Lesson 19: Nonparametric tests

Pagona TB, Chapter 13

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Learning Objectives

1. Understand the difference between and appropriate use of parametric and nonparametric tests
2. Use the (Wilcoxon) Signed-rank test to determine if a single sample or paired sample are symmetric around some value.
3. Use the Wilcoxon Rank-Sum test to compare two independent numeric samples.
4. Use the Fisher's Exact test to determine if two categorical variables are associated.
5. Use the Kruskal-Wallis test to compare two or more independent numeric samples.

Where are we?

Data
- Collecting data
- Categorical vs. Numeric
- Summary statistics
- Data visualization

Probability
- Probability rules
- Independence, conditional
- Random variables and probability distributions
- Linear combinations
- Binomial, Normal, and Poisson

Sampling Variability, and Statistical Inference
- Sampling distributions
- Central Limit Theorem
- Confidence Intervals
- Hypothesis tests

Inference for continuous data/outcomes
- One sample t-test
- 3+ independent samples
- Simple linear regression / correlation
- 2 sample tests: paired and independent
- Power and sample size
- Non-parametric tests

Inference for categorical data/outcomes
- One proportion test
- Fisher's exact test
- Non-parametric tests
- Chi-squared test
- 2 proportion test
- Power and sample size

R
- Basics
- Reproducibility
- Quarto
- Packages
- Data visualization
- Data wrangling
- R Projects
- …

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Background: parametric vs nonparametric

- Parametric vs. nonparametric
  - Basically saying: assuming a distribution for our data vs. not assuming a distribution for our data
- In all of our inference so far, we have assumed the population (that the data come from) has a specific distribution
  - Normal distribution, T-distribution, Chi-squared distribution, F-distribution
- Each of those distribution can be **parameterized** from certain population parameters
  - For example: Normal distribution is completely described (parameterized) by two parameters: μ and σ
- Our inference and analysis was all based in the assumed distribution
  - But remember: we have specific assumptions that we need to check in order to use those distributions!
- **Nonparametric** procedures
  - Make fewer assumptions about the structure of the underlying population from which the samples were collected
  - Work well when distributional assumptions are in doubt.

Nonparametric tests: Pros vs. cons

Pros

- Fewer assumptions
  - Can handle smaller sample sizes
  - No assumptions about the distribution of the data's population
- Tests are based on ranks
  - Therefore outliers have no greater influence than non-outliers.
  - Since tests are based on ranks we can apply these procedures to ordinal data

Cons

- Less powerful than parametric tests (due to loss of information when data are converted to ranks)
- While the test is laid out for us, it may require substantial (computer) work to develop a confidence interval
- Ties in ranks make the test harder to implement
- Some nonparametric methods can be computationally intensive, especially for large datasets or complex designs

Parametric and nonparametric tests

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We still follow the general hypothesis test process

1. Check the **assumptions**
    - We will not meet the parametric assumptions!
    - There are some assumptions for the nonparametric tests
2. Set the **level of significance** α
3. Specify the **null** (H_0) and **alternative** (H_A) **hypotheses**
    - In symbols
    - In words
    - Alternative: one- or two-sided?
4. Calculate the **test statistic** and **p-value**
    - We will not discuss the test statistic's equation
5. Write a **conclusion** to the hypothesis test
    - Do we reject or fail to reject H_0?
    - Write a conclusion in the context of the problem

Poll Everywhere Question 1

Poll Everywhere Question 2

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(Wilcoxon) Signed-rank test

- The (Wilcoxon) signed-rank test is used for
  - Paired samples (i.e., a single set of differences)
  - One-sample comparison against a specified value

- If we want to see if data are symmetric (centered) around a certain value
  - For paired data, we may want to see if the data are symmetric around 0 to determine a difference
  - For one sample, we may have an idea of a median value that our data may follow

- **Think back to the parametric parallel of these!**
  - If we apply the body temperature example to this: We would check if the data were symmetric around 98.6

- Data do NOT need to be approximately normal

Example: Intraocular pressure of glaucoma patients

- Intraocular pressure of glaucoma patients is often reduced by treatment with adrenaline.
- A **new synthetic drug** is being considered, but it is more expensive than the **current adrenaline alternative**.
- 7 glaucoma patients were treated with both drugs:
  - one eye with adrenaline and
  - the other with the synthetic drug
- **Reduction in pressure** was recorded in each eye after following treatment (larger numbers indicate greater reduction)

