Counts and Proportions

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Plan for lecture

- Summary of Day 1.
  - Recap of T-tests.
  - Solution to Exercise 1.2 and 1.5.

- Discussion of papers.
  - Stern & Smith: “Sifting the evidence — What’s wrong with significance tests?”
  - Gelman & Carlin: “Beyond Power Calculations: Assessing Type S (Sign) and Type M (Magnitude) Errors”

- Non-parametric tests:
  - Wilcoxon / Mann-Whitney, Kruskal-Wallis.

- Analysis of 2-way tables.
  - More assumptions $\Longrightarrow$ more power.
  - Interpretations and associated tests.

Summary of Day 1

- Statistics answers four important questions:
  1. Is there an effect? (falsification of null hypothesis, p-value)
  2. Where is the effect? (p-values from post hoc analyses)
  3. What is the effect? (confidence and prediction intervals)
  4. Can the conclusions be trusted? (model validation)

- We do model based frequentist statistics: Interpretation of p-values and confidence intervals via the meta-experiment.

- Tidy data: Datasets consists of variables (columns) and observations (rows).

- T-tests, data transformation, and validation of normality assumption.
  - Due to lack of time this was only superficially discussed on Day 1.
  - We will recap one and two sample T-tests today, and return to data transformation later in the course.

Data example 4 from Day 1: Phosphor in lakes

Two independent samples, not necessarily of the same length

```
> lakes
# A tibble: 627 x 2
   location     phosphor
   <chr>           <dbl>
 1 East-Denmark    255
 2 East-Denmark    102.
 3 East-Denmark    166.
 4 East-Denmark     42.5
 5 East-Denmark    102.
 6 East-Denmark     60.6
 7 East-Denmark     89.8
 8 East-Denmark    182.
 9 East-Denmark    243.
10 East-Denmark     30.9
# ... with 617 more rows
```

R code (here log-transformation needed to have normality)

```
t.test(log(phosphor)~location,data=lakes)
```

Solution to Exercise 1.2

- Example 1: Growth of rats, $N = 12$.

Variable	**Type**	**Range**	**Usage**
antibiotica	Nominal	0, 40	fixed effect
vitamin	Nominal	0, 5	fixed effect
growth	Continuous	[1.00 ; 1.56]	response

- Example 2 (for paired analysis): Tenderness of meat, $N = 24$.

Variable	**Type**	**Range**	**Usage**
pH.group	Nominal	low, high	fixed effect
Tunnel	Continuous	[3.11 ; 8.78]	response
Fast	Continuous	[3.33 ; 8.44]	response

- Example 2 (for mixed model): Tenderness of meat, $N = 48$.

Variable	**Type**	**Range**	**Usage**
Pork	Nominal	24 levels	random effect
pH.group	Nominal	low, high	fixed effect
method	Nominal	tunnel, fast	fixed effect
tenderness	Continuous	[3.11 ; 8.44]	response

Solution to Exercise 1.2 (continued)

- Example 3: Weight loss (raw binary data), $N = 160$.

Variable	Type	Range	Usage
diet	Nominal	2 levels	fixed effect
week	Ordinal	$1 < \ldots < 8$	fixed effect
person	Nominal	20 levels	random effect
weight.loss	Binary	no, yes	response

- Example 3: Weight loss (for binomial analysis), which is also available from the table, $N = 20$.

Variable	Type	Range	Usage
diet	Nominal	2 levels	fixed effect
weeks.with.weight.loss	Count	$0 < \ldots < 8$	response

Solution to Exercise 1.2 (continued)

- Example 4 (with univariate end-point): Stress and metabolism, $N = 8 * 96 = 768$.

Variable	Type	Range	Usage
number.of.rats	Continuous	5,6	weight (!?)
group	Nominal	8 levels	random effect
sex	Nominal	male, female	fixed effect
stabeling	Nominal	no, yes	fixed effect
food.additive	Nominal	no, yes	fixed effect
gene	Nominal	96 levels	fixed effect
expression	Continuous	[–5.7060 ; 13.2240]	response

Solution to Exercise 1.5 (slide 1 of 4)

- Open data frame `hypertension` from the R datafile `hypertension.RData` to see the variables:

  change1 = change of blood pressure over study period 1
  change2 = change of blood pressure over study period 2
  average = (change1+change2)/2
  diff = change1 − change2
  E_diff_N = changeE − changeN

- Four tests:

Two sample test:	E_diff_N	in E/N-group vs. N/E-group
Two sample test:	average	in E/N-group vs. N/E-group
Two sample test:	diff	in E/N-group vs. N/E-group
One sample test:	E_diff_N	against 0

- Question: What do the four hypotheses mean?

