Drug Rating Comparisons for Depression, Pain, and ADHD

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1 Introduction

For many individuals, pharmaceutical drugs are the typical go to remedy in regards to treating various conditions the are relevant for them. For relatively mild conditions such as a headache or sore throat, over the counter drugs may suffice. These drugs may not be enough for more extreme conditions such as major depression, severe post-surgical pain, or ADHD. Conditions such as these may necessitate drugs that require receiving permission from a medical practitioner in the form of a prescription.

Prescription drug manufacturing and use has increased substantially over the years. The total expenditure by pharmaceutical companies in 2020 was $535.3 billion which was a 4.9% increase in expenditure in comparison to 2019 [1]. For conditions such as depression, pain and ADHD, there are a multitude of drugs that can be used to treat each of them. They typically differ by producing the desired effects through variations of generic chemical interaction mechanisms or their own unique chemical interaction mechanisms. For example, most prescription drugs that are used to treat depression interact with neurological pathways as a selective serotonin inhibitor. However, the anti-depressant Bupropion approaches neurological pathways as an norepinepherine dopamine re-uptake inhibitor [2].

With this in mind, sentiment towards various prescription drugs for a particular condition may not be equal. Patients may not react well to the side effects of one drug and may prefer an alternative. In many cases, patients may not have the financial means to acquire a prescription drug they prefer. They would have to settle with cheaper alternatives that they may not respond well to. Typically brand-name prescriptions cost more than generic drug prescriptions. However many generic drugs have currently received price increases [3] thereby financially limiting patients to other potential alternatives. This report uses statistical analysis methods such as permutation testing and t-test's in order to compare drug sentiments for specified drugs that are used to treat depression, pain, and ADHD.

2 Algorithm Description

Permutation tests [4] are conducted in order to compare the rating for different drugs of interest for depression, pain and ADHD. Since all the samples of interest were drawn from the same population [5], we can assume exchangeability of the data [4] and conduct permutations. A permutation function was created in order to conduct the various permutation tests on the drugs of interest. The function inputs were the number of permutations to conduct, the ratings for one drug of interest, the ratings for another drug of interest, and the test statistic of interest. The test statistic in every case was the difference in mean ratings between the drugs of interest. This can be done safely since there is no situation where the means for any of the samples are equal to each other. This was done for each of the previously mentioned conditions.

The function first determines the number of samples from each drug vector. It then labels samples from one of the drug vectors as 1 and the other drug vector as 0. Once the vectors have been labeled, they are combined into one data frame. The labels are then permuted and a new test statistic is generated. The previous step occurs as many times as specified by the number of permutations parameter in the function. The observed test statistic is then calculated. A p-value with 95% confidence is then calculated from there. If there is a significant difference between the drugs of interest, a t-test[6] with 95% confidence was then conducted to determine whether one drug had a significantly greater or smaller average rating than the other.

For depression, the drug that was reviewed the most was Bupropion. Three permutation tests were conducted in order to determine whether Bupropion had significantly better ratings than the other specified drugs of interest. The first permutation test was conducted between Bupropion and Sertraline, the second permutation test was conducted between Bupropion and Lexapro, and the third permutation test was conducted between Bupropion and Effexor. In all three permutation tests, the null hypothesis was that Bupropion does not have significantly different ratings in comparison to the other specified drugs. A t-test was conducted accordingly if a significant difference was found.

For pain, the drug that was reviewed the most was Tramadol. Three permutation tests were conducted in order to determine whether Tramadol had significantly better ratings than the other specified drugs of interest. The first permutation test was conducted between Tramadol and Oxycodone, the second permutation test was conducted between Tramadol and Gabapentin, and the third permutation test was conducted between Tramadol and Fentanyl. In all three permutations tests the null hypothesis was that Tramadol does not have significantly different ratings in comparison to the other specified drugs. A t-test was conducted accordingly if a significant difference was found.

For ADHD, the drug that was reviewed the most was Lisdexamfetamine. Three permutations tests were conducted in order to determine whether Lisdexamfetamine had significantly better ratings than the other specified drugs of interest. The first permutation test was conducted between Lisdexamfetamine and Methylphenidate, the second permutation test was conducted between Lisdexamfetamine and Adderal, the third permutation test was conducted between Lisdexamfetamine and Bupropion. In all three permutation tests, the null hypothesis was that Lisdexamfetamine does not have significantly different ratings in comparison to the other drugs of interest. A t-test was conducted accordingly

if a significant difference was found.

All relevant code pertaining to the previously described procedures can be found in the Appendix section. Values mentioned in the report may differ slightly from those found in the Appendix section due to the nature of permutation testing.

3 Data description

The data set that will be used for this project is the Drug Review Dataset from the UCI Machine Learning Repository[5]. This data set provides patient reviews on various drugs for different medical conditions including a 10-star patient rating of drug satisfaction. The attributes in the data set include drugName(name of drug), condition(medical condition), review(comments on drug satisfaction), rating(numerical rating of drug from 1 to 10), date(date of review entry), and usefulCount(number of users who found review useful). There are a total 215,063 cases in the entire data set. The data was collected by scraping online pharmaceutical reviews with the intention of studying drug sentiment analysis. The particular conditions of focus for this project are depression, pain, and ADHD.

For depression, there were 12,164 reviews and 115 unique drugs. The drugs focus for depression were Bupropion, Sertraline, Lexapro, and Effexor. There were 747 reviews for Bupropion, 663 reviews for Sertraline, 408 reviews for Lexapro, and 259 reviews for Effexor.

For pain, there were 8,245 reviews and 219 unique drugs. The drugs of focus for pain were Tramadol, Oxycodone, Gabapentin, and Fentanyl. There were 501 reviews for Tramadaol, 380 reviews for Oxycodone, 239 reviews for Gabapentin, and 155 reviews for Fentanyl.

For ADHD, there were 4,509 reviews and 58 unique drugs. The drugs of focus for ADHD were Lisdexamfetamine, Methylphendiate, Adderal, and Bupropion. There were 548 reviews for Lisdexamfetamine, 513 review for Methylphendiate, 227 reviews for Adderall, and 72 reviews for Bupropion.

4 Results

4.1 Depression

The permutation test for the average rating of Bupropion versus Sertraline is displayed below in Figure 1. The p-value for this test was 0.0569 which is greater than a significance of 5%. Therefore, we fail to reject the null and conclude that there is no significant difference between average ratings for Bupropion and Sertraline.

The permutation test for the average rating of Bupropion versus Lexapro is displayed below in Figure 2. The p-value for this test was 0.0903 which is greater than a significance of 5%. Therefore, we fail to reject the null and conclude that there is no significant difference between average ratings for Bupropion and Lexapro.

The permutation test for the average rating of Bupropion versus Effexor is displayed below in Figure 3. The p-value for this test was 0 which is smaller than a significance

of 5%. Therefore, we reject the null and conclude that there is a significant difference between Bupropion and Effexor. A t-test was then conducted in order to determine whether Bupropion had a significantly greater average rating than Effexor. The p-value was calculated to be 2.78e-11 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that Bupropion does a significantly greater average rating than Effexor.

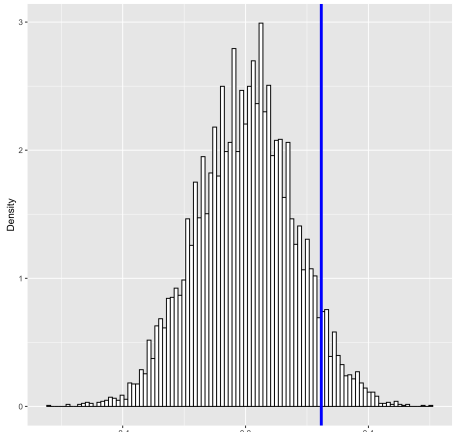

Figure 1. Average rating for Bupropion vs. Sertraline

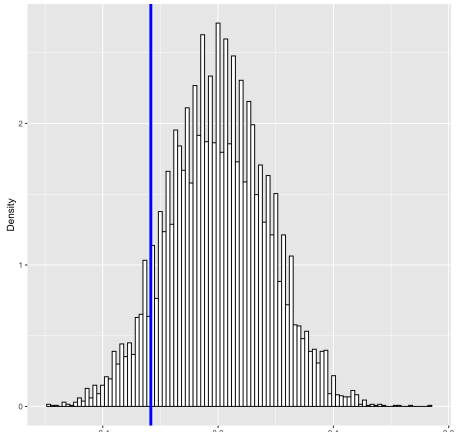

Figure 2. Average rating for Bupropion vs. Lexapro

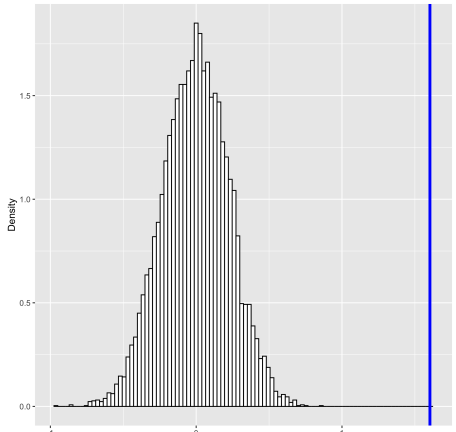

Figure 3. Average rating for Bupropion vs. Effexor

4.2 Pain

The permutation test for the average rating of Tramadol versus Oxycodone is displayed below in Figure 4. The p-value for this test was 0 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that there is a significant difference between average ratings for Tramadol and Oxycodone. A t-test was then conducted in order to determine whether Tramadol had a significantly smaller average rating than Oxycodone. The p-value was calculated to be a value smaller than 2.2e-16 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that Tramadol does have a significantly smaller average rating than Oxycodone.

