Binomial tests
Chi square tests
P-values
Confidence Intervals
Null Hypothesis testing

Biostatistics Course 2024
Lecture 2
Tuesday, 9 July 2024
10:00am - 12:00pm

Example 1: Human Sex Ratio

Computing sex ratio of humans is one of the oldest applications of statistics

year	male	female
1629	5218	4683
1630	4858	4457
1631	4422	4102
1632	4994	4590
1633	5158	4839
1634	5035	4820
1635	5106	4928
1636	4917	4605
1637	4703	4457

⋮

Arbuthnott J (1711). An Argument for Divine Providence, taken from the Constant Regularity observed in the Births of both Sexes.

https://www.openintro.org/stat/data/?data=arbuthnot

sex_ratio.pzfx — Edited

Search

Data Tables
- Data 1
- New Data Table...

Info
- Project info 1
- New Info...

Results
- New Analysis...

Graphs
- a 1
- ew Graph...

Layouts
- New Layout...

Family
- Data 1
- Data 1

Table format: Parts of whole

		A	B	C	D	E	F	G	H	I
		year 1634	total	Title	Title	Title	Title	Title	Title	Title
		Y	Y	Y	Y	Y	Y	Y	Y	Y
1	boys	5035	484382							
2	girls	4820	453841							
3	Title									
4	Title									
5	Title									
6	Title									
7	Title									
8	Title									
9	Title									
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21	Title									
22	Title									
23	Title									
24	Title									
25	Title									
26	Title									
27	Title									

Data 1

Row --, A: year 1634
Selected: Rows 1073741827, Columns 1

Create New Analysis

Data to analyze

Table: Data 1

Type of analysis

Which analysis?

- ▼ **Transform, Normalize...**
  - Transform
  - Transform concentrations (X)
  - Normalize
  - Prune rows
  - Remove baseline and column math
  - Transpose X and Y
  - Fraction of Total
- ▶ **XY analyses**
- ▶ **Column analyses**
- ▶ **Grouped analyses**
- ▶ **Contingency table analyses**
- ▶ **Survival analyses**
- ▼ **Parts of whole analyses**
  - Fraction of Total
  - Compare observed distribution with ex...
- ▶ **Multiple varia analyses**
- ▶ **Nested analy**
- ▶ **Generate curve**
- ▶ **Simulate data**
- ▶ **Recently used**

Analyze which data sets?

- A:year 1634
- B:total

Select All | Deselect All

?

Cancel | OK

Parameters: Compare observed distribution with expected

This analysis expects that each value in the data table is an actual number of events or items, and is not normalized in any way.

Data set to analyze

A: year 1634

Enter expected values as

- ○ Actual numbers of objects or events
- ◉ Percentages

Wit o rows, perform

- ◉ nomial test (recommended)
- ○ Ch -square test for goodness of fit

Expected distribution

Row	Outcome	Observed %	Expected %
1	boys	51.09	50
2	girls	48.91	50

Output

Method to calculate CI: Wilson/Brown (recommended)

Show this many significant digits (for everything except P values): 4

P value style: GP: 0.1234 (ns), 0.0332 (*), 0.0021 (**), 0.000... N= 6

?

Cancel

O

sex_ratio.pzfx — Edited

Search

- Data Tables
  - Data 1
  - *New Data Table...*
- Info
  - Project info 1
  - *New Info...*
- Results
  - O vs. E of Data 1
  - *New Analysis...*
- Graphs
  - Data 1
  - *New Graph...*
- Layouts
  - *New Layout...*