Solution of Exercise 1.5 (slide 2 of 4)

- Let's do some algebra:

$$\begin{aligned} \text{e1} &= \text{effect of drug E in period 1} \\ \text{e2} &= \text{effect of drug E in period 2} \\ \text{n1} &= \text{effect of drug N in period 1} \\ \text{n2} &= \text{effect of drug N in period 2} \end{aligned}$$

- E/N patients experience effects (e1,n2)
- N/E patients experience effects (n1,e2)
- Two first null hypotheses stipulate the following:

Test 1: e1−n2 = e2−n1 (No spill-over: e1+n1 = e2+n2)
Test 2: e1+n2 = e2+n1 (No interaction: e1−n1 = e2−n2)

- If these hypotheses are not rejected, then e1=e2=e and n1=n2=n
- Thereafter two last null hypotheses stipulate:

Test 3: e−n = n−e (No difference: e=n)
Test 4: e−n = 0 (No difference: e=n)

Solution to Exercise 1.5 (slide 3 of 4): R code

Test 1: Example of a two-sample test

```
# T-test
ggplot(hypertension,aes(sample=E_diff_N)) + geom_qq() + facet_grid(.~order)
t.test(E_diff_N~order,data=hypertension)

# Wilcoxon Rank Sum test
wilcox.test(E_diff_N~order,data=hypertension)
```

Test 4: Example of a one-sample test

```
# T-test
ggplot(hypertension,aes(sample=E_diff_N)) + geom_qq()
t.test(hypertension$E_diff_N)

# Wilcoxon Signed Rank test
wilcox.test(hypertension$E_diff_N)
```

Recommendation: Only use Wilcoxon tests if the t-tests are not valid.

Solution to Exercise 1.5 (4/4): Conclusion from analysis

Test number: null hypothesis	Statistical test	Assumptions	p-value
1: No spill-over	Welch T-test	Normality ok(!?)	0.2011
	Wilcoxon	None	0.0981
2: No interaction	Welch T-test	Normality questionable	0.5136
	Wilcoxon	None	0.6791
3: No drug difference	Welch T-test	Normality questionable	0.0932
	Wilcoxon	None	0.0826
4: No drug difference	T-test	Normality ok!	0.1108
	Wilcoxon	None	0.1328

- Neither spill-over (although significant at $\alpha = 0.10$) nor interaction.
- However, drug effect is non-significant.
- Here the two-sample test is more powerful than the one-sample test (0.0932 vs. 0.1108). But personally I prefer the one-sample test due to its interpretation (e.g. confidence interval for drug difference).

Questions?

- And then a break.

- After the break we discuss the two papers. These papers address problems that may arise in experiments with low statistical power:
  - Is there an effect? (Sterne & Smith)
  - What is the effect? (Gelman & Carlin)

What's wrong with significance tests?

Table 2, Sterne & Smith, BMJ, 226–231, 2001

		Null hypothesis:	
		True	False
Test:	Don't reject	Correct	Type II error
	Reject	Type I error (significance level)	Correct (power)

- Specificity = P(don't reject | hypothesis true) = 1 − significance level
- Sensitivity = P(reject | hypothesis false) = power

- The p-value is not the probability that the hypothesis is true. As a "counterexample" consider the following 1000 tests ($\frac{45}{95} > 0.05$):

Result of experiment	**Null hypothesis true (no association)**	**Null hypothesis false (association!)**	**Total**
Don't reject null hypothesis	855	50	905
Reject null hypothesis	45	50	95
Total	900	100	1000

Percentage of significant results that are false positives

Table 3, Sterne & Smith, BMJ, 226–231, 2001

		Significance level		
Ideas correct	**Power**	$\alpha = 5\%$	$\alpha = 1\%$	$\alpha = 0.1\%$
80%	20%	5.9	1.2	0.10
	50%	2.4	0.5	0.05
	80%	1.5	0.3	0.03
50%	20%	20.0	4.8	0.50
	50%	9.1	2.0	0.20
	80%	5.9	1.2	0.10
10%	20%	69.2	31.0	4.30
	50%	47.4	15.3	1.80
	80%	36.0	10.1	1.10
1%	20%	96.1	83.2	33.10
	50%	90.8	66.4	16.50
	80%	86.1	55.3	11.00

Type S (sign) and Type M (magnitude) errors

Gelman & Carlin, Persp. Psych. Science, 1–11, 2014.

- Sterne & Smith discuss risk of false positive (Is there an effect?), i.e. the proportion of true null hypothesis among rejected tests.

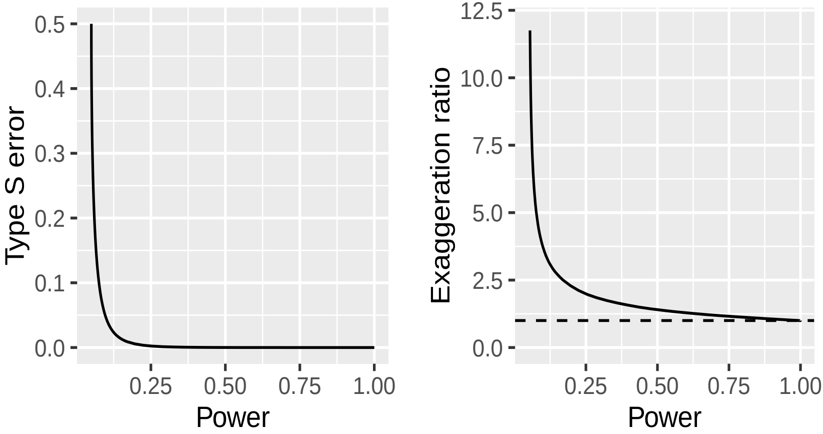
		Null hypothesis:	
		True	False
Test:	Don't reject	Correct	Type II error
	Reject	False positive	Possibly Type S/M error