The permutation test for the average rating of Tramadol versus Gabapentin is displayed below in Figure 5. The p-value for this test was calculated to be 0.3116 which is greater than a significance of 5%. Therefore, we fail to reject the null and conclude that there is no significant difference between average ratings for Tramadol and Gabapentin.

The permutation test for the average rating of Tramadol versus Fentanyl is displayed below in Figure 6. The p-value for this test was calculated to be 0 which is smaller than a significance of 5%. A t-test was then conducted in order to determine whether Tramadol had a significantly smaller average rating than Fentanyl. The p-value was calculated to be a value significantly smaller 2.2e-16 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that Tramadol does have a significantly smaller average rating than Oxycodone.

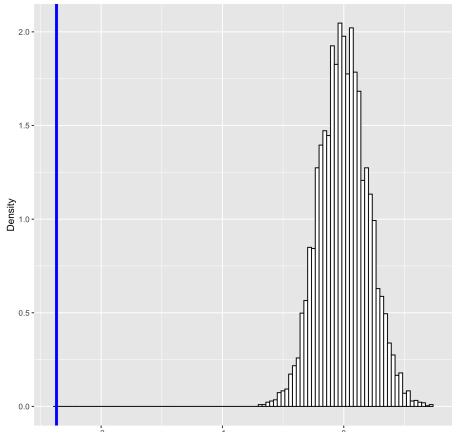

Figure 4. Average rating for Tramadol vs. Oxycodone

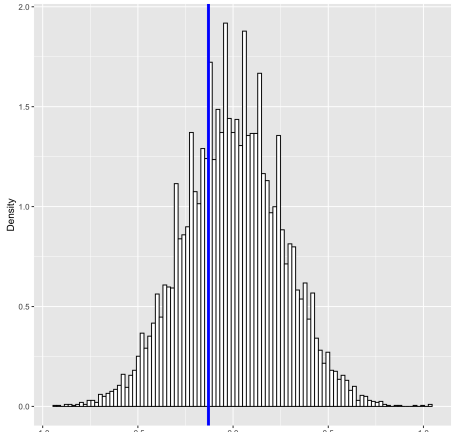

Figure 5. Average rating for Tramadol vs. Gabapentin

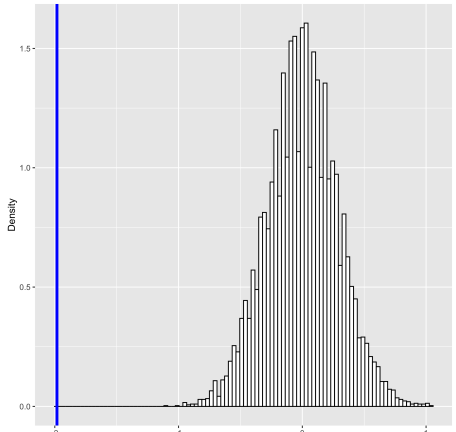

Figure 6. Average rating for Tramadol vs. Fentanyl

4.3 ADHD

The permutation test for average rating of Lisdexamfetamine versus Methylphenidate is displayed below in Figure 7. The p-value for this test was calculated to be 0.0306 which is smaller than a significance of 5%. Therefore we reject the null and conclude that there is a significant difference between average ratings for Lisdexamfetamine and Methylphenidate. A t-test was then conducted in order to determine whether Lisdexamfetamine had a significantly larger average rating than Methylphenidate. The p-value was calculated to be 0.02926 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that Lisdexamfetamine does have a significantly greater average rating than Methylphenidate.

The permutation test for the average rating of Lisdexamfetamine versus Adderall is displayed below in Figure 8. The p-value for this test was calculated to be 0.0037 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that there is a significant difference between average ratings for Lisdexamfetmanine and Adderall. A t-test was then conducted in order to determine whether Lisdexamfetamine had a significantly smaller average rating than Adderall. The p-value was calculated to be 0.003105 which is smaller than a significance of 5%. Therefore, we reject the null and conclude that Lisdexamfetamine does have a significantly smaller average rating than Adderall.

The permutation test for average rating of Lisdexamfetamine versus Bupropion is displayed below in Figure 9. The p-value for this test was calculated to be 0.2813 which is larger than a significance of 5%. Therefore, we fail to reject the null and conclude that there is not a significant significant difference between average ratings for Lisdexamfetamine and Bupropion.

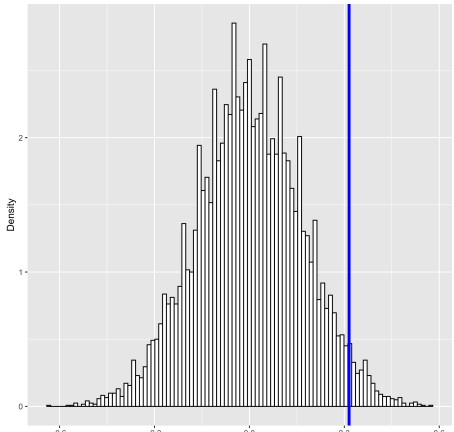

Figure 7. Average rating for Lisdexamfetamine vs. Methylphenidate

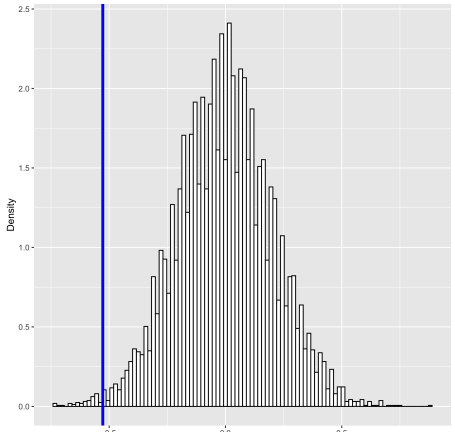

Figure 8. Average rating for Lisdexamfetamine vs. Adderall

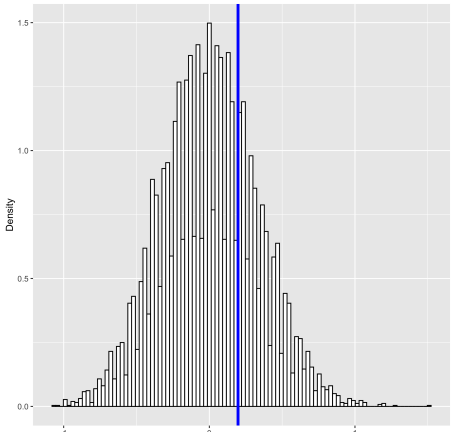

Figure 9. Average rating for Lisdexamfetamine vs. Bupropion

5 Discussion

5.1 Depression

When comparing the average ratings for Bupropion and Sertraline, it was observed that there was no significant difference between them. This was also observed when comparing the average ratings for Bupropion and Lexapro. This is most likely because these three drugs are fairly common treatments that have been extensively commercialized as prescription drugs for depression. Bupropion is a single drug that is marketed as 4 different brand names [7]. Each one of these brands has a similar chemical structure but has been marketed for different purposes. Bupropion is marketed as Wellbutrin and Prolev for depression. It is also marketed as Zyban and Quomem as a smoking-cessation aid. Sertraline is typically marketed with the brand name Zoloft [8] under Pfizer which is one of the largest pharmaceutical manufacturing companies. Lexapro is the brand name for the drug Escitalopram [9] which has been extensively studied as an effective treatment for major depression. Considering how these drugs are marketed for depression, it makes sense that there is no significant difference in the average ratings Bupropion with each respective drug.

When comparing the average ratings for Bupropion and Effexor, it was observed that Bupropion had significantly greater average ratings than Effexor. This is probably due to negative side effects that are accompanied with taking Effexor. A key side-effect that differentiates Effexor and Bupropion (Wellbutrin) is that Effexor may cause drowsiness and sexual dysfunction [10]. Considering these side-effects, it makes sense that Bupropion had a significantly greater average rating than Effexor.