Patient	Adren	Synth	d	Sign
1	3.5	3.2	-0.3	-
2	2.6	3.1	0.5	+
3	3.0	3.3	0.3	+
4	1.9	2.4	0.5	+
5	2.9	2.9	0.0	NA
6	2.4	2.8	0.4	+
7	2.0	2.6	0.6	+

- **d** is the difference in reduction of pressure: **Synth - Adren**
- **Sign** is + if the difference is positive and – if the difference is negative

(Wilcoxon) Signed-rank test: Hypotheses

General wording for hypotheses

H_0 : population is **symmetric around some value** $\tilde{\mu}_0$
H_a : population is **not symmetric around some value** $\tilde{\mu}_0$

Hypotheses test for example

H_0 : the population difference in reduction of intraocular pressure in treatment with adrenaline vs. new synthetic drug is **symmetric around** $\tilde{\mu}_0 = 0$
H_a : the population difference in reduction of intraocular pressure in treatment with adrenaline vs. new synthetic drug is **not symmetric around** $\tilde{\mu}_0 = 0$

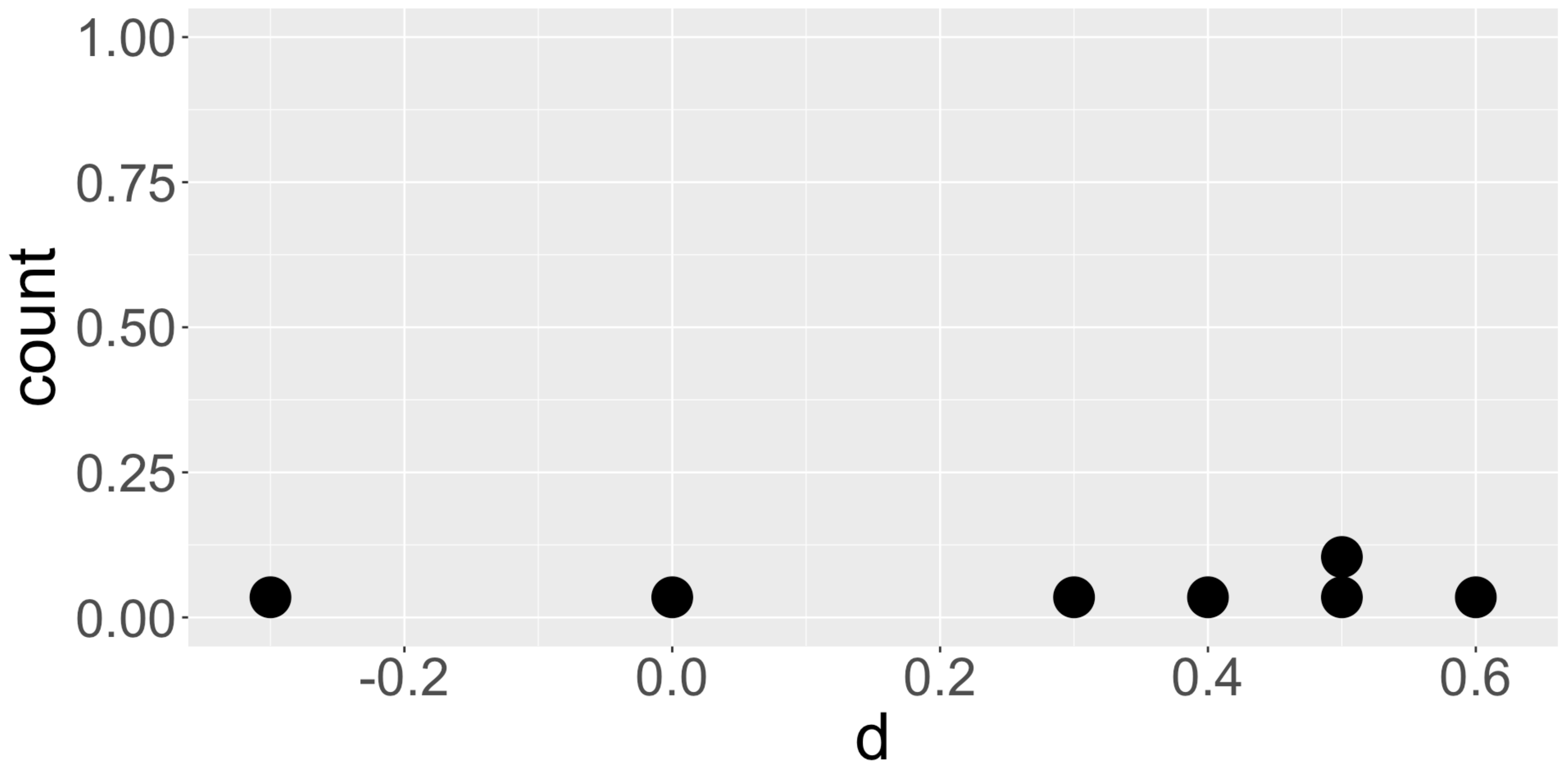
- Even if the population has a mean/median equal to $\tilde{\mu}_0$, the test may reject the null if the population isn't symmetric, thus only use if the data (differences) are symmetric.
- If the population is symmetric
  - then the mean and median coincide,
  - thus often the null hypothesis is phrased in terms of the median (or median difference) being 0

