# A COMPARATIVE ANALYSIS OF DRUG EFFICACY IN SYSTOLIC BLOOD PRESSURE REDUCTION

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## INTRODUCTION

This study aims to evaluate the effectiveness of three different drugs: Ramipril, Lisinopril, and Moexipril in lowering systolic blood pressure (BP). The drugs were administered to four subjects, who were randomly assigned to each treatment group. Systolic BP was recorded both before and after the intervention. The main objectives of this analysis are:

1. To assess whether the three drugs have the same level of effectiveness in reducing mean blood pressure.
2. If not, to identify which drug produces the most significant reduction.
3. To conduct a statistical analysis to determine if the random assignment of subjects to drug groups was successful.

## METHODS

### 1. Data

The dataset includes three variables: systolic BP before and after treatment, and the drug administered. Each drug group consists of four subjects, totaling 12 subjects in the study.

### 2. Statistical Analysis

A one-way ANCOVA was chosen as the primary model for analysis. This model was selected because it adjusts for baseline BP differences and allows for a clearer evaluation of the effect of the three drugs on change in systolic BP. The covariate in the ANCOVA model is the pre-treatment systolic BP, and the response variable is the change in systolic BP. The primary factor is the drug administered (Ramipril, Lisinopril, or Moexipril).

In this analysis, the emmeans procedure was applied to estimate the average change in systolic blood pressure (BP) for each drug group, while adjusting for differences in pre-treatment BP (used as a covariate). By calculating the marginal means, we obtain a clearer understanding of the treatment effects (i.e., the BP change caused by each drug) after accounting for baseline variations between subjects. This helps provide more accurate comparisons of the drugs' effectiveness.

To verify the claim of randomization, pre-treatment BP values were compared among the drug groups using the Kruskal-Wallis Test which is a nonparametric alternative to ANOVA that tests for differences in median values. The Kruskal-Wallis test only compares group

medians, ignoring other distribution aspects like variance, which could affect the verification of randomization. Additionally, with small sample sizes, the test may lack sufficient power to detect significant differences. The level of significance we will use to draw conclusions in this report is 0.05.

3. **Software**

R Core Team (2023). _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.

# RESULTS

## Mean and standard deviation change

Before presenting the ANCOVA results, it's essential to report the baseline data and changes in BP for each drug group. Table 1 summarizes the mean change and standard deviation (SD) of systolic blood pressure (BP) for each drug group: Lisinopril, Moexipril, and Ramipril. Moexipril shows the greatest average BP reduction (-44.50 mmHg), while Ramipril has the smallest (-32.00 mmHg). The standard deviation values indicate the variability in the BP changes, with Lisinopril having the highest variability (SD = 14.95) and Ramipril showing the most consistent BP reductions (SD = 6.38).

Table 1 is important as it provides a quick overview of how each drug impacts systolic BP and the consistency of these effects across subjects. From here, we will conduct the one-way ANCOVA test that will help confirm whether the observed differences between the drugs are statistically significant and guide in determining the most effective treatment.

*Table 1*

| Drug | Mean BP Change | SD BP Change |
|---|---|---|
| **Lisinopril** | -38.75 | 14.95 |
| **Moexipril** | -44.50 | 8.81 |
| **Ramipril** | -32.00 | 6.38 |

## ANCOVA Results

The ANCOVA model was run with the change in systolic BP as the dependent variable (response variable), pre-treatment systolic BP as a covariate, and drug type as the independent variable. The purpose of the model is to determine whether the type of drug has a significant effect on the BP change, while accounting for any differences in pre-treatment BP levels. By adjusting for the covariate, we aim to isolate the effect of each drug on BP reduction and assess whether the observed changes in BP are influenced by

the initial BP levels of the subjects. Table 2 shows the results from running the ANCOVA model.

*Table 2*

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|---|---|---|---|---|---|
| SysBP.pre | 1 | 360.3 | 360.3 | 7.046 | 0.0291 |
| Drug | 2 | 569.5 | 284.7 | 5.568 | 0.0305 |
| Residuals | 8 | 409.1 | 51.1 | | |

The F-value for pre-treatment systolic BP is 7.046 (with 1df) and the p-value is 0.0291 (which is less than 0.05). This suggests that pre-treatment systolic BP has a significant effect on the change in BP. In other words, the initial BP level of the subjects influences how much their BP changes after treatment. Therefore, including this covariate was appropriate and helps to account for baseline differences in BP between subjects.

Also, the F-value for the drug type is 5.568 (with 2df), and the p-value is 0.0305 (which is also less than 0.05). This means that, after adjusting for pre-treatment BP, there is a significant difference in BP changes across the different drug groups. The type of drug administered influences the reduction in systolic BP.

The one-way ANCOVA analysis indicates that both pre-treatment systolic BP and drug type significantly affect the change in systolic BP. This means that the drugs differ in their effectiveness at reducing systolic BP, even after adjusting for differences in baseline BP.

Since the drug type has a significant effect, it would be useful to perform a multiple comparison test to determine which specific drugs differ from each other in terms of BP reduction. This will help to identify the most effective drug. We will use the Tukey's HSD test.

**Multiple Comparisons**

Pairwise comparisons are shown in table 3 and they indicate that the difference between Moexipril and Ramipril was statistically significant (p-value = 0.0282), with Moexipril being more effective. However, the difference between Lisinopril and Moexipril was not statistically significant (p-value = 0.7021), indicating similar effectiveness. The comparison between Lisinopril and Ramipril was also not significant (p-value = 0.0992). Overall, the results indicate that Moexipril was the most effective drug in reducing systolic BP, especially when compared to Ramipril.