5.2 Pain

When comparing the average ratings for Tramadol and Gabapentin, it was observed that there was no significant difference between them. This is probably because both these drugs are used to treat different types of pain so there is not much competition between their use [11]. Gabapentin is typically used for nerve pain. Specifically, it is used to treat

pain that is a result of shingles. On other hand, Tramadol is typically used for more general pain symptoms.

When comparing the average ratings for Tramadol and Oxycodone, it was observed that Tramadol had a significantly smaller average rating than Oxycodone. This is probably because Oxycodone is significantly more potent than Tramdol in regards to treating pain. While Tramadol is 10% as strong as morphine, Oxycodone is 1.5 times more potent than morphine. Therefore, it is considered to be significantly more effective in treating pain.

When comparing the average ratings for Tramadol and Fentanyl, it was observed that Tramadol had a significantly smaller average rating than Fentanyl. This may also be due to the potency difference between Fentanyl and Tramadol. Fentanyl is a significantly more potent pain reliever than Tramadol. In addition, Fentanyl's analgesia occurs more rapidly than Tramadol [12]. Considering the potency and onset time differences, Fentanyl is most likely prescribed in situations where Tramadol may not be enough for pain treatment. It is worth noting that both these drugs are considered to be highly addictive when abused. Particularly Fentanyl which is classified 100 times more potent than morphine and classified as a Schedule II controlled substance [13]. This means that there is high potential for abuse and can cause severe psychological or physical dependence [14]. Tramadol on the other hand is classified as a Schedule IV drug which indicates a significantly smaller potential for abuse and dependence.

5.3 ADHD

When comparing the average ratings for Lisdexamfetamine and Methylphenidate, it was observed that Lisdexamfetamine has a significantly greater average rating than Methylphenidate. The brand names for Lisdexamfetamine and Methylphidate are Vyvanse and Ritalin. Vyvanse is shown to have a more effective symptom relief when treating ADHD as compared to Ritalin [15]. Since Vyvanse is more expensive than Ritalin, patients may settle with being prescribed Ritalin due to cost limitations.

When comparing the average ratings for Lisdexamfetamine and Adderall, it was observed that Lisdexamfetamine has a significantly smaller average rating than Adderall. Both drugs are considered to have similar effectiveness when treating symptoms associated with ADHD. They both also have similar side effects. A key difference is that Vyvanse is sold as a name-brand prescription drug and Adderall is sold as a generic drug [16]. Typically, generic drugs are much less expensive than brand-name drugs. Therefore, it makes sense that Adderall would have a significantly higher average rating than Lisedexamfetamine.

When comparing the average ratings for Lisdexamfetamine and Bupropion, it was observed that there is no significant difference between them. Wellbutrin has been studied extensively as a non-stimulant alternative for ADHD treatment [17]. While there is evidence that Bupropion is a valid treatment for ADHD, further studies need to be conducted in order to determine whether it is as good as other stimulant drugs [18].

5.4 Future Works

Statistical analysis was conducted on only a small portion of drugs and conditions from the drug review data set. Further studies should be conducted on other conditions and drugs found in the data set. More in depth studies should also be conducted on why certain drugs are prescribed more than others. These reasons can range from healthcare limitations to potential side effects. Further studies should also be conducted on potential alternatives to effective drugs that are associated with high risk. Studies in to how pharmaceutical companies market their drugs and how consumers respond to the marketing can also be a potentially useful route of research.

References

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[13] Facts about fentanyl.

[14] Dea drug schedules.

[15] Kristi C. Torres. Vyvanse vs. ritalin: Which is better?, May 2021.

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[17] James G Waxmonsky. Nonstimulant therapies for attention-deficit hyperactivity disorder (adhd) in children and adults. *Essential Psychopharmacology*, 6(5):262–276, 2005.

[18] Amanda L Hile. Bupropion for the treatment of adhd. *Lynchburg Journal of Medical Science*, 2(1):15, 2020.

Appendix

Libraries

```
library(dplyr)
```

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
library(plyr)
```

```
## ------------------------------------------------------------------------------

## You have loaded plyr after dplyr - this is likely to cause problems.
## If you need functions from both plyr and dplyr, please load plyr first, then dplyr:
## library(plyr); library(dplyr)

## ------------------------------------------------------------------------------

##
## Attaching package: 'plyr'

## The following objects are masked from 'package:dplyr':
##
##     arrange, count, desc, failwith, id, mutate, rename, summarise,
##     summarize
```

```
library(tidyverse)
```

```
## -- Attaching packages --------------------------------------- tidyverse 1.3.1 --

## v ggplot2 3.3.5     v purrr   0.3.4
## v tibble  3.1.6     v stringr 1.4.0
## v tidyr   1.2.0     v forcats 0.5.1
## v readr   2.1.2
```

```
## -- Conflicts ---------------------------------------- tidyverse_conflicts() --
## x plyr::arrange()   masks dplyr::arrange()
## x purrr::compact()  masks plyr::compact()
## x plyr::count()     masks dplyr::count()
## x plyr::failwith()  masks dplyr::failwith()
## x dplyr::filter()   masks stats::filter()
## x plyr::id()        masks dplyr::id()
## x dplyr::lag()      masks stats::lag()
## x plyr::mutate()    masks dplyr::mutate()
## x plyr::rename()    masks dplyr::rename()
## x plyr::summarise() masks dplyr::summarise()
## x plyr::summarize() masks dplyr::summarize()
```

```
library(ggplot2)
```

EDA

```
train <- read.csv("/Users/shivramiyer/Documents/Stat440/drugsCom_raw/drugsComTest_raw.tsv", sep = "\t")
#train <- train[order(-train$usefulCount),]
test <- read.csv("/Users/shivramiyer/Documents/Stat440/drugsCom_raw/drugsComTrain_raw.tsv", sep = "\t")
#test <- test[order(-test$usefulCount),]
joint_df <- rbind(train, test)
drug_freq <- count(joint_df, 'drugName')
drug_freq <- drug_freq[order(-drug_freq$freq),]
condition_freq <- count(joint_df, 'condition')
condition_freq <- condition_freq[order(-condition_freq$freq),]
```

condition = Depression

```
depression_df <- joint_df[which(joint_df$condition=='Depression'),]
depression_df <- depression_df[order(-depression_df$rating),]
depression_drug_freq <- count(depression_df, 'drugName')
depression_drug_freq <- depression_drug_freq[order(-depression_drug_freq$freq),]
```

condition = Pain

```
pain_df <- joint_df[which(joint_df$condition=='Pain'),]
pain_df <- pain_df[order(-pain_df$rating),]
pain_drug_freq <- count(pain_df, 'drugName')
pain_drug_freq <- pain_drug_freq[order(-pain_drug_freq$freq),]
```

condition = ADHD

```r
adhd_df <- joint_df[which(joint_df$condition=='ADHD'),]
adhd_df <- adhd_df[order(-adhd_df$rating),]
adhd_drug_freq <- count(adhd_df, 'drugName')
adhd_drug_freq <- adhd_drug_freq[order(-adhd_drug_freq$freq),]
```

Functions

```r
same_dist_perms_test = function(
    n_perms,
    xs,
    ys,
    test_stat){
  #' generic permutation test
  #' @param n_perms number of permutations
  #' @param xs vector of samples for distribution X
  #' @param ys vector of samples from distribution Y
  #' @param test_stat function that calculates the test stat

  # calculate the number of samples in X and Y
  n = length(xs)
  m = length(ys)

  # define labels (1 = X samples, 0 = y samples)
  labels = c(rep(1, n), rep(0, m))
  all_data = c(xs, ys)

  # for every permutation replication
  replicate(
    n_perms, {
      # permute label orders
      permuted_labels = sample(labels)
      # generate new test statistic under permutation
      test_stat(all_data[permuted_labels == 1],
                all_data[permuted_labels == 0])
      }
    )
}
```

Permutation Tests for Depression Drugs

Bupropion Vs. Sertraline Ratings

```r
dp_BpVSe <- depression_df[depression_df$drugName %in% c("Bupropion", "Sertraline"),]

dp_BpVSe_ratings_perms = same_dist_perms_test(
  10000,
  dp_BpVSe[dp_BpVSe$drugName == "Bupropion", "rating"],
  dp_BpVSe[dp_BpVSe$drugName == "Sertraline", "rating"],
```

```
  function(a, b) {mean(a) - mean(b)}
)

observed_dp_BpVSe_ratings = (
  mean(dp_BpVSe[dp_BpVSe$drugName == "Bupropion", "rating"])-
    mean(dp_BpVSe[dp_BpVSe$drugName == "Sertraline", "rating"])
)