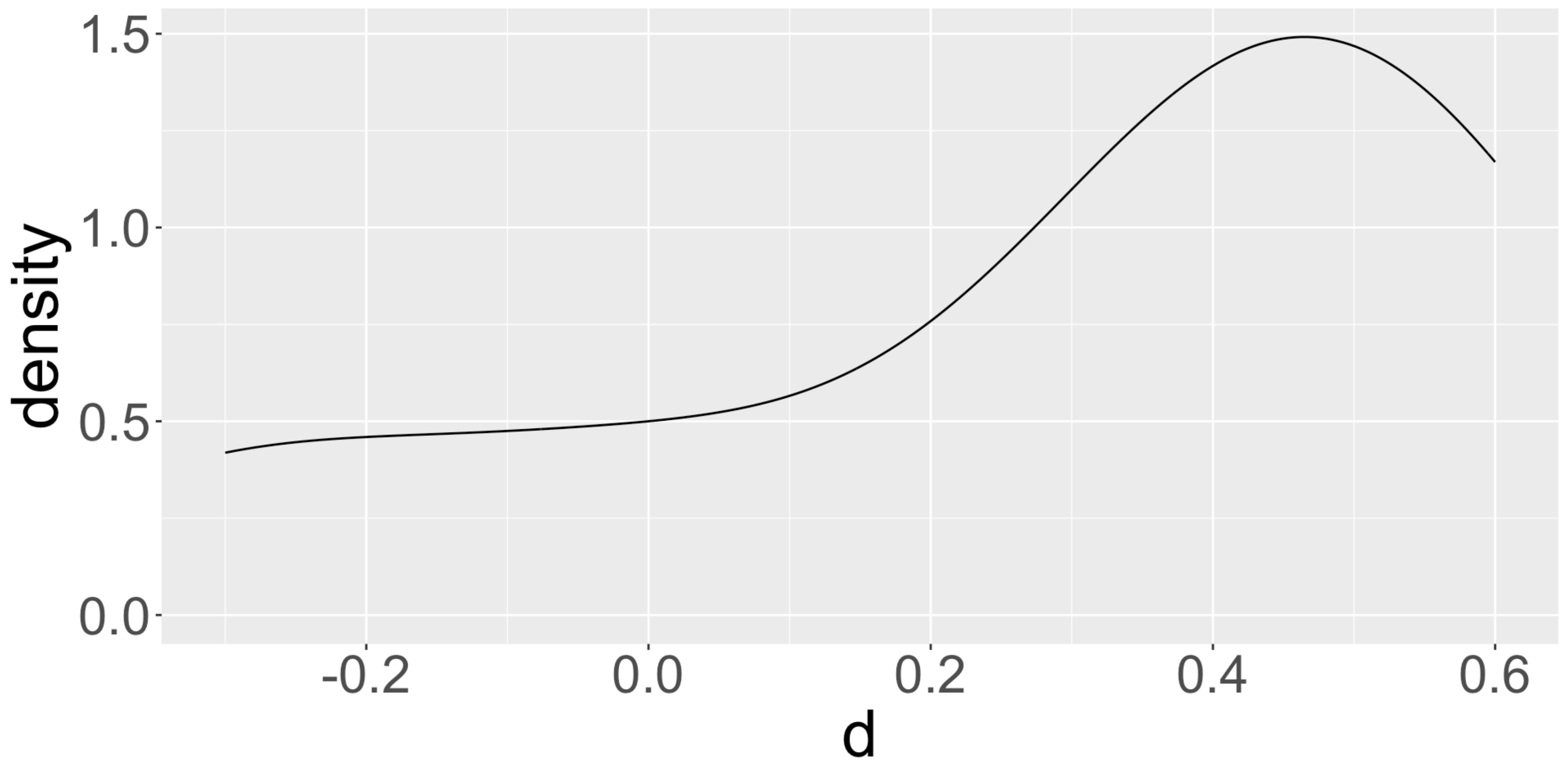
Example: Visualize the differences

Visualize the differences in reduction of pressure d : **Synth - Adren**

```r
ggplot(IOP_table, aes(x = d)) +
  geom_dotplot() +
  theme(text = element_text(size = 30))
```

```r
ggplot(IOP_table, aes(x = d)) +
  geom_density() +
  theme(text = element_text(size = 30))
```