*Table 3*

| **Pairwise Comparisons of Drugs** | | | | | |
|---|---|---|---|---|---|
| **contrast** | **estimate** | **SE** | **df** | **t.ratio** | **p.value** |
| **Lisinopril - Moexipril** | 4.161991 | 5.077354 | 8 | 0.8197165 | 0.7020515 |

| | | | | | |
|---|---|---|---|---|---|
| **Lisinopril - Ramipril** | -12.784435 | 5.347005 | 8 | -2.3909522 | 0.0992435 |
| **Moexipril - Ramipril** | -16.946426 | 5.216330 | 8 | -3.2487260 | 0.0282393 |

### Assessment of Randomization

The Kruskal-Wallis test was conducted to evaluate whether the pre-treatment systolic blood pressure levels were comparable across the different drug groups. This serves as a check for the effectiveness of randomization. It allows us to determine whether there are significant differences in pre-treatment BP distributions between the drug groups, which would suggest problems with randomization. The test yielded a p-value of 0.668, which is significantly greater than 0.05. This indicates that there is no statistically significant difference in pre-treatment BP between the drug groups. Thus, we conclude that the groups were comparable at baseline, suggesting that the randomization process was successful.

This result supports the integrity of the study design, ensuring that any observed differences in post-treatment outcomes are likely because of the drugs rather than pre-existing differences between the groups.

*Table 4*

| | **Statistic** | **DF** | **p-value** |
|---|---|---|---|
| **Kruskal-Wallis chi-squared** | 0.808 | 2 | 0.668 |

## CONCLUSION

### Implications and Findings

The analysis assessed the effectiveness of three drugs: Ramipril, Lisinopril, and Moexipril in reducing systolic blood pressure (BP) using ANCOVA, adjusting for pre-treatment BP. The results indicated that Moexipril had the largest average reduction in systolic BP, followed by Lisinopril, with Ramipril being the least effective. The emmeans (estimated marginal means) method was used for multiple comparisons, and the pairwise contrasts revealed that Moexipril was significantly more effective than Ramipril. However, the difference between Moexipril and Lisinopril was not statistically significant, indicating similar effectiveness between these two drugs.

The Kruskal-Wallis test was used to verify the randomization of subjects, and it confirmed no significant differences in pre-treatment BP between the drug groups, suggesting that the randomization was successful.

## Limitations of the study

There are several limitations to this analysis. The small sample size (four subjects per group) limits the power of the statistical tests, making it harder to detect smaller differences between the drugs. Additionally, the Kruskal-Wallis test compares medians but does not consider differences in variances, which could have influenced the findings. Moreover, while emmeans offers more refined comparisons than basic methods, the results are specific to these three drugs and may not generalize to other treatments for systolic BP without further research.

# APPENDIX

## References

Hughes, M. (2024). *R Code for Statistical Analysis*. STA 660, Miami University, Oxford-Ohio.

## Code for Statistical Analysis

```
# Load necessary libraries
library(dplyr)
library(knitr)
library(car)
library(emmeans)

# Read in data
bpdata <- read.csv("/Users/presidentoliver/Desktop/Practicum in Data
Analysis/Project 1 - Blood pressure study/bloodpressurestudy.csv")
#names(bpdata)

bpdata <- bpdata %>%
  mutate(subject = factor(subject),
         BPchange = after-before,                                    #
straight pre/post diff
         rel.BPchange = (after-before)/before,                       #
change relative to initial
         BP.pct.drop.120 = 100*(before-after)/(before-120)) %>%   # %
drop rel to 120 (interp?)
  rename(ID = subject,
         Drug = drug,
         SysBP.pre = before,
         SysBP.post = after)



# calculate both mean and standard deviation for BP_Change by Drug
formatted_table <- bpdata %>%
  group_by(Drug) %>%
  summarize(
    mean_BP_Change = mean(BPchange, na.rm = TRUE),
    sd_BP_Change = sd(BPchange, na.rm = TRUE)
  ) %>%
  kable(format = "html", digits = 2, caption = "Table 1")  # Adding a
caption

# Print formatted table
formatted_table
```

```
### Model 5: One-way ANCOVA on change in BP, using pre-study BP as a
covariate

# Visualization
ggplot(bpdata, aes(x=SysBP.pre, y=BPchange, shape=Drug, colour=Drug,
fill=Drug)) +
  geom_smooth(method="lm") +
  geom_point() +
  labs(x = "Pre-study Systolic BP (mmHg)",
       y = "Change in Systolic BP (mmHg)")

# Modeling
ancova2 <- aov(BPchange ~ SysBP.pre + Drug, data = bpdata)



# Multiple comparison - simultaneous CIs
emmeans(ancova2, specs = pairwise ~ Drug)

# Get the emmeans output
emmeans_output <- emmeans(ancova2, specs = pairwise ~ Drug)

# Format the contrast results using kable
contrast_table <- as.data.frame(emmeans_output$contrasts)

# Use kable to format the table for Word
kable(contrast_table, format = "markdown", caption = "Pairwise
Comparisons of Drugs") %>%
  print()

# Nonparametric test to compare distributions of pre-study BP
kruskal_result <- kruskal.test(SysBP.pre ~ Drug, data = bpdata)


# Extract the necessary values
kruskal_df <- data.frame(
  Statistic = kruskal_result$statistic,
  Degrees_of_Freedom = kruskal_result$parameter,
  P_value = kruskal_result$p.value
)
kable(kruskal_df, format = "html", digits = 3, caption = "Kruskal-
Wallis Test for Pre-treatment BP") %>%
  print()
```