Fig1<-
  ggplot(data=data.frame(x=dp_BpVSe_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_dp_BpVSe_ratings,
             color="blue", size=1.5) +
  xlab("Figure 1. Average rating for Bupropion vs. Sertraline") +
  ylab("Density")

ggsave("Fig1.png", Fig1)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig1
```

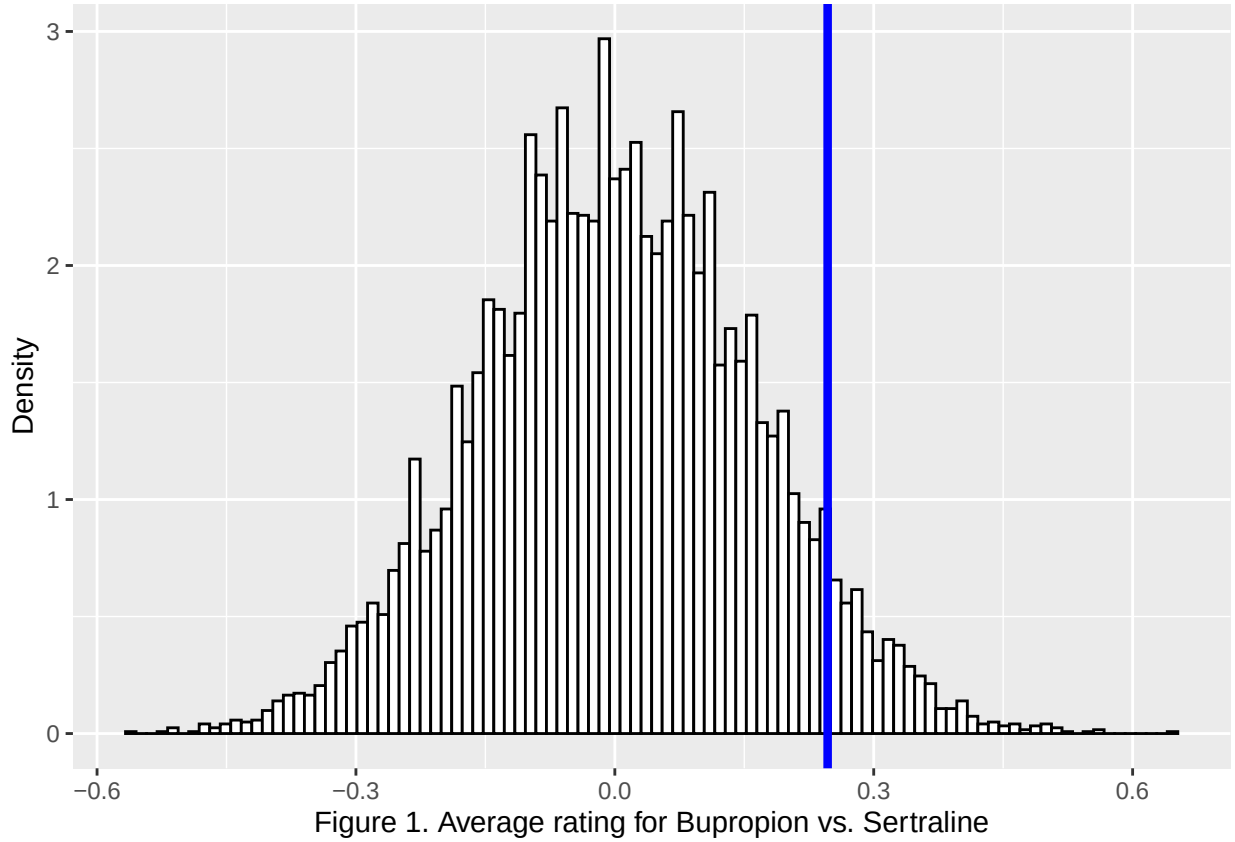

Figure 1. Average rating for Bupropion vs. Sertraline

```
mean(dp_BpVSe_ratings_perms >= observed_dp_BpVSe_ratings)
```

p-value

```
## [1] 0.0626
```

Bupropion Vs. Lexapro Ratings

```
dp_BpVLx <- depression_df[depression_df$drugName %in% c("Bupropion", "Lexapro"),]

dp_BpVLx_ratings_perms = same_dist_perms_test(
  10000,
  dp_BpVLx[dp_BpVLx$drugName == "Bupropion", "rating"],
  dp_BpVLx[dp_BpVLx$drugName == "Lexapro", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_dp_BpVLx_ratings = (
  mean(dp_BpVLx[dp_BpVLx$drugName == "Bupropion", "rating"])-
    mean(dp_BpVLx[dp_BpVLx$drugName == "Lexapro", "rating"])
)

Fig2<-
  ggplot(data=data.frame(x=dp_BpVLx_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_dp_BpVLx_ratings,
             color="blue", size=1.5) +
  xlab("Figure 2. Average rating for Bupropion vs. Lexapro") +
  ylab("Density")

ggsave("Fig2.png", Fig2)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig2
```

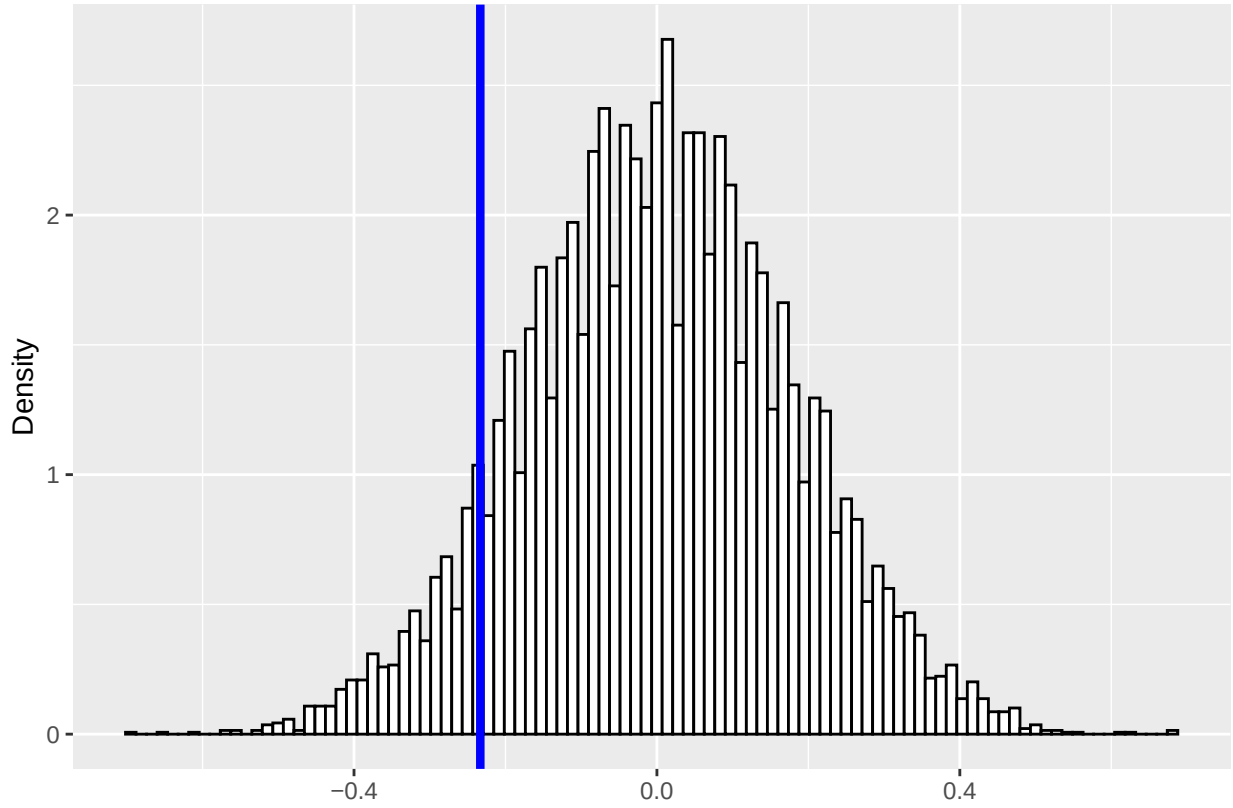

Figure 2. Average rating for Bupropion vs. Lexapro

```
1-mean(dp_BpVLx_ratings_perms >= observed_dp_BpVLx_ratings)
```

p-value

```
## [1] 0.0876
```

Buproprion Vs. Effexor

```
dp_BpVEx <- depression_df[depression_df$drugName %in% c("Bupropion", "Effexor"),]

dp_BpVEx_ratings_perms = same_dist_perms_test(
  10000,
  dp_BpVEx[dp_BpVEx$drugName == "Bupropion", "rating"],
  dp_BpVEx[dp_BpVEx$drugName == "Effexor", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_dp_BpVEx_ratings = (
  mean(dp_BpVEx[dp_BpVEx$drugName == "Bupropion", "rating"])-
    mean(dp_BpVEx[dp_BpVEx$drugName == "Effexor", "rating"])
)
```