Example: Calculate signed ranks

- Rank the **absolute values** of the differences from smallest to largest
- For ties, take the average of the highest and lowest tied ranks
  - I.e. if ranks 3-7 are tied, then assign (3+7)/2 = 5 as the rank
- Then calculate the **signed ranks** as +/- the rank depending on whether the sign is +/-

```r
IOP_ranks <- IOP %>%
  mutate(
    Rank = c(1.5, 4.5, 1.5,
             4.5, NA, 3, 6),
    Signed_rank = case_when(
      d < 0 ~ -Rank,
      d > 0 ~ Rank
      )
    )
```

Patient	Adren	Synth	d	Sign	Rank	Signed_rank
1	3.5	3.2	-0.3	-	1.5	-1.5
2	2.6	3.1	0.5	+	4.5	4.5
3	3.0	3.3	0.3	+	1.5	1.5
4	1.9	2.4	0.5	+	4.5	4.5
5	2.9	2.9	0.0	NA	NA	NA
6	2.4	2.8	0.4	+	3.0	3.0
7	2.0	2.6	0.6	+	6.0	6.0

(Wilcoxon) Signed-rank test: Test statistic

- If the null is true:
  - The population is symmetric around some point ($\tilde{\mu}_0 = 0$, typically), and
  - The **overall size of the positive ranks should be about the same as the overall size of negative ranks.**
- We can split the positive and negative ranks
  - T^+ = sum of the positive ranks
  - T^- = sum of the negative ranks
- Thus, any of the following can be used as a test statistic and will lead to the same conclusion:
  - T^+ (what R is using)
  - T^-
  - $T^+ - T^-$
  - $\min(T^+, |T^-|) = T_0$

Example: calculate sums of signed ranks

- Sum of the positive ranks
  - T^+ = 1.5 + 3 + 4.5 + 4.5 + 6 = 19.5
- Sum of the negative ranks
  - T^- = -1.5
- $\min(T^+, |T^-|) = T_0 = 1.5$

Patient	Adren	Synth	d	Sign	Rank	Signed_rank
1	3.5	3.2	-0.3	-	1.5	-1.5
2	2.6	3.1	0.5	+	4.5	4.5
3	3.0	3.3	0.3	+	1.5	1.5
4	1.9	2.4	0.5	+	4.5	4.5
5	2.9	2.9	0.0	NA	NA	NA
6	2.4	2.8	0.4	+	3.0	3.0
7	2.0	2.6	0.6	+	6.0	6.0

(Wilcoxon) Signed-rank test: Exact p-value (fyi)

- **Exact p-value** is preferable
  - This is the default method in R's `wilcox.test()`
    - if the samples contain less than 50 finite values
    - and **there are no ties**
      - *R will automatically use normal approximation method if there are ties*
- *We will not be calculating the exact p-value "by hand." We will be using R for this.*

$$p - value = 2 * P(\min(T^+, T^-) \leq t)$$

- t is the smaller of the calculated sums of the positive and negative ranks
- To calculate the exact p-value, we need the probability of each possible sum of ranks

(Wilcoxon) Signed-rank test in R: Glaucoma example

"Attempt" with exact p-value & running one sample test with differences

```
# Exact p-value
wilcox.test(x = IOP$d,
        alternative = c("two.sided"), mu = 0,
        exact = TRUE, correct = TRUE)
```

```
    Wilcoxon signed rank test with continuity correction

data:  IOP$d
V = 19.5, p-value = 0.07314
alternative hypothesis: true location is not equal to 0
```

(Wilcoxon) Signed-rank test: Conclusion

Recall the hypotheses to the (Wilcoxon) Signed-rank test:

H_0 : the population difference in reduction of intraocular pressure in treatment with adrenaline vs. new synthetic drug is **symmetric around** $\tilde{\mu}_0 = 0$
H_a : the population difference in reduction of intraocular pressure in treatment with adrenaline vs. new synthetic drug is **not symmetric around** $\tilde{\mu}_0 = 0$

- Significance level: α = 0.05
- p-value = 0.07314
- Do we reject or fail to reject H_0?