- Gelman & Carlin discuss risk of wrong conclusions (What is the effect?) given correctly rejected (and false) null hypothesis!
  - Type S error = the estimate (from a rejected false null hypothesis) has the wrong sign.
  - Type M error = the estimate (from a rejected false null hypothesis) has a too large magnitude.

- Risk of false positives and of Type S and Type M errors is only problematic when the power of the test is low.

Risk of Type S and Type M error

Figure 2, Gelman & Carlin, 2014: Effect size from 0 to 100, SE=1, $\alpha = 0.05$, df=∞



Remark: Exaggeration ratio approaches ∞ as effects size approaches 0.

Questions?

- And then a break.
- After the break we discuss non-parametric tests that may by used in replacement of T-tests and 1-way ANOVA when the normality assumption is not satisfied:
  - Wilcoxon's signed rank test (one sample).
  - Wilcoxon's rank sum test (two independent samples). Also known as Mann-Whitney test.
  - Kruskal-Wallis test (1-way design with more than 2 groups).

Data example: Density of nerve cells

Motivation for non-parametric tests

Density of nerve cells measured at two sites of the intestine, midregion/mesentric region of jejunum (“tyndtarm”), for n=9 horses.

horse	mid	mes	diff
1	50.6	38.0	12.6
2	39.2	18.6	20.6
3	35.2	23.2	12.0
4	17.0	19.0	-2.0
5	11.2	6.6	4.6
6	14.2	16.4	-2.2
7	24.2	14.4	9.8
8	37.4	37.6	-0.2
9	35.2	24.4	10.8

Densities of nerve cells are significantly different at the two sites:

$$p = 2 \cdot P\left(T_{\mathrm{df}=8} > \frac{7.33 - 0}{2.60} \right) = 0.0222$$

This conclusion, however, relies on the assumption that `diff` is normally distributed.

But what if this assumption fails?
Usually, I either see if $\log(\frac{\text{mid}}{\text{mes}})$ is normal, or use a non-parametric test.

Non-parametric methods

Tests that do not assume normality

Pro and Cons:

+ “No” assumptions, no distribution checks needed.
– Only available for some situations.
– Often less powerful (but not always!).
– No model, no estimates, no confidence intervals, no predictions.
– Two sample T-test with unequal variances (known as Welch T-test) may be less restrictive when applicable.

Today:

- One sample: Sign test (appealing, but very weak and never used),
  Wilcoxon signed rank test (preferable).
- Two samples: Wilcoxon rank sum test (Mann-Whitney).
- 1-way ANOVA: Kruskal-Wallis test.

Sign test for the density of nerve cells example

Paired two sample T-test gives p=0.0222

horse	mid	mes	diff	sign
1	50.6	38.0	12.6	+
2	39.2	18.6	20.6	+
3	35.2	23.2	12.0	+
4	17.0	19.0	-2.0	-
5	11.2	6.6	4.6	+
6	14.2	16.4	-2.2	-
7	24.2	14.4	9.8	+
8	37.4	37.6	-0.2	-
9	35.2	24.4	10.8	+

- Test statistic r = number of positive signs $= 6$
- If H_0 ($+/-$ are exchangeable) is true, then $r \sim \text{bin}(n, 0.5)$:

$$\text{p} = 2 \cdot P\big(\text{bin}(9, 0.5) \geq 6\big) = 0.5078$$

- Absolutely no evidence against H_0.

Wilcoxon's signed rank test for Data example 2

Paired two sample T-test gives p=0.0222

horse	mid	mes	diff	abs_diff	sign	rank
1	50.6	38.0	12.6	12.6	+	8
2	39.2	18.6	20.6	20.6	+	9
3	35.2	23.2	12.0	12.0	+	7
4	17.0	19.0	-2.0	2.0	-	2
5	11.2	6.6	4.6	4.6	+	4
6	14.2	16.4	-2.2	2.2	-	3
7	24.2	14.4	9.8	9.8	+	5
8	37.4	37.6	-0.2	0.2	-	1
9	35.2	24.4	10.8	10.8	+	6

- Test statistic $S_+ =$ sum of ranks of positive diff.'s
  $= 8+9+7+4+5+6 = 39$ (out of total=45)
- If H_0 (distribution of diff's is symmetric) is true, then

$$\text{p} = 2 \cdot P(S_+ \geq 39) = 0.05469$$

- Almost significant at 5%. Some evidence of larger values at "mid".