```
Fig3<-
  ggplot(data=data.frame(x=dp_BpVEx_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_dp_BpVEx_ratings,
             color="blue", size=1.5) +
  xlab("Figure 3. Average rating for Bupropion vs. Effexor") +
  ylab("Density")

ggsave("Fig3.png", Fig3)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig3
```

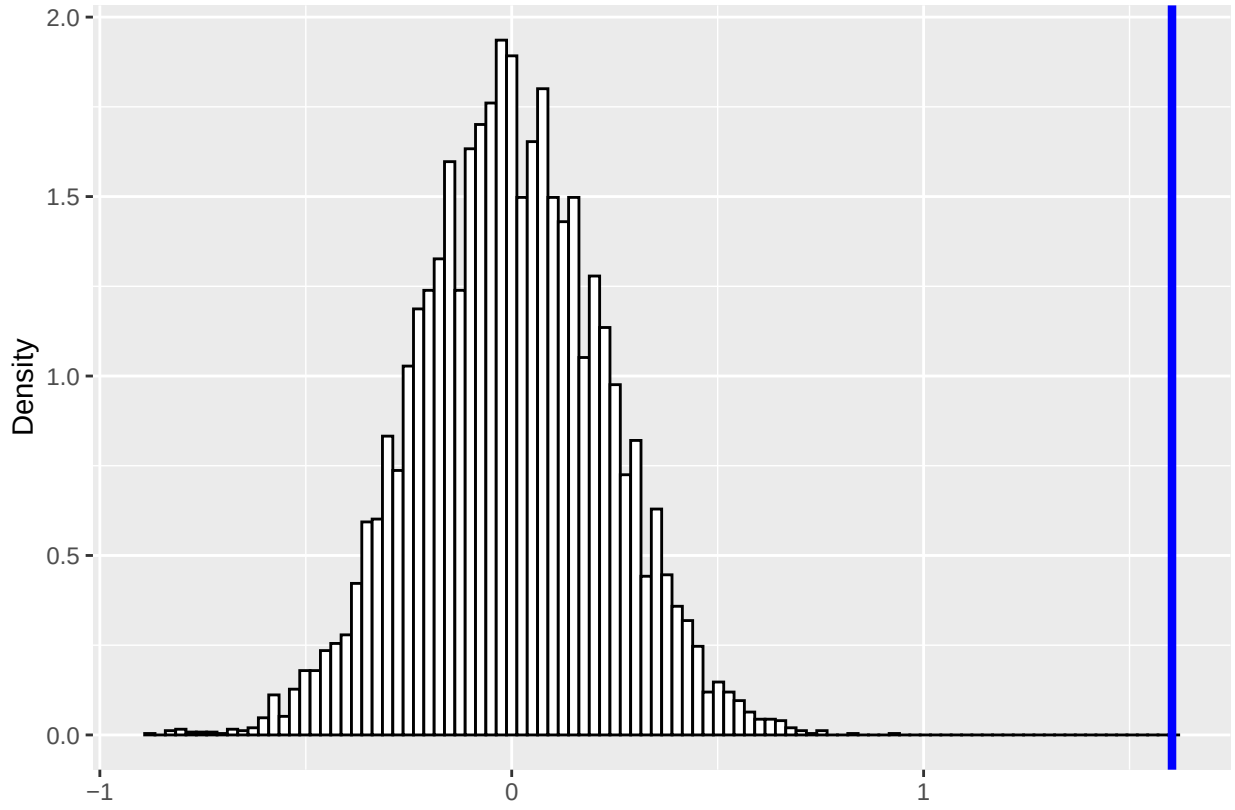

Figure 3. Average rating for Bupropion vs. Effexor

```
mean(dp_BpVEx_ratings_perms >= observed_dp_BpVEx_ratings)
```

p-value

```
## [1] 0
```

```
t.test(x=dp_BpVEx[dp_BpVEx$drugName == "Bupropion", "rating"],
       y=dp_BpVEx[dp_BpVEx$drugName == "Effexor", "rating"],
       alternative = "greater",
       conf.level = 0.95)
```

t-test for whether Bupropion has a significantly greater average rating than Effexor

```
##
##  Welch Two Sample t-test
##
## data:  dp_BpVEx[dp_BpVEx$drugName == "Bupropion", "rating"] and dp_BpVEx[dp_BpVEx$drugName == "Effex
## t = 6.7421, df = 393.76, p-value = 2.788e-11
## alternative hypothesis: true difference in means is greater than 0
## 95 percent confidence interval:
##  1.211071      Inf
## sample estimates:
## mean of x mean of y
##  7.386881  5.783784
```

Permutation Tests For Pain Drugs

Tramadol Vs. Oxycodone

```
pn_TrVOx <- pain_df[pain_df$drugName %in% c("Tramadol", "Oxycodone"),]

pn_TrVOx_ratings_perms = same_dist_perms_test(
  10000,
  pn_TrVOx[pn_TrVOx$drugName == "Tramadol", "rating"],
  pn_TrVOx[pn_TrVOx$drugName == "Oxycodone", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_pn_TrVOx_ratings = (
  mean(pn_TrVOx[pn_TrVOx$drugName == "Tramadol", "rating"])-
    mean(pn_TrVOx[pn_TrVOx$drugName == "Oxycodone", "rating"])
)

Fig4<-
  ggplot(data=data.frame(x=pn_TrVOx_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_pn_TrVOx_ratings,
             color="blue", size=1.5) +
  xlab("Figure 4. Average rating for Tramadol vs. Oxycodone") +
  ylab("Density")

ggsave("Fig4.png", Fig4)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig4
```

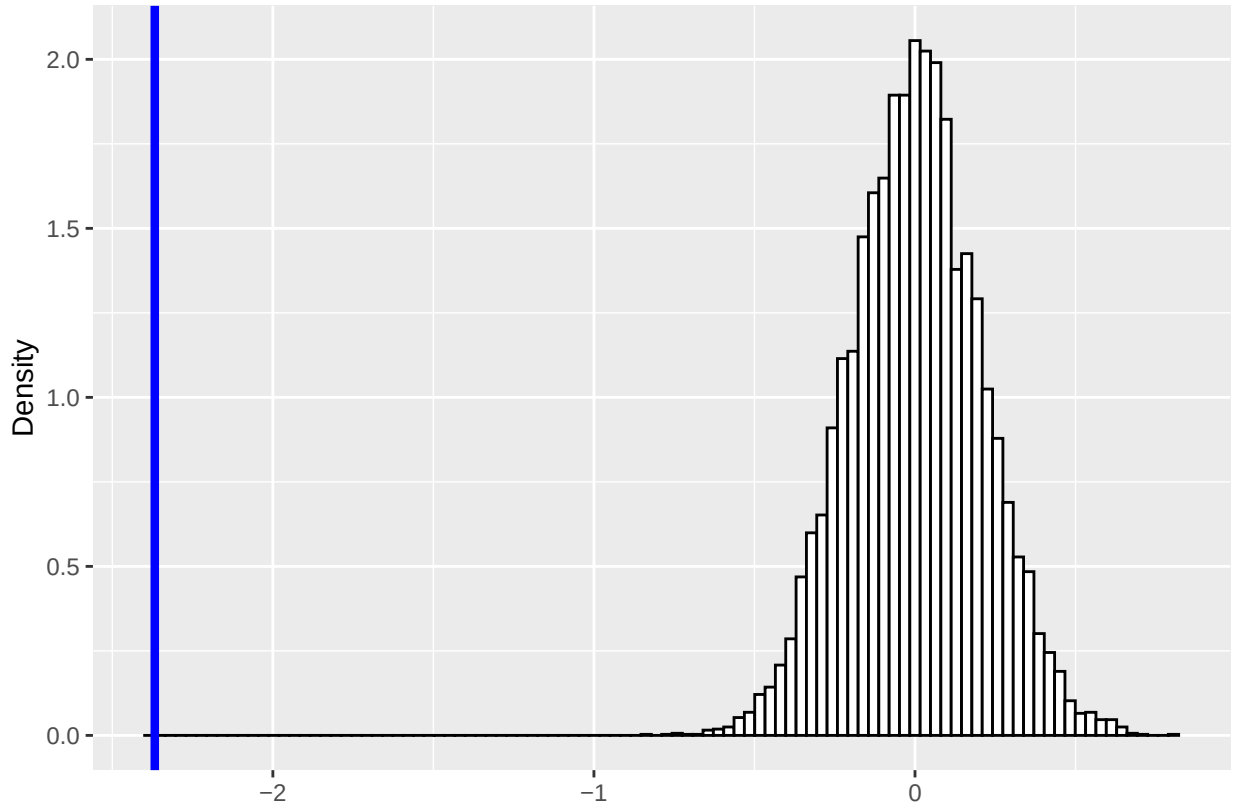

Figure 4. Average rating for Tramadol vs. Oxycodone