Conclusion:

There is insufficient evidence the differences in reduction in intraocular pressure differs between the synthetic drug and adrenaline are symmetric about 0 (2-sided Wilcoxon signed rank test p-value = 0.07314)

(Wilcoxon) Signed-rank test with one sample

- One can use the (Wilcoxon) Signed-rank test when testing just one sample
- Note that we did this when in R: Ran the (Wilcoxon) Signed-rank test using just the differences
- For one sample, we can specify the null population median value:

H_0 : The population median is m
H_a : The population median is NOT m

Not-so-real example: Run (Wilcoxon) Signed-rank test for paired data with null $m = 0.7$

```r
wilcox.test(x = IOP$d, mu = 0.7, alternative = "two.sided")
```

```
	Wilcoxon signed rank test with continuity correction

data:  IOP$d
V = 0, p-value = 0.02225
alternative hypothesis: true location is not equal to 0.7
```

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Wilcoxon rank-sum test

- The nonparametric alternative to the two-sample t-test
  - used to analyze two samples selected from separate (independent) populations
- **Also called the Mann-Whitney U test**
- Unlike the signed-rank test, there is no need to assume symmetry
- Necessary **condition** is that the two populations being compared
  - have the same shape (both right skewed, both left skewed, or both symmetric),
  - so any noted difference is due to a shift in the median
- Since they have the same shape, when summarizing the test, we can describe the results in terms of a difference in medians.

Hypotheses:

H_0 : the two populations have the same median
H_a : the two populations do NOT have the same median

Example

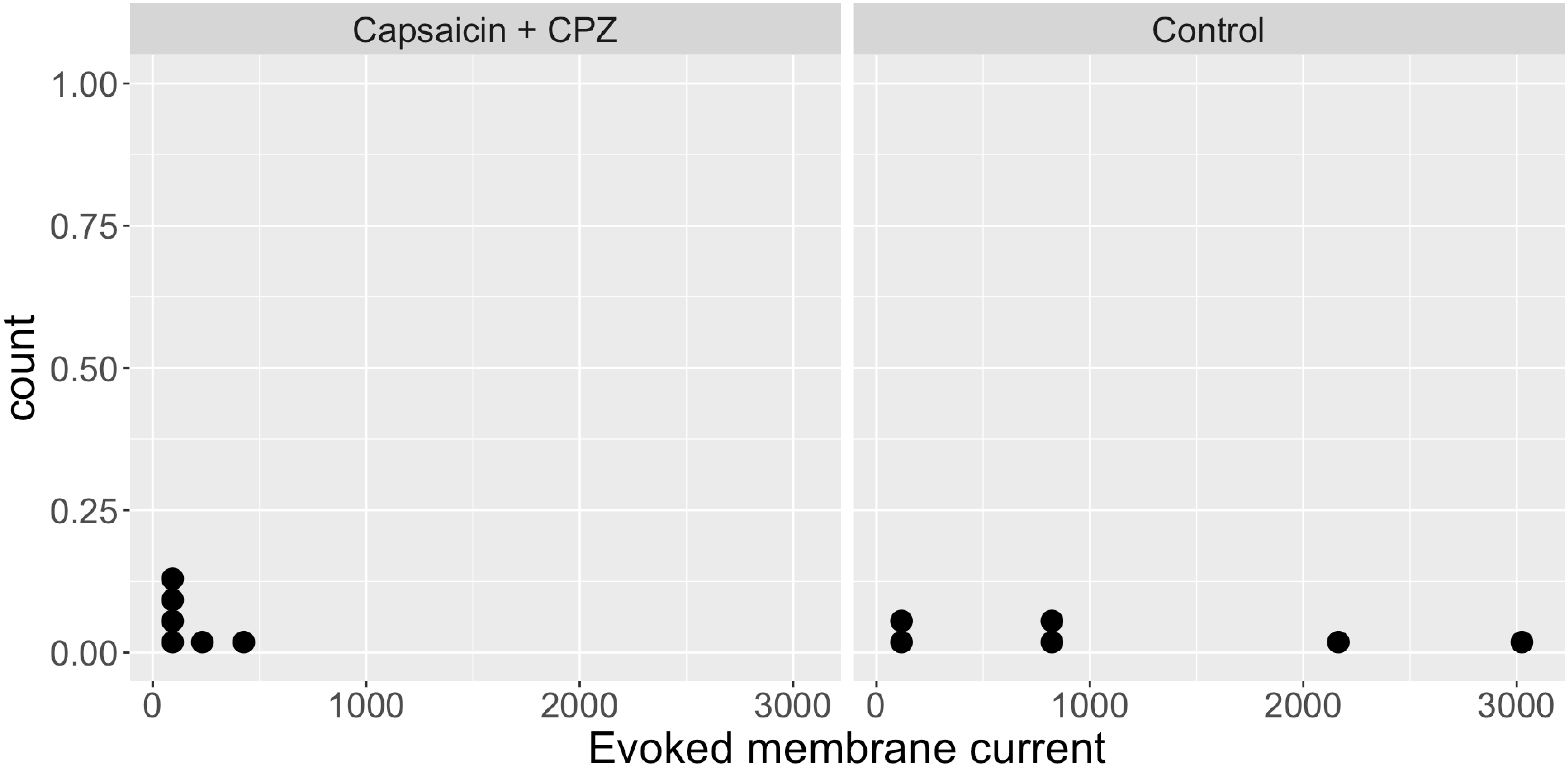
Dr. Priya Chaudhary (OHSU) examined the evoked membrane current of dental sensory neurons (in rats) under control conditions and a mixture of capsaicin plus capsazepine (CPZ). J. Dental Research} 80:1518–23, 2001.