R code available in script: cellDensity.R

Try to execute the script on your own laptop and locate the results

```
# Hard code data into two vectors
mid <- c(50.6,39.2,35.2,17.0,11.2,14.2,24.2,37.4,35.2)
mes <- c(38.0,18.6,23.2,19.0, 6.6,16.4,14.4,37.6,24.2)

# Make t-test
qqnorm(mid-mes)
shapiro.test(mid-mes)
t.test(mid,mes,paired=TRUE)

# Sign test: Is never used!
binom.test(sum(mid>mes),length(mid))

# Make Wilcoxon rank sum test
wilcox.test(mid,mes,paired=TRUE)
```

Non-parametric two sample tests

2 groups of observations

- Null hypothesis: Both groups have the same continuous distribution.

- The Wilcoxon rank sum test, also know as Mann-Whitney test, is based on the ranks R_j (among all observations) via the test statistic

$$S = \sum_{\text{observations } j \text{ from the first group}} R_j$$

- To compute p-value we need the distribution of S under the null hypothesis. On slide 24 we discuss how this may be done.

- There exists many other non-parametric test statistics. Doing several tests and choosing the one with the minimal p-value is cheating!
  - Quiz: Can you explain why?

p-values: Exact / Simulated exact / Approximate

- In some situations, e.g. two sample T-test with equal variances, the distribution of the test statistics is known mathematically. In these situations we may compute the exact p-value.

- Simulated p-values:
  1. Simulate 10000 datasets, say, assuming the null hypothesis.
  2. Compute the test statistic for each simulated dataset.
  3. Is the observed test statistic extreme among the 10000 simulated test statisitcs?
  4. Leads to estimate and confidence interval for the exact p-value.

  On Day 1 we tried this for the milk yield example.

- Use an approximation of the test statistic distribution, e.g.

$$\mathrm{p} = 2 \cdot P\big(Z \geq |z_{\mathrm{obs}}|\big), \qquad Z = \frac{S - \mathrm{mean}(S)}{\sqrt{\mathrm{var}(S)}} \underbrace{\sim \mathcal{N}(0,1)}_{\text{approximatively}},$$

  but several other approximations (Satterthwaite, Kenward-Roger, . . .) appear in various situations.

Non-parametric equivalent for 1-way ANOVA

When there are more than 2 groups

- Null hypothesis: All groups have the same continuous distribution.
- Test statistic constructed via the ranks of the observations.
- Approximative p-value via χ^2-distribution.
- The equivalent (when more than 2 groups) of the Wilcoxon test is also known as Kruskal-Wallis test.

Remarks:

1. A falsification of the null hypothesis only tell us that the groups do not have the same continuous distribution.
2. In principle none of the non-parametric methods discussed today tolerate ties, e.g. that two observations are identical. However, there of course exists remedies for this.

Questions?

- And then a break.
- After the break we discuss tests for 2-way contingency tables. Doing this we consider the following principles:
  - Can the p-values be trusted?
  - Using ordinal instead of nominal structure $\Longrightarrow$ more power!

Statistics and tests for 2-way contingency tables

Multi-way tables: Graphical models (not covered in this course)

- Overview:

Number of categories		See slide
Variable 1	Variable 2	
2	2	30–35
2+ (nominal)	2+ (nominal)	37
2+ (nominal)	2+ (ordinal)	38
2+ (ordinal)	2+ (ordinal)	39–40
2 (paired)	2 (paired)	43–47
2+ (paired)	2+ (paired)	48–49

- Statistical principles: Validity and Power.

- Data representation and R functions.

How to describe these methods in publications?

- The methods discussed today are so simple/standard that I wouldn't include a description in the Method section.
  - In particular, these methods do not require model validation.
  - However, the simulated χ^2-test is not yet standard. So you perhaps need to make a comment if you use that test (see later).

- In the Results section I would present tables with both raw observations and model estimates. Together with a statement like (cf. gait score example):

  Spearman's rank correlation shows strong evidence of treatment effect on gait score ($\hat{r}_s = -0.1968$, $p = 0.00066$).

Table-of-Variables: Overview of data examples

- Data example 1: Avadex and cancer

Variable	Type	Range	Usage
Avadex	nominal	no, yes	fixed effect
Tumor	nominal	no, yes	response

- Data example 2: Activity of chicken

Variable	Type	Range	Usage
Treatment	ordinal	$A < B < C < D$	fixed effect
Gait.score	ordinal	$0 < 1 < 2 < 3.5$	response

- Data example 3: Marijuana and sleeping problems

Variable	Type	Range	Usage
Marijuana	nominal	no, yes	response
Control	nominal	no, yes	response

Data example 1: Fungicide Avadex given to mice

Comparing two proportions (2×2-tabel). Notice treatment and response.

		Tumor		
		$+$	$-$	Total
Avadex	$+$	4	12	16
	$-$	5	74	79
Total		9	86	95

$n_1 = 16$ mice got Avadex in their food
$n_2 = 79$ mice got no Avadex (controls)

Presumably, most of you have learned (in your basic statistics course) about the three tests listed below. What are the differences, and which test should we use for the example above?