```
1 - mean(pn_TrVOx_ratings_perms >= observed_pn_TrVOx_ratings)
```

p-value

```
## [1] 0
```

```
t.test(x=pn_TrVOx[pn_TrVOx$drugName == "Tramadol", "rating"],
       y=pn_TrVOx[pn_TrVOx$drugName == "Oxycodone", "rating"],
       alternative = "less",
       conf.level = 0.95)
```

t-test for whether Tramadol has a significantly smaller average rating than Oxycodone

```
##
##  Welch Two Sample t-test
##
```

```
## data:  pn_TrVOx[pn_TrVOx$drugName == "Tramadol", "rating"] and pn_TrVOx[pn_TrVOx$drugName == "Oxycod
## t = -13.685, df = 795.23, p-value < 2.2e-16
## alternative hypothesis: true difference in means is less than 0
## 95 percent confidence interval:
##       -Inf -2.082862
## sample estimates:
## mean of x mean of y
##  6.469062  8.836842
```

Tramadol Vs. Gabapentin

```
pn_TrVGb <- pain_df[pain_df$drugName %in% c("Tramadol", "Gabapentin"),]

pn_TrVGb_ratings_perms = same_dist_perms_test(
  10000,
  pn_TrVGb[pn_TrVGb$drugName == "Tramadol", "rating"],
  pn_TrVGb[pn_TrVGb$drugName == "Gabapentin", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_pn_TrVGb_ratings = (
  mean(pn_TrVGb[pn_TrVGb$drugName == "Tramadol", "rating"])-
    mean(pn_TrVGb[pn_TrVGb$drugName == "Gabapentin", "rating"])
)

Fig5<-
  ggplot(data=data.frame(x=pn_TrVGb_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_pn_TrVGb_ratings,
             color="blue", size=1.5) +
  xlab("Figure 5. Average rating for Tramadol vs. Gabapentin") +
  ylab("Density")

ggsave("Fig5.png", Fig5)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig5
```

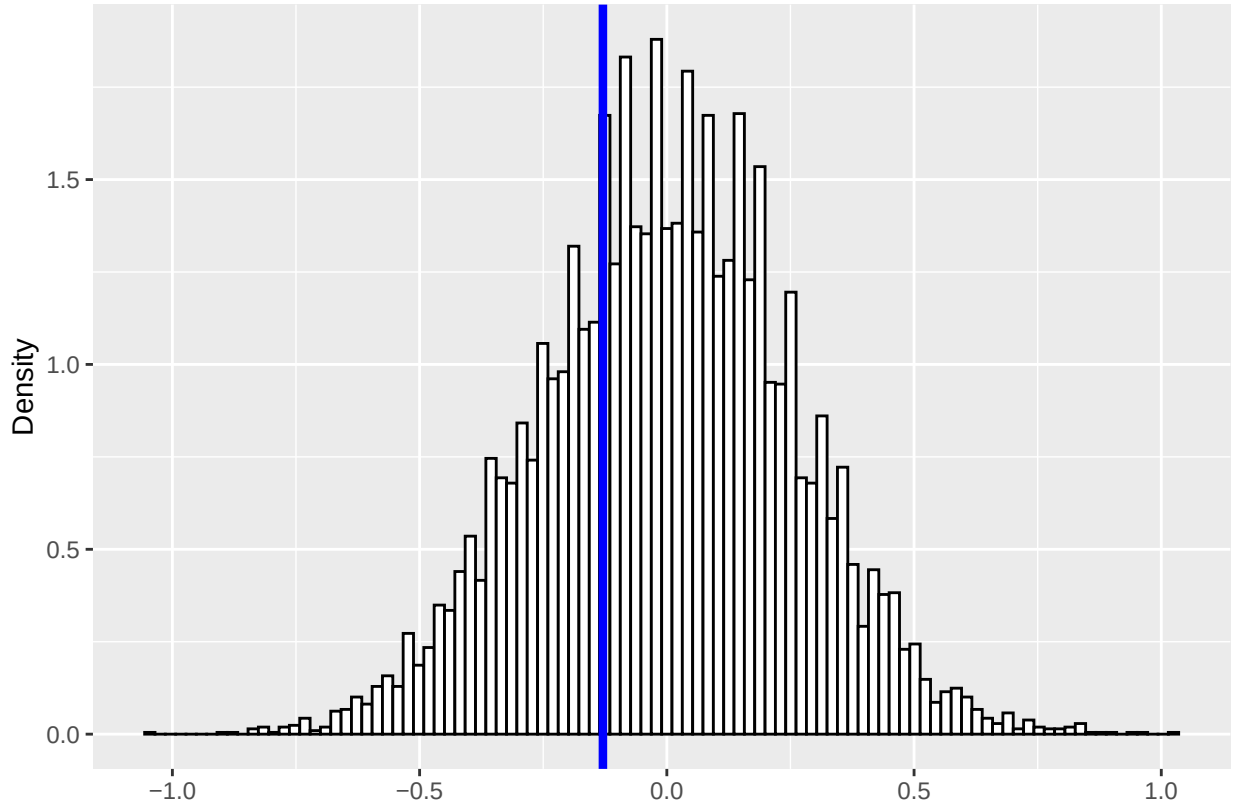

Figure 5. Average rating for Tramadol vs. Gabapentin

```
1-mean(pn_TrVGb_ratings_perms >= observed_pn_TrVGb_ratings)
```

p-value

```
## [1] 0.2992
```

Tramadol Vs. Fentanyl

```
pn_TrVFn <- pain_df[pain_df$drugName %in% c("Tramadol", "Fentanyl"),]

pn_TrVFn_ratings_perms = same_dist_perms_test(
  10000,
  pn_TrVFn[pn_TrVFn$drugName == "Tramadol", "rating"],
  pn_TrVFn[pn_TrVFn$drugName == "Fentanyl", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_pn_TrVFn_ratings = (
  mean(pn_TrVFn[pn_TrVFn$drugName == "Tramadol", "rating"])-
    mean(pn_TrVFn[pn_TrVFn$drugName == "Fentanyl", "rating"])
)
```

```
Fig6<-
  ggplot(data=data.frame(x=pn_TrVFn_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_pn_TrVFn_ratings,
             color="blue", size=1.5) +
  xlab("Figure 6. Average rating for Tramadol vs. Fentanyl") +
  ylab("Density")

ggsave("Fig6.png", Fig6)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig6
```

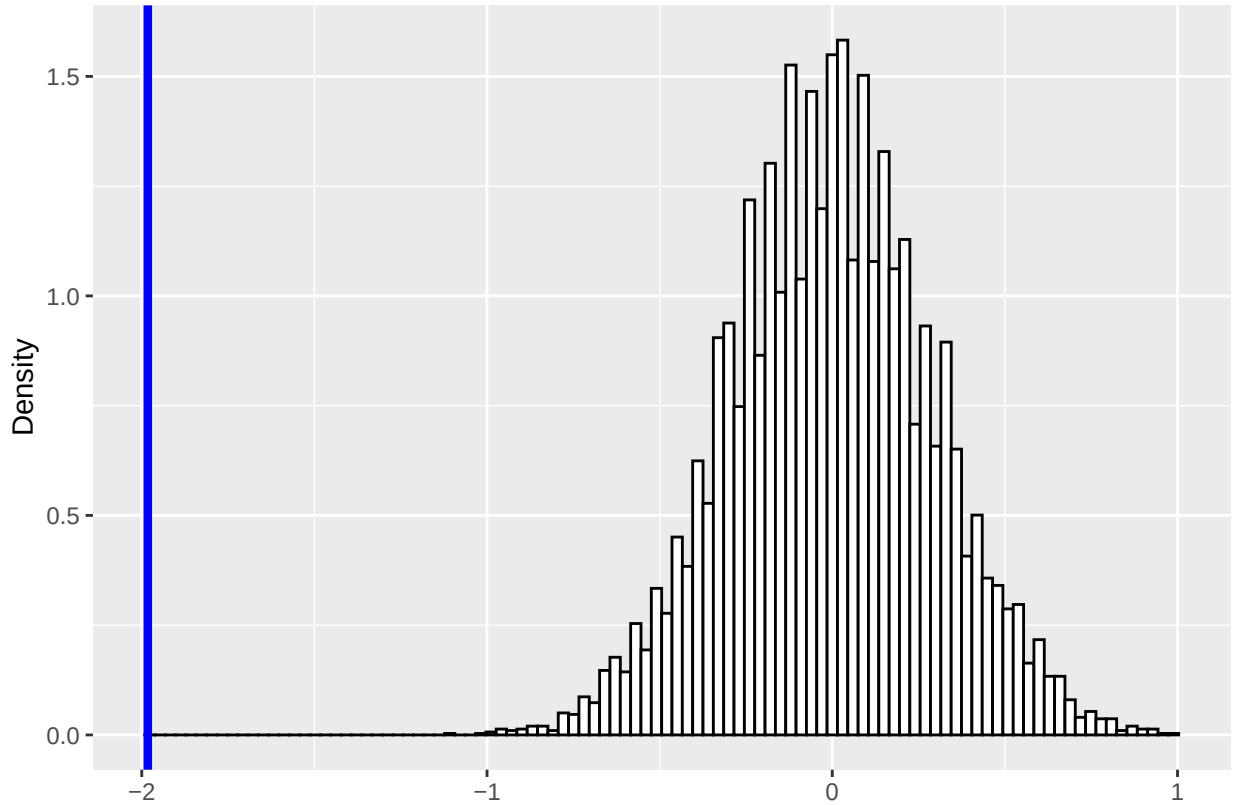

Figure 6. Average rating for Tramadol vs. Fentanyl