Family
- Data 1
  - O vs. E

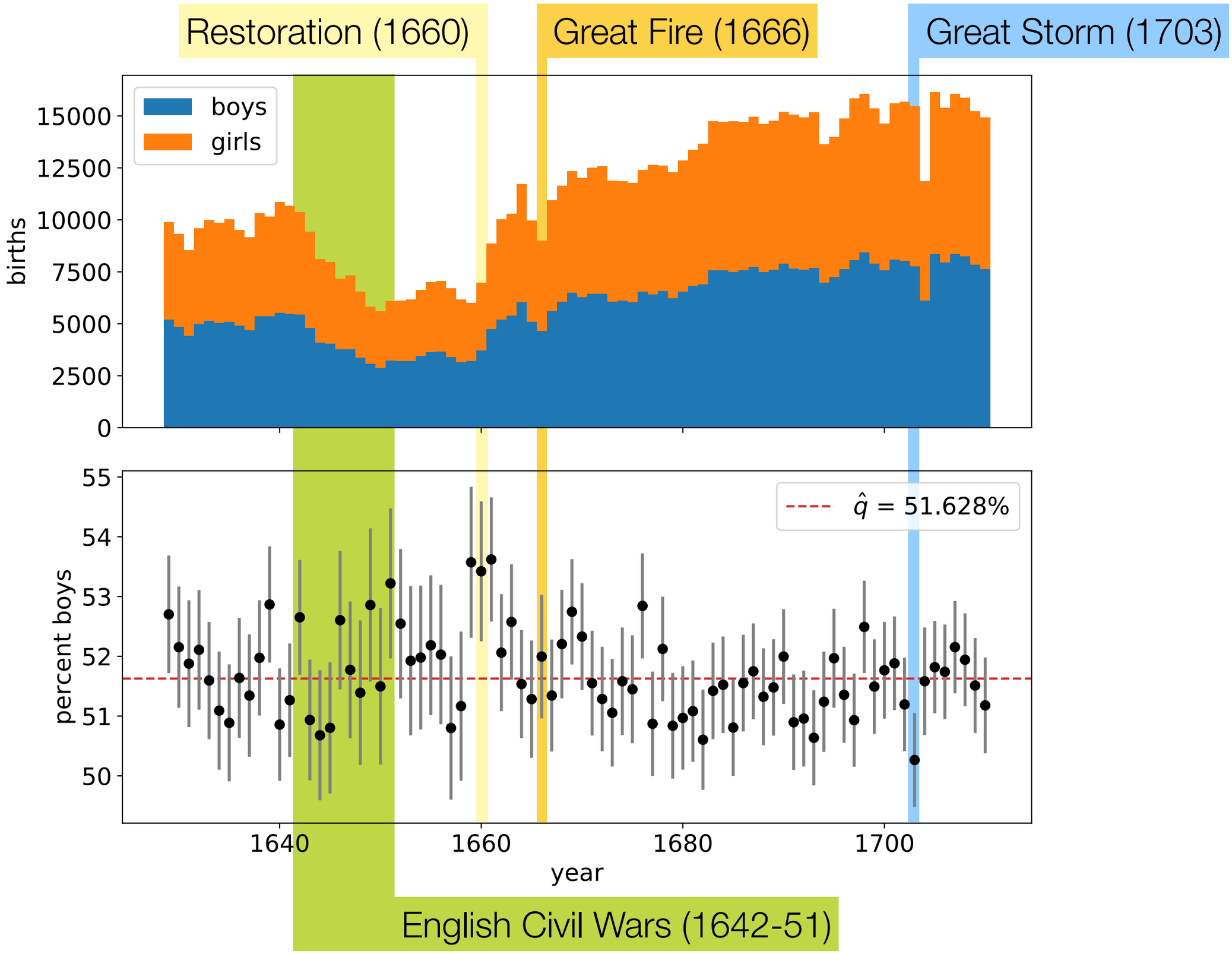
O vs. E

1	Table analyzed	Data 1					
2	Column analyzed	Column A					
3							
4	**Binomial test**						
5	P (one-tailed)	0.0156					
6	P (two-tailed)	0.0311					
7	P value summary	*					
8	Is discrepancy significant (P < 0.05)?	Yes					
9							
10	**Outcome**	**Expected #**	**Observed #**	**Expected %**	**Observed %**	**95% CI of Observed %**	
11	boys	4928	5035	50.00	51.09	50.10 to 52.08	
12	girls	4928	4820	50.00	48.91	47.92 to 49.90	
13	TOTAL	9855	9855	100.0	100.00		
14							
15							
16							
17							
18							
19							
20							
21							
22							
23							
24							
25							
26							
27							