Group	variable	n	median
Capsaicin + CPZ	Memb_current	6	112
Control	Memb_current	6	822

Rat_ID	Group	Current
1	Control	3024
2	Control	2164
3	Control	864
4	Control	780
5	Control	125
6	Control	110
7	Capsaicin + CPZ	426
8	Capsaicin + CPZ	232
9	Capsaicin + CPZ	130
10	Capsaicin + CPZ	94
11	Capsaicin + CPZ	75
12	Capsaicin + CPZ	55

Example: Visualize the data

Do the independent samples have the same distribution?



Wilcoxon rank-sum test: Calculating test statistic W

1. Combine the two samples together (keep track of which observations came from each sample).
2. Rank the full set of $N = n_1 + n_2$ observations.
   - If ties exist, assign average ranks to tied values (like signed-rank test)
3. Sum the ranks corresponding to those observations from the smaller sample.
   - This is a time-saving step; you could also have used the larger sample.
   - Call this sum W
4. If n_1, n_2 are both less than 10, then use an exact test (can only be done if no ties are present)
   - Otherwise use the large-sample normal approximation.

In our example, both groups have equal n; choose either for computing W.

$$W_{CPZ} = 1 + 2 + 3 + 6 + 7 + 8 = 27$$

$$W_{control} = 4 + 5 + 9 + 10 + 11 + 12 = 51$$

Rat_ID	Group	Current	Rank
12	Capsaicin + CPZ	55	1
11	Capsaicin + CPZ	75	2
10	Capsaicin + CPZ	94	3
6	Control	110	4
5	Control	125	5
9	Capsaicin + CPZ	130	6
8	Capsaicin + CPZ	232	7
7	Capsaicin + CPZ	426	8
4	Control	780	9
3	Control	864	10
2	Control	2164	11
1	Control	3024	12

Wilcoxon rank-sum test: Exact p-value approach

- **If** n_1, n_2 are both less than 10, then use an exact test,
  - otherwise use the large-sample normal approximation.
  - However, exact method can only be done if **no ties** are present
- p-value is the probability of getting a rank sum W as extreme or more extreme than the observed one.
  - Multiply the 1-tail probability by 2 for the 2-tailed probability

$$p - value = 2 \cdot P(W_{CPZ} \leq 27)$$

- To calculate $P(W_{CPZ} \leq 27)$,
  - we need to enumerate all possible sets ranks for the sample size,
  - calculate the sum of ranks for each set of possible ranks,
  - and then the probability for each sum (assuming each set of ranks is equally likely).

Wilcoxon rank-sum test: using R

Exact p-value

```
wilcox.test(Current ~ Group,
            data = CPZdata2,
            alternative = c("two.sided"), mu = 0,
            exact = TRUE)
```

```
    Wilcoxon rank sum exact test

data:  Current by Group
W = 6, p-value = 0.06494
alternative hypothesis: true location shift is not equal to 0
```

Wilcoxon rank-sum test: Conclusion

Recall the hypotheses to the Wilcoxon rank-sum test:

H_0 : the control and treated populations have the same median
H_a : the control and treated populations do NOT have the same median

- Significance level: α = 0.05
- p-value = 0.06494
- Do we reject or fail to reject H_0?