```
1-mean(pn_TrVFn_ratings_perms >= observed_pn_TrVFn_ratings)
```

p-value

```
## [1] 0
```

```
t.test(x=pn_TrVFn[pn_TrVFn$drugName == "Tramadol", "rating"],
       y=pn_TrVFn[pn_TrVFn$drugName == "Fentanyl", "rating"],
       alternative = "less",
       conf.level = 0.95)
```

t-test for whether Tramadol has a significantly smaller average rating than Fentanyl

```
##
##  Welch Two Sample t-test
##
## data:  pn_TrVFn[pn_TrVFn$drugName == "Tramadol", "rating"] and pn_TrVFn[pn_TrVFn$drugName == "Fentany
## t = -9.4361, df = 465.71, p-value < 2.2e-16
## alternative hypothesis: true difference in means is less than 0
## 95 percent confidence interval:
##       -Inf -1.636275
## sample estimates:
## mean of x mean of y
##  6.469062  8.451613
```

Permutation Tests For ADHD Drugs

Lisdexamfetamine Vs. Methylphenidate

```
ad_LsVMe <- adhd_df[adhd_df$drugName %in% c("Lisdexamfetamine", "Methylphenidate"),]

ad_LsVMe_ratings_perms = same_dist_perms_test(
  10000,
  ad_LsVMe[ad_LsVMe$drugName == "Lisdexamfetamine", "rating"],
  ad_LsVMe[ad_LsVMe$drugName == "Methylphenidate", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_ad_LsVMe_ratings = (
  mean(ad_LsVMe[ad_LsVMe$drugName == "Lisdexamfetamine", "rating"])-
    mean(ad_LsVMe[ad_LsVMe$drugName == "Methylphenidate", "rating"])
)

Fig7<-
  ggplot(data=data.frame(x=ad_LsVMe_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_ad_LsVMe_ratings,
             color="blue", size=1.5) +
  xlab("Figure 7. Average rating for Lisdexamfetamine vs. Methylphenidate") +
  ylab("Density")

ggsave("Fig7.png", Fig7)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig7
```

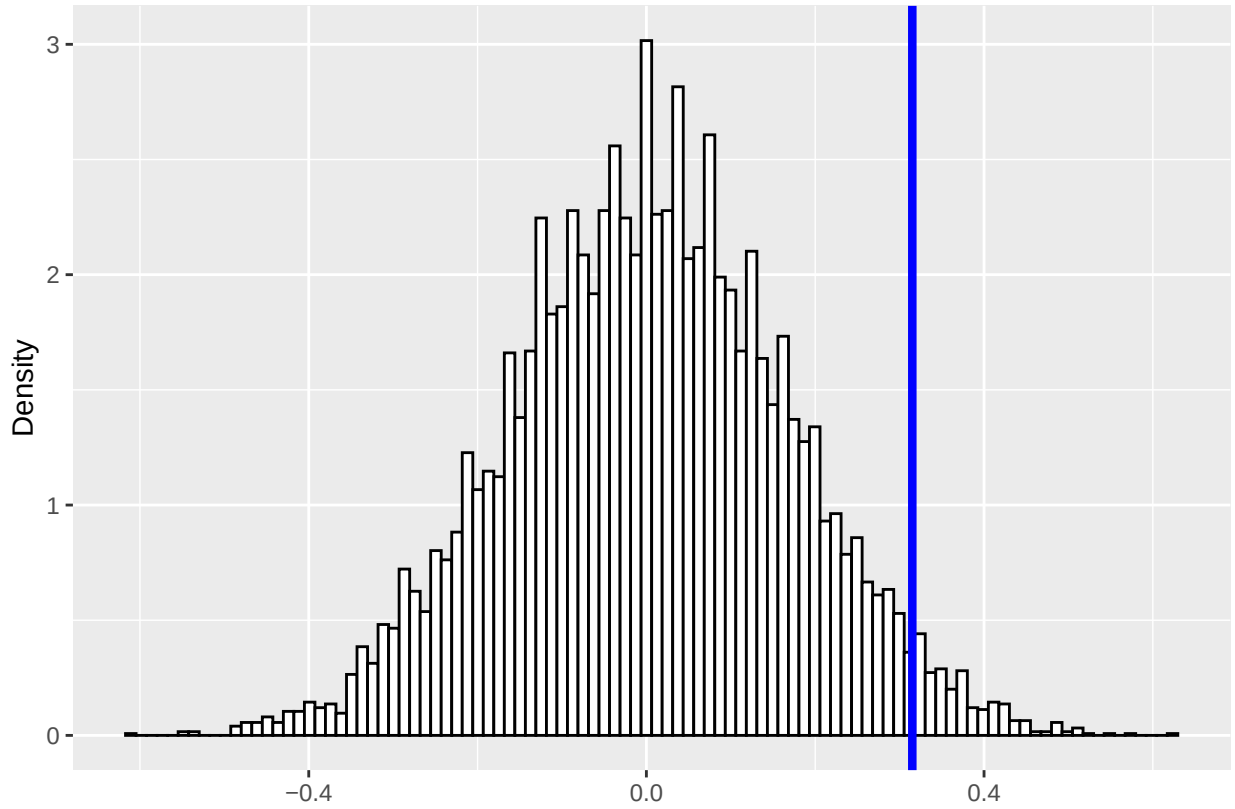

Figure 7. Average rating for Lisdexamfetamine vs. Methylphenidate

```
mean(ad_LsVMe_ratings_perms >= observed_ad_LsVMe_ratings)
```

p-value

```
## [1] 0.0304
```

```
t.test(x=ad_LsVMe[ad_LsVMe$drugName == "Lisdexamfetamine", "rating"],
       y=ad_LsVMe[ad_LsVMe$drugName == "Methylphenidate", "rating"],
       alternative = "greater",
       conf.level = 0.95)
```

t-test for whether Lisdexamfetamine has a significantly greater average rating than Methylphenidate

```
##
##  Welch Two Sample t-test
```

```
##
## data:  ad_LsVMe[ad_LsVMe$drugName == "Lisdexamfetamine", "rating"] and ad_LsVMe[ad_LsVMe$drugName ==
## t = 1.8939, df = 1042.6, p-value = 0.02926
## alternative hypothesis: true difference in means is greater than 0
## 95 percent confidence interval:
##  0.04117369        Inf
## sample estimates:
## mean of x mean of y
##  7.697080  7.382066
```

Lisdexamfetamine Vs. Adderall

```
ad_LsVAl <- adhd_df[adhd_df$drugName %in% c("Lisdexamfetamine", "Adderall"),]

ad_LsVAl_ratings_perms = same_dist_perms_test(
  10000,
  ad_LsVAl[ad_LsVAl$drugName == "Lisdexamfetamine", "rating"],
  ad_LsVAl[ad_LsVAl$drugName == "Adderall", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_ad_LsVAl_ratings = (
  mean(ad_LsVAl[ad_LsVAl$drugName == "Lisdexamfetamine", "rating"])-
    mean(ad_LsVAl[ad_LsVAl$drugName == "Adderall", "rating"])
)