- χ^2-test for independence (between Tumor and Avadex).
- χ^2-test for homogeneity (of Tumor risks across the Avadex groups).
- Fishers exact test.

Chi square test (2×2 tables)

Null hypothesis: Independence / Null hypothesis: Homogeneity of proportions.

	Var. 2		Total
Var. 1	a	b	a+b
	c	d	c+d
Total	a+c	b+d	n

Rule of thumb: Valid when

$$\begin{aligned} \text{80\% of cells:} &\quad \text{expected} \geq 5 \\ \text{all cells:} &\quad \text{expected} \geq 1 \end{aligned}$$

For 2×2 tables: all expected ≥ 5.

- **Chi square test statistic:**

$$X^2 = \sum_{\text{cells}} \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

- **Yates' continuity correction (classically only for 2×2 tables):**

$$X^2_{\text{Yates}} = \sum_{\text{cells}} \frac{(|\text{observed} - \text{expected}| - \frac{1}{2})^2}{\text{expected}}$$

Independence test using R

If you don't want the (recommended) continuity correction use option: `correct=FALSE`

```
> chisq.test(matrix(c(4,5,12,74),2,2))

Pearson's Chi-squared test with Yates' continuity correction

data:  matrix(c(4, 5, 12, 74), 2, 2)
X-squared = 3.4503, df = 1, p-value = 0.06324

Warning message:
In chisq.test(matrix(c(4, 5, 12, 74), 2, 2)) :
  Chi-squared approximation may be incorrect
```

Homogeneity test in 2 × 2-table using R

If you don't want the (recommended) continuity correction use option: `correct=FALSE`

```
> prop.test(c(4,5),n=c(16,79))

2-sample test for equality of proportions with continuity correction

data:  c(4, 5) out of c(16, 79)
X-squared = 3.4503, df = 1, p-value = 0.06324
alternative hypothesis: two.sided
95 percent confidence interval:
 -0.06973073  0.44314845
sample estimates:
    prop 1     prop 2
0.25000000 0.06329114

Warning: In prop.test(c(4, 5), n = c(16, 79)) :
  Chi-squared approximation may be incorrect
```

What if the Chi-square test is invalid?

Classically, Fisher's Exact Test is recommended

```
fisher.test(matrix(c(4,5,12,74),2,2))
```

- However, Fisher's test has a slightly different interpretation of the null hypothesis!
- Alternative approach, which is always valid: keep the X^2-statistic and simulate the p-value. This gives different tests for the hypotheses of independence of variables and homogeneity of proportions:
  - Testing for independence between tumors and avadex requires conditioning on the total sum.
  - Comparing proportions of tumors requires conditioning on the row marginals.
  - Quiz: What is correct in the present example?

Implemented in `LabApplStat`-package

```
chisq.test.simulate(matrix(c(4,5,12,74),2,2),"row")
```

R function for power computations: `power.chisq.test.simulate()`

Avadex: Presentation of results

		Tumor		
		+	−	Total
Avadex	+	4 (25%)	12 (75%)	16 (100%)
	−	5 (6%)	74 (94%)	79 (100%)
Total		9 (9%)	86 (91%)	95 (100%)

Chi-square:	$X^2 = 5.4083$,	p=0.0200 (*, validity questionable)
Yates:	$X^2_{\text{Yates}} = 3.4503$,	p=0.0632 (NS, validity questionable)
Fisher:		p=0.0411 (*, “wrong” null hypothesis)
Simulated Chi-square:	$X^2 = 5.4083$,	p=0.0224 (*, valid)

- Only the simulated Chi-square is needed, and we conclude that Avadex increase risk of tumors (p=0.02).

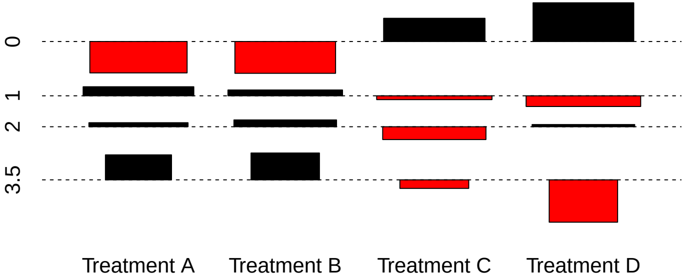
- Estimated tumor probabilities:

Avadex	p(tumor)	95% confidence interval
+	0.250	(0.083 ; 0.526)
−	0.063	(0.024 ; 0.148)

Data example 2: Activity of chicken

Graphical display using R: `assocplot()`

Treatment	GAIT-score:	0	1	2	3.5	Total
A (ad libitum feeding)		12	26	20	12	70
B (fasting 8 H/day, 1 week)		13	27	22	13	75
C (fasting 8 H/day, 2 weeks)		25	25	18	8	76
D (fasting 8 H/day, 3 weeks)		28	23	21	3	75
Total		78	101	81	36	296



Unordered categories ($r \times k$ table)

Null hypothesis: No association between row and column variables

- **Chi square test statistic:**

$$X^2 = \sum_{\text{cells}} \frac{(\text{observed} - \text{expected})^2}{\text{expected}}, \quad \text{expected} = \frac{\text{row total} \cdot \text{column total}}{\text{grand total}}$$

Under the null hypothesis, X^2 approximately follows a χ^2-distribution with $\text{df} = (r-1)\cdot(k-1)$.