Conclusion:

There is suggestive but inconclusive evidence that the evoked membrane current of dental sensory neurons (in rats) differs between the control group and the group exposed to a mixture of capsaicin plus capsazepine (2-sided Wilcoxon rank-sum test p-value = 0.06494).

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Fisher's Exact Test

- Only necessary when expected counts in one or more cells is less than 5
- Given row and column totals fixed, computes exact probability that we observe our data or more extreme data
- Consider a general 2 x 2 table:

Group	Outcome		Total
	Died	Alive	
Treatment	a	b	a+b
Control	c	d	c+d
Total	a+c	b+d	n

- The exact probability of observing a table with cells (a, b, c, d) can be computed based on the hypergeometric distribution

$$P(a, b, c, d) = \frac{(a+b)! \cdot (c+d)! \cdot (a+c)! \cdot (b+d)!}{n! \cdot a! \cdot b! \cdot c! \cdot d!}$$

- Numerator is fixed and denominator changes

Some notes on the Fisher's Exact Test

- This is always a two-sided test
- There is no test statistic nor CI
- There is no continuity correction since the hypergeometric distribution is discrete

Recall our example from Lesson 4 and 16

Question: Is there an association between age group and hypertension?

- Let's pretend that we actually had the following numbers

Table: Contingency table showing hypertension status and age group.

Age Group	Hypertension	No Hypertension	Total
18-39 yrs	1	11	12
40-59 yrs	4	9	13
60+ yrs	4	2	6
Total	9	22	31

Fisher's Exact test: Hypertension

1. Check expected cell counts threshold

```
hyp_data2 %>% expected()
```

```
     Hypertension No_Hypertension
[1,]     3.483871        8.516129
[2,]     3.774194        9.225806
[3,]     1.741935        4.258065
```

We're going to pretend they are less than 5.

2. $\alpha = 0.05$

3. Hypothesis test:

- H_0 : There is no association between age group and hypertension
- H_1 : There is an association between age group and hypertension

4. Calculate the test statistic and p-value for Chi-squared test in R

```
fisher.test(x = hyp_data2)
```

```
	Fisher's Exact Test for Count Data

data:  hyp_data2
p-value = 0.04062
alternative hypothesis: two.sided
```

5. Conclusion to the hypothesis test

We reject the null hypothesis that age group and hypertension are not associated ($p = 0.04062$). There is sufficient evidence that age group and hypertension are associated.

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Kruskal-Wallis test: nonparametric ANOVA test

- Recall that an ANOVA tests means from 2 or more groups
- Conditions for ANOVA include
  - Sample sizes in each group group are large (each $n \geq 30$),
    - OR the data are relatively normally distributed in each group
  - Variability is "similar" in all group groups
- If these conditions are in doubt, or if the response is ordinal, then the Kruskal-Wallis test is an alternative.

$$\begin{aligned} H_0 &: \text{pop median}_1 = \text{pop median}_2 = \ldots = \text{pop median}_k \\ \text{vs. } H_A &: \text{At least one pair pop median}_i \neq \text{pop median}_j \text{ for } i \neq j \end{aligned}$$

- K-W test is an extension of the (Wilcoxon) rank-sum test to more than 2 groups
  - With $k = 2$ groups, the K-W test is the same as the rank-sum test

