 19, p-value = 3.481e-08
## alternative hypothesis: true mean difference is not equal to 0
## 95 percent confidence interval:
##  3.66777 5.93223
## sample estimates:
## mean difference
##             4.8
```

A paired t-test shows a statistically significant decrease in diastolic blood pressure from baseline (DBP1) to the final measurement (DBP5) in the Placebo group, with a mean reduction of 4.8 mmHg.

Both groups show a significant reduction in diastolic blood pressure from baseline to the final time point; however, the decrease is substantially greater in the Drug group compared to the Placebo group, suggesting a stronger treatment effect of the drug.

After comparing baseline (DBP1) and final (DBP5) values using a paired t-test, we proceeded to assess whether diastolic blood pressure changed significantly over time across all five timepoints (DBP1–DBP5).

To meet the assumptions of repeated measures ANOVA, we first tested the normality of the within-subject difference scores using the Shapiro–Wilk test.

```
group_drug$d12 <- group_drug$DBP1-group_drug$DBP2

group_drug$d13 <- group_drug$DBP1-group_drug$DBP3

group_drug$d14 <- group_drug$DBP1-group_drug$DBP4

group_drug$d15 <- group_drug$DBP1-group_drug$DBP5


shapiro.test(group_drug$d12)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  group_drug$d12
## W = 0.95877, p-value = 0.5195
```

```
shapiro.test(group_drug$d13)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  group_drug$d13
## W = 0.83358, p-value = 0.002864
```

```
shapiro.test(group_drug$d14)
```

```
##
##  Shapiro-Wilk normality test
```

```
## 
## data:  group_drug$d14
## W = 0.95478, p-value = 0.4455
```

```
shapiro.test(group_drug$d15)
```

```
## 
##  Shapiro-Wilk normality test
## 
## data:  group_drug$d15
## W = 0.9741, p-value = 0.8379
```

Normality of difference scores was tested using Shapiro-Wilk test. All comparisons were normal except DBP1–DBP3 (p = 0.0028), which showed slight deviation.

Upon confirming approximate normality, we conducted a repeated measures ANOVA using the ezANOVA() function.

```
df_dbp$Subject <- as.factor(df_dbp$Subject)

df_dbp$Time <- as.factor(df_dbp$Time)


anova_results <- ezANOVA(
  data = df_dbp,
  dv = DBP, # dependent variable
  wid = Subject, # Within ID subject
  within = Time, # Repeated Measure Factor
  detailed = TRUE
)


print(anova_results)
```

```
## $ANOVA
##        Effect DFn DFd       SSn      SSd          F           p p<.05
## 1 (Intercept)   1  39 2503203.1 1379.075 70790.14693 3.551105e-65     *
## 2        Time   4 156    2514.1 1228.700    79.79971 9.883983e-37     *
##         ges
## 1 0.9989593
## 2 0.4908554
## 
## $`Mauchly's Test for Sphericity`
##   Effect         W            p p<.05
## 2   Time 0.1075557 3.686644e-14     *
## 
## $`Sphericity Corrections`
##   Effect       GGe       p[GG] p[GG]<.05       HFe       p[HF] p[HF]<.05
## 2   Time 0.4783073 7.577155e-19         * 0.5023972 1.125439e-19         *
```

The effect of time is statistically significant ($F(4, 156) = 79.80$, $p < 2e\text{-}16$), indicating that DBP changed significantly over time.

In summary, both the paired t-tests and repeated measures ANOVA demonstrate a significant reduction in diastolic blood pressure over time in both treatment groups, with a markedly stronger effect observed in the Drug group. These findings suggest that the drug may be effective in lowering DBP more substantially than placebo. Further investigation with a larger sample and additional covariates may help confirm and extend

these results.