Chicken example: $X^2_{\text{obs}} = 17.68$, p-value $= P\left(\chi^2_{\text{df}=9} \geq X^2_{\text{obs}}\right) = 0.04$ (*)

	GAIT-score				
Treatment	0	1	2	3.5	Total
A	12	26	20	12	70
B	13	27	22	13	75
C	25	25	18	8	76
D	28	23	21	3	75
Total	78	101	81	36	296

Can we do better than this, i.e.

- Get more power?
- Get more precise statement of the effect?

One ordered category ($r \times k$ table)

Compare rank sums of treatment groups using **Kruskal-Wallis**

- **Chicken example:** GAIT-score is an ordinal variable.
- Ranks for GAIT-score with resolved ties:

$$
\begin{array}{ll}
\text{A:} & \underbrace{39.5, \ldots, 39.5}_{12}, \underbrace{129, \ldots, 129}_{26}, \underbrace{220, \ldots, 220}_{20}, \underbrace{278.5, \ldots, 278.5}_{12} \\
\text{B:} & \underbrace{39.5, \ldots, 39.5}_{13}, \underbrace{129, \ldots, 129}_{27}, \underbrace{220, \ldots, 220}_{22}, \underbrace{278.5, \ldots, 278.5}_{11} \\
\text{C:} & \underbrace{39.5, \ldots, 39.5}_{25}, \underbrace{129, \ldots, 129}_{25}, \underbrace{220, \ldots, 220}_{18}, \underbrace{278.5, \ldots, 278.5}_{8} \\
\text{D:} & \underbrace{39.5, \ldots, 39.5}_{28}, \underbrace{129, \ldots, 129}_{23}, \underbrace{220, \ldots, 220}_{21}, \underbrace{278.5, \ldots, 278.5}_{3}
\end{array}
$$

- Test statistic = 13.0272.
- P-value = 0.00457 (**)

Two ordered categories ($r \times k$ table)

- Arguably, treatment is also an ordinal variable:
  (A: ad libitum feeding, B:fasting 8 H/day, 1 week, C: 2 weeks, D: 3 weeks)

- Separate ranks for both variables (also resolving ties):

$$
\begin{array}{rl}
35.5: & \underbrace{39.5,\ldots,39.5}_{12},\underbrace{129,\ldots,129}_{26},\underbrace{220,\ldots,220}_{20},\underbrace{278.5,\ldots,278.5}_{12} \\
108: & \underbrace{39.5,\ldots,39.5}_{13},\underbrace{129,\ldots,129}_{27},\underbrace{220,\ldots,220}_{22},\underbrace{278.5,\ldots,278.5}_{11} \\
183.5: & \underbrace{39.5,\ldots,39.5}_{25},\underbrace{129,\ldots,129}_{25},\underbrace{220,\ldots,220}_{18},\underbrace{278.5,\ldots,278.5}_{8} \\
259: & \underbrace{39.5,\ldots,39.5}_{28},\underbrace{129,\ldots,129}_{23},\underbrace{220,\ldots,220}_{21},\underbrace{278.5,\ldots,278.5}_{3}
\end{array}
$$

Two ordered categories ($r \times k$ table)

Null hypothesis: $r_s = 0$. Alternative hypothesis: $r_s \neq 0$.

- **Spearmans rank correlation** r_s:

$$\hat{r}_s = \underbrace{\frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}}}_{\textbf{Pearson correlation} \text{ of the ranks } x \text{ and } y}$$

- Test statistic and p-value done using either an exact algorithm or an approximative T-test.
  - In R the exact algorithm is used if there are no ties and if the sample size n is less than 1290.
  - For applications it is of minor importance which tests is used. So we simply ignore the issue. Also when the Spearman rank correlation is used in papers!

- **Chicken example:** $\hat{r}_s = -0.1969$, $p = 0.0006596$ (***)

Activity of Chicken: Comparison of hypothesis tests

Statistical power gained when using that both treatment and response are ordinal

Test	$\mathbf{X}^2$	Effective **DF**	**p-value**	
Spearman rank correlation	NA	1	0.00066	(***)
Kruskal-Wallis	13.0272	3	0.00458	(**)
Chi-square	17.6187	9	0.03909	(*)

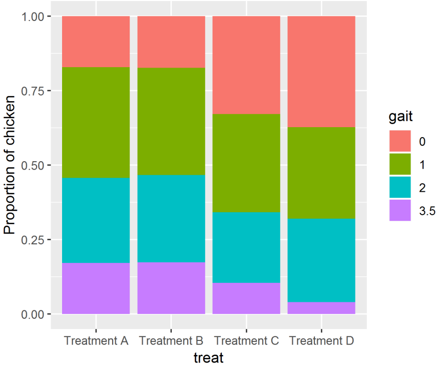
- How to do these tests is exemplified in the R script "`chicken.R`".
- To my knowledge Kruskal-Wallis and Spearman rank correlation require that data is given with individual observations, i.e. in a data frame with 2 variables and 296 observations.
  - One way of transforming *table data* to *individual data* is shown in the R script "`chicken.R`".