Ranks for the K-W test

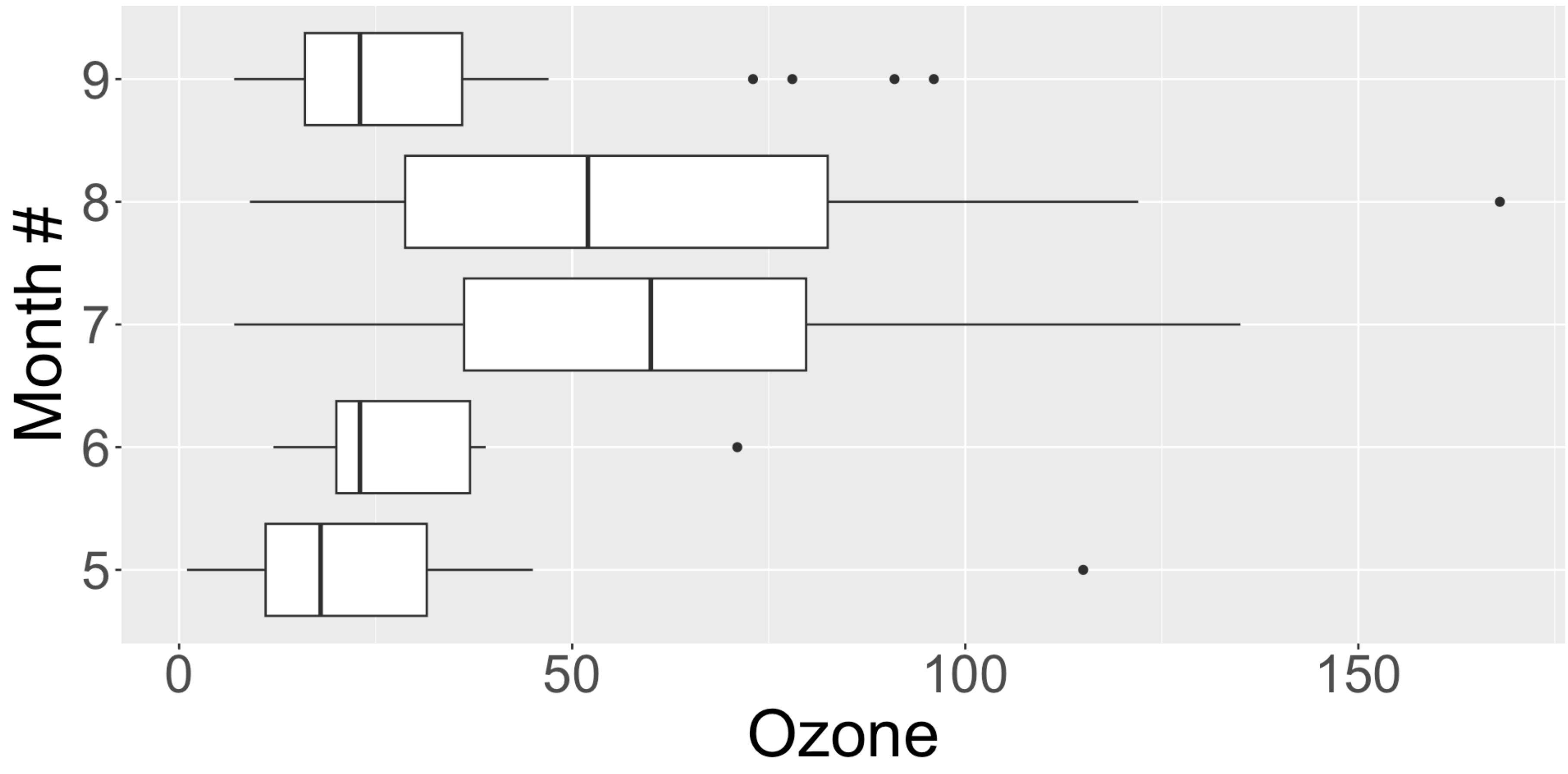
1. Combine the k samples together (keep track of which observations came from each sample).
2. Rank the full set of $N = n_1 + \ldots + n_k$ observations.
   - If ties exist, assign average ranks to the tied values (as with the signed-rank test).
3. Then sum the ranks within each of the k groups
   - Label the sums of the ranks for each group as $R_1, \ldots + R_k$.

If H_0 is true, we expect the populations to have the same medians, and thus the ranks to be similar as well.

Example: Ozone levels by month

- `airquality` data included in base R - no need to load it
- Daily air quality measurements in New York, May to September 1973.
- Question: Do ozone levels differ by month?

Month	variable	n	mean	median	sd
5	Ozone	26	23.615	18	22.224
6	Ozone	9	29.444	23	18.208
7	Ozone	26	59.115	60	31.636
8	Ozone	26	59.962	52	39.681
9	Ozone	29	31.448	23	24.142



- Does not look like each month has equal variance so we cannot use ANOVA

```
max(Oz_mnth$sd) / min(Oz_mnth$sd)
```

```
[1] 2.179317
```

K-W test in R

```r
kruskal.test(Ozone ~ Month, data = airquality)
```

```
	Kruskal-Wallis rank sum test

data:  Ozone by Month
Kruskal-Wallis chi-squared = 29.267, df = 4, p-value = 6.901e-06
```

There is sufficient evidence that the median ozone levels are different in at least two months from May - September, 1973 in New York City ($p < 0.001$; Kruskal-Wallis test).

- (fyi) Since the K-W test is significant, follow-up with pairwise (Wilcoxon) rank-sum tests using a multiple comparison procedure to identify which months have different medians.