Fig8<-
  ggplot(data=data.frame(x=ad_LsVAl_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_ad_LsVAl_ratings,
             color="blue", size=1.5) +
  xlab("Figure 8. Average rating for Lisdexamfetamine vs. Adderall") +
  ylab("Density")

ggsave("Fig8.png", Fig8)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig8
```

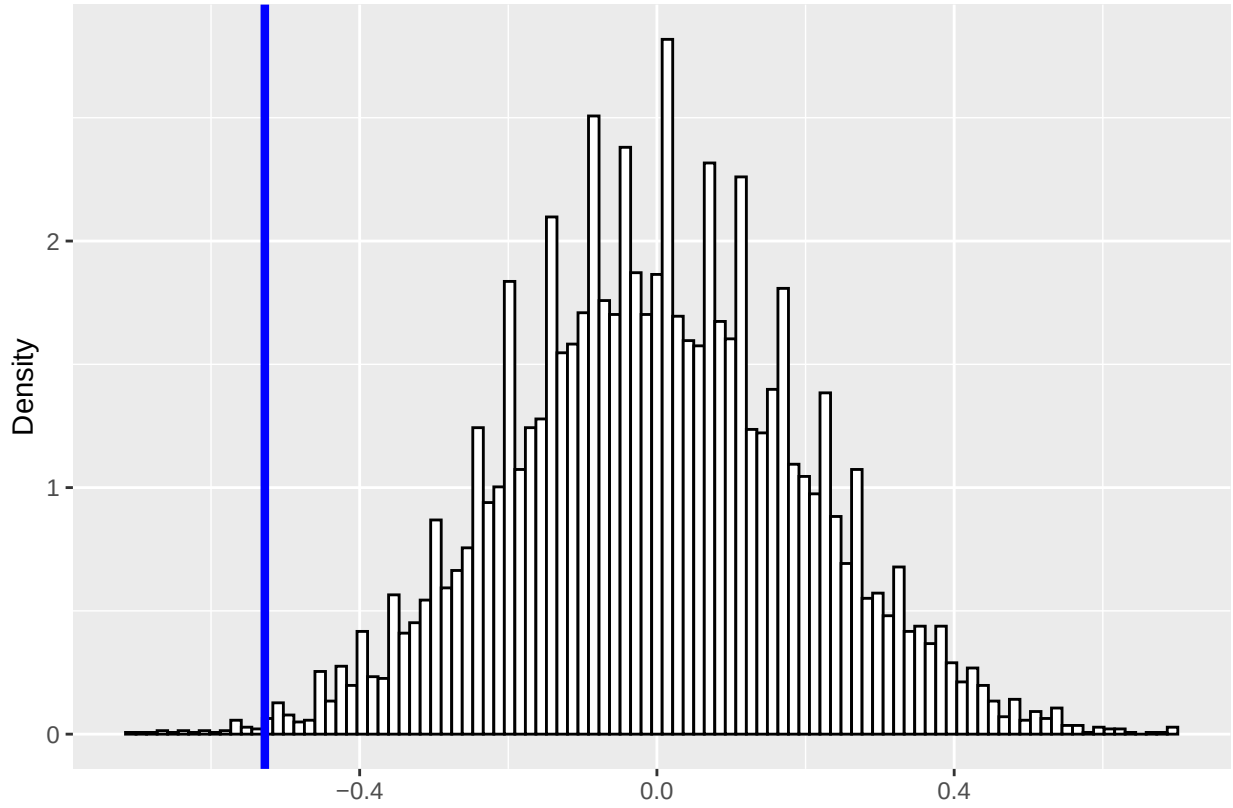

Figure 8. Average rating for Lisdexamfetamine vs. Adderall

```
1-mean(ad_LsVAl_ratings_perms >= observed_ad_LsVAl_ratings)
```

p-value

```
## [1] 0.0029
```

```
t.test(x=ad_LsVAl[ad_LsVAl$drugName == "Lisdexamfetamine", "rating"],
       y=ad_LsVAl[ad_LsVAl$drugName == "Adderall", "rating"],
       alternative = "less",
       conf.level = 0.95)
```

t-test for whether Lisdexamfetamine has a significantly smaller average rating than Adderall

```
##
##  Welch Two Sample t-test
##
## data:  ad_LsVAl[ad_LsVAl$drugName == "Lisdexamfetamine", "rating"] and ad_LsVAl[ad_LsVAl$drugName ==
## t = -2.749, df = 468.44, p-value = 0.003105
## alternative hypothesis: true difference in means is less than 0
```

```
## 95 percent confidence interval:
##       -Inf -0.211278
## sample estimates:
## mean of x mean of y
##   7.69708   8.22467
```

Lisdexamfetamine Vs. Bupropion

```
ad_LsVBp <- adhd_df[adhd_df$drugName %in% c("Lisdexamfetamine", "Bupropion"),]

ad_LsVBp_ratings_perms = same_dist_perms_test(
  10000,
  ad_LsVBp[ad_LsVBp$drugName == "Lisdexamfetamine", "rating"],
  ad_LsVBp[ad_LsVBp$drugName == "Bupropion", "rating"],
  function(a, b) {mean(a) - mean(b)}
)

observed_ad_LsVBp_ratings = (
  mean(ad_LsVBp[ad_LsVBp$drugName == "Lisdexamfetamine", "rating"])-
    mean(ad_LsVBp[ad_LsVBp$drugName == "Bupropion", "rating"])
)

Fig9<-
  ggplot(data=data.frame(x=ad_LsVBp_ratings_perms)) +
  geom_histogram(aes(x=x, y=..density..),
                 bins=100, color="black", fill="white") +
  geom_vline(xintercept=observed_ad_LsVBp_ratings,
             color="blue", size=1.5) +
  xlab("Figure 9. Average rating for Lisdexamfetamine vs. Bupropion") +
  ylab("Density")

ggsave("Fig9.png", Fig9)
```

```
## Saving 6.5 x 4.5 in image
```

```
Fig9
```

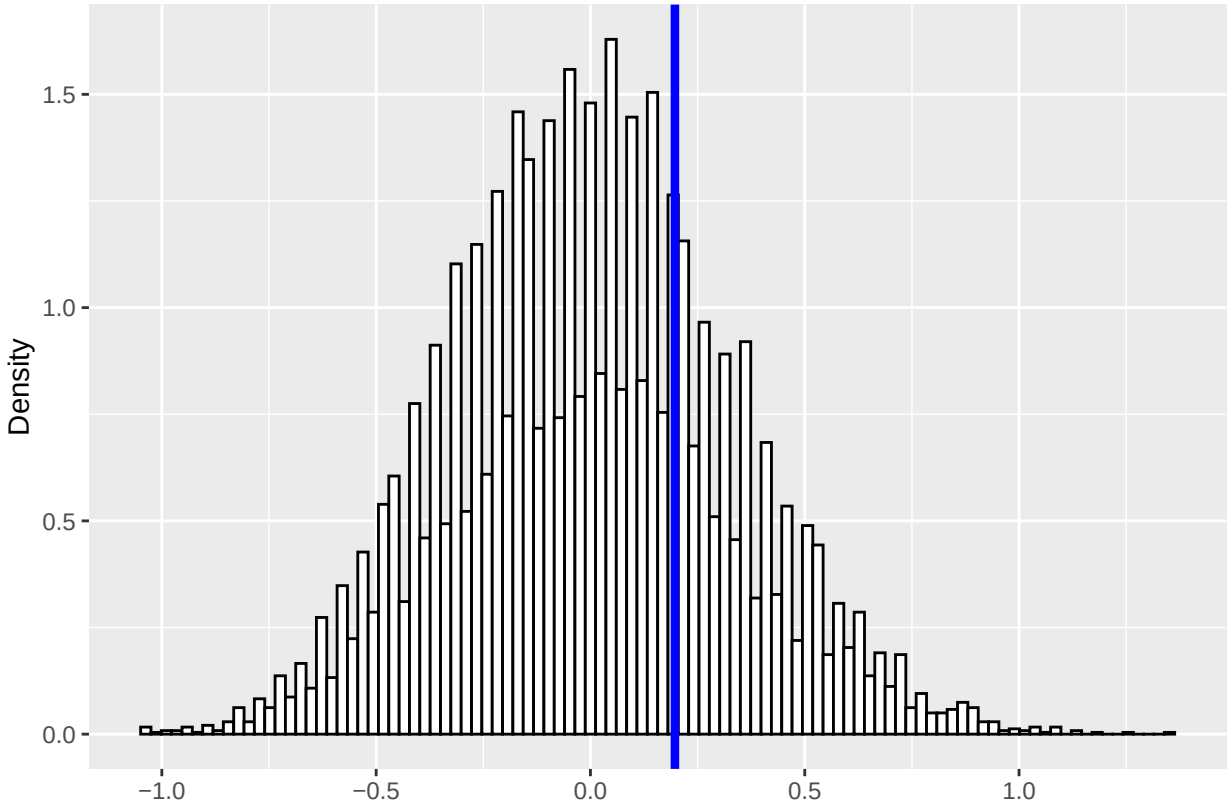

Figure 9. Average rating for Lisdexamfetamine vs. Bupropion

```
mean(ad_LsVBp_ratings_perms >= observed_ad_LsVBp_ratings)
```

p-value

```
## [1] 0.277
```