Activity of Chicken: Presentation of results

Spearman's rank correlation shows strong evidence of treatment effect on gait score ($\hat{r}_s = -0.1968$, $p = 0.00066$).

The estimated proportions are given in the following table:

Count,	GAIT-score				
Row %	0	1	2	3.5	Total
A	12	26	20	12	70
	17.14	37.14	28.57	17.14	100
B	13	27	22	13	75
	17.33	36.00	29.33	17.33	100
C	25	25	18	8	76
	32.89	32.89	23.68	10.53	100
D	28	23	21	3	75
	37.33	30.67	28.00	4.00	100
Total	78	101	81	36	296
	26.35	34.12	27.36	12.16	100



- Confidence intervals on the proportions might be given.
- Quantification of the association might be improved.
- Analysis might be refined by pairwise comparisons of the treatment groups (plot suggests: A=B, C=D).

Agreement between two binary responses

```
           Correct answer
Student   Pre-test  Post-test
  1          No        No
  2          No       Yes
  3          No        No
  4          No       Yes
  5          No       Yes
  6         Yes       Yes
  7          No        No
...
...
 30          No       Yes
```

Correct answer		Post-test		
of question		Yes	No	Total
Pre-test	Yes	2	0	2
	No	21	7	28
Total		23	7	30

- Did the teaching improve the students performance, or is there agreement between performance before and after the teaching?
  - Are the responses the same at the two time points? (See slides 44–45)
  - Is there a direction of the disagreement? (See slides 46–47)
- Similar issues arise when two raters categorize the same probes, either on nominal or ordinal scale. Possibly with more than 2 categories.

Measuring agreement: Kappa coefficient

How many of the observations are on the diagonal?

		Variable 2		
		+	−	Total
Variable 1	+	a	b	a+b
	−	c	d	c+d
Total		a+c	b+d	n

- Observed fraction on the diagonal:

$$p_{\text{obs}} = \frac{a+d}{n}$$

- Expected fraction on the diagonal (given the marginals):

$$p_{\text{exp}} = \frac{a+b}{n} \cdot \frac{a+c}{n} + \frac{c+d}{n} \cdot \frac{b+d}{n}$$

- Kappa coefficient (R: `kappa2()` from `irr`-package)

$$\kappa = \frac{p_{\text{obs}} - p_{\text{exp}}}{1 - p_{\text{exp}}}$$

Measuring agreement: Kappa coefficient (II)

- Maximal agreement if $\kappa = 1$. Positive agreement if $\kappa > 0$.
- How large κ should be to claim strong agreement is contextual. However, here is a guideline:

Value of κ	Strength of agreement
< 0.20	Poor
0.21–0.40	Fair
0.41–0.60	Moderate
0.61–0.80	Good
0.81–1.00	Very good

- Making hypothesis tests on κ makes less sense (why?). But we may of course make confidence intervals.
- If there is more than two levels we may also use the weighted kappa coefficient, which incorporates the distance to the diagonal.

Is there a direction of the disagreement?

McNemar's test for paired binary observations

		Variable 2		Total
		+	−	
Variable 1	+	a	b	a+b
	−	c	d	c+d
Total		a+c	b+d	n

- **Null hypothesis:**

$$P(+,-) = P(-,+)$$

- **Estimates (under the model):**

$$\hat{P}(+,-) = \frac{b}{n}, \qquad \hat{P}(-,+) = \frac{c}{n}$$

- **Test statistic and continuity correction:**

$$z = \frac{b-c}{\sqrt{b+c}}, \qquad z_c = \frac{|b-c|-1}{\sqrt{b+c}}$$

Squared test statistic evaluated in a chi-square distribution with 1 degree of freedom.

Data example 3: Marijuana and sleeping problems

Matched case-control study. Null hypothesis: $p_{\text{marijuana}} = p_{\text{controls}}$

- **Design:** 32 cases (marijuane users)
  32 controls (cases matched: age, sex, job, ...)
- **Observation:**

Sleeping problems		Marijuana group Yes	No	Total
Controls	Yes	4	9	13 (41 %)
	No	3	16	19
Total		7 (22 %)	25	32 (100 %)

- **Estimates:** $\hat{p}_{\text{marijuana}} = \frac{7}{32} = 0.22, \;\; \hat{p}_{\text{controls}} = \frac{13}{32} = 0.41$
- **McNemar's test with continuity correction:**

$$z_c = \frac{|9-3|-1}{\sqrt{9+3}} = \frac{5}{\sqrt{12}}$$

- **P-value:** $p = 2 \cdot P\left(Z^2 > z_c^2 = \frac{25}{12}\right) = 0.1489$ (NS)

Stuart-Maxwell test for marginal homogeneity

Paired observations with more than 2 categories (I)

Eye-testing (unaided distance vision performance) of $N = 7477$ female employees in Royal Ordnance factories between 1943 and 1946.

	Left eye				
Right eye	1st grade	2nd grade	3rd grade	4th Grade	Total
1st grade	1520	266	124	66	1976
2nd grade	234	1512	432	78	2256
3rd grade	117	362	1772	205	2456
4th Grade	36	82	179	492	789
Total	1907	2222	2507	841	7477

- Null hypothesis: green distribution = blue distribution.
- Here this means that left and right eyes perform equally well.
- R analysis: `stuart.maxwell.mh()` from `irr`-package.

Bowker's test for asymmetry.

Paired observations with more than 2 categories (II)

	Left eye				
Right eye	1st grade	2nd grade	3rd grade	4th Grade	Total
1st grade	1520	266	124	66	1976
2nd grade	234	1512	432	78	2256
3rd grade	117	362	1772	205	2456
4th Grade	36	82	179	492	789
Total	1907	2222	2507	841	7477

- Null hypothesis: green counts and blue counts mirror each other across the diagonal.
- Here this means that there is complete "symmetry" between joint performance of left and right eyes. Note that this hypothesis is more restrictive than marginal homogeneity.
- R analysis: `mcnemar.test()`

Summary of lecture

- Non-parametric test can be used when normality assumption isn't satisfied.
  - Common non-parametric tests available for designs corresponding to T-tests and 1-way ANOVA.
- Risk of wrong conclusions when the statistical power is low.
  - Gelman & Carlin even recommend retrospective power analysis. This is, however, somewhat controversial.
- Analysis of 2-way contingency tables.
  - Association vs. marginal homogeneity (what is the relevant null hypothesis?)
  - Simulation of p-value available in the `LabApplStat`-package in cases, where the approximation by the χ^2-distribution is invalid.
  - Nominal vs. ordinal variables (power to be gained!)
- The remaining slides contain solutions to some of the exercises.

Solution to Exercise 2.3

- There are 64 observations of 2 variables: **treatment**, **seasick**

- Chi-square test, here on the “long” dataset

  ```
  chisq.test(table(read.table("dramanine.txt",header=T)))
  ```

  gives $X^2_{\text{Yates}} = 6.9827$, df $= 1$, p$=$ 0.0082.

- Since there is a significant effect of **treatment** we estimate proportion of seasickness in each subgroup:

Group	$\hat{p}$(seasick)	Lower 95% CL	Upper 95% CL
draminine	0.0882	0.0231	0.2481
placebo	0.4000	0.2322	0.5925

- Confidence intervals are found by R calls:

  ```
  prop.test(3,n=34)
  prop.test(12,n=30)
  ```

Solution to Exercise 2.4

The described data consists of 85 case-control pairs (boldface numbers are stated in the exercise text):

	Sibling		
Patient	No tonsillectomy	Tonsillectomy	Total
No tonsillectomy	**37**	7	**44**
Tonsillectomy	15	26	**41**
Total	**52**	**33**	**85**

McNemar's test gives p=0.1356 (so still non-significant):

```
mcnemar.test(matrix(c(37,15,7,26),2,2))
```

Concerning the data organisation please note that the rows from the table in the exercise text now are the marginals in the paired design. Moreover, we have 85 pairs (instead of 170 persons).

Solution to Exercise 2.6

```
> library(LabApplStat)
> retrodesign(c(0.001,0.003,0.01),SE=0.033)
       power     typeS exaggeration
1 0.05010520 0.4646377    76.682346
2 0.05094724 0.3953041    25.502874
3 0.06058446 0.1950669     7.751928
> power.prop.test(p1=0.49,p2=0.491,power=0.80)

     Two-sample comparison of proportions power calculation

              n = 3923022
             p1 = 0.49
             p2 = 0.491
      sig.level = 0.05
          power = 0.8
    alternative = two.sided

NOTE: n is number in *each* group
```

Solution to Exercise 2.7

Categorization of the continuous height measurements results in the following table:

Count	Sons		
(row pct)	Small	Tall	Total
Parents: small	247 (62%)	152 (38%)	399 (100%)
tall	189 (34%)	364 (66%)	553 (100%)
Total	436	516	952

Chi-square test for association: $\chi^2 = 70.6704$, df=1, $p < 2.2 \cdot 10^{-16}$:

```
chisq.test(matrix(c(247,189,152,364),2,2))
```

Thus, the association is highly significant. Inspection of the row percentages shows that tall parents tend to get tall sons.

- In this situation McNemar's test is non-significant (p=0.05123). What is the interpretation of this test?