O vs. E of Data 1

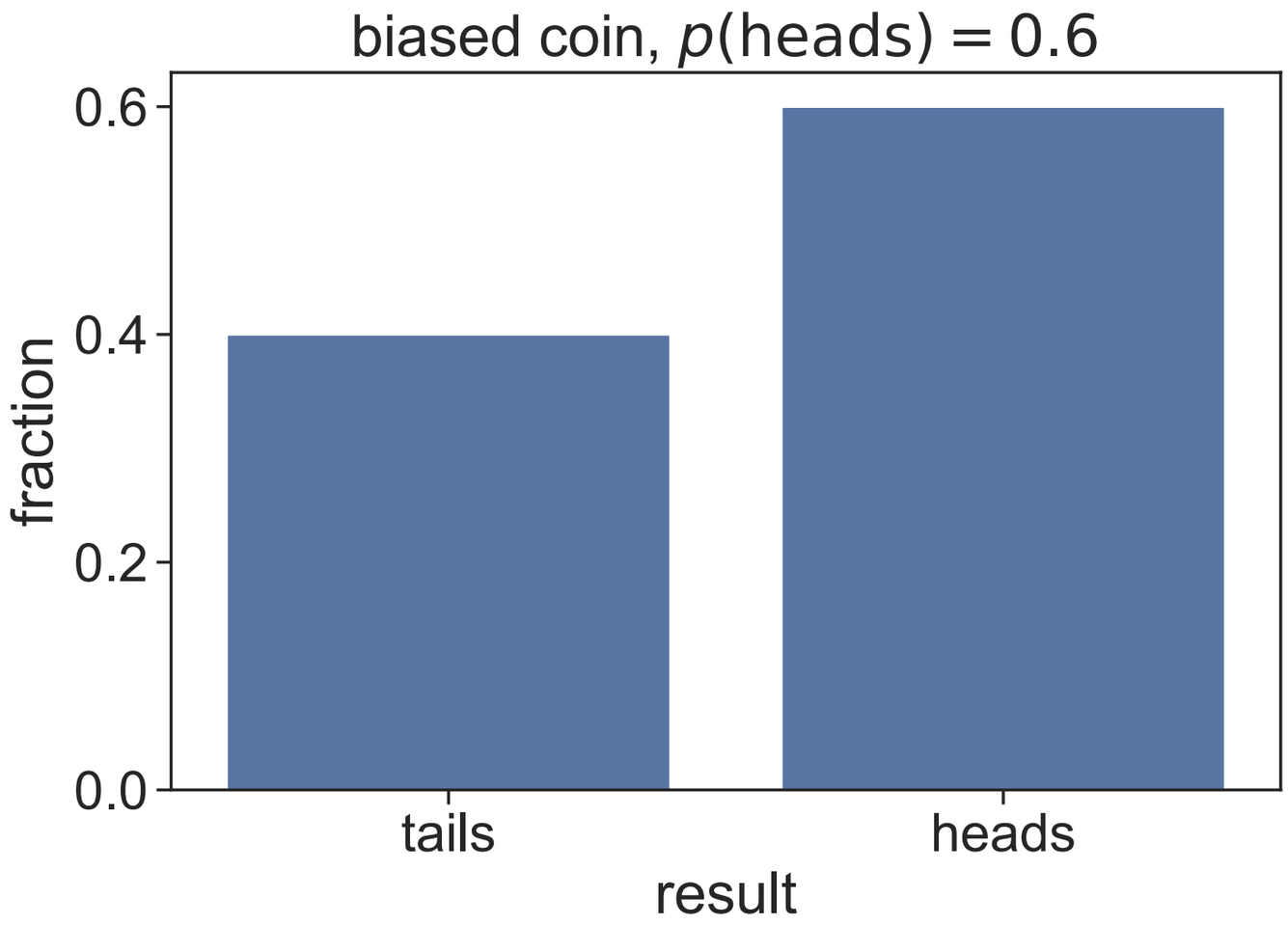
Row 1, Column A

Births in London, 1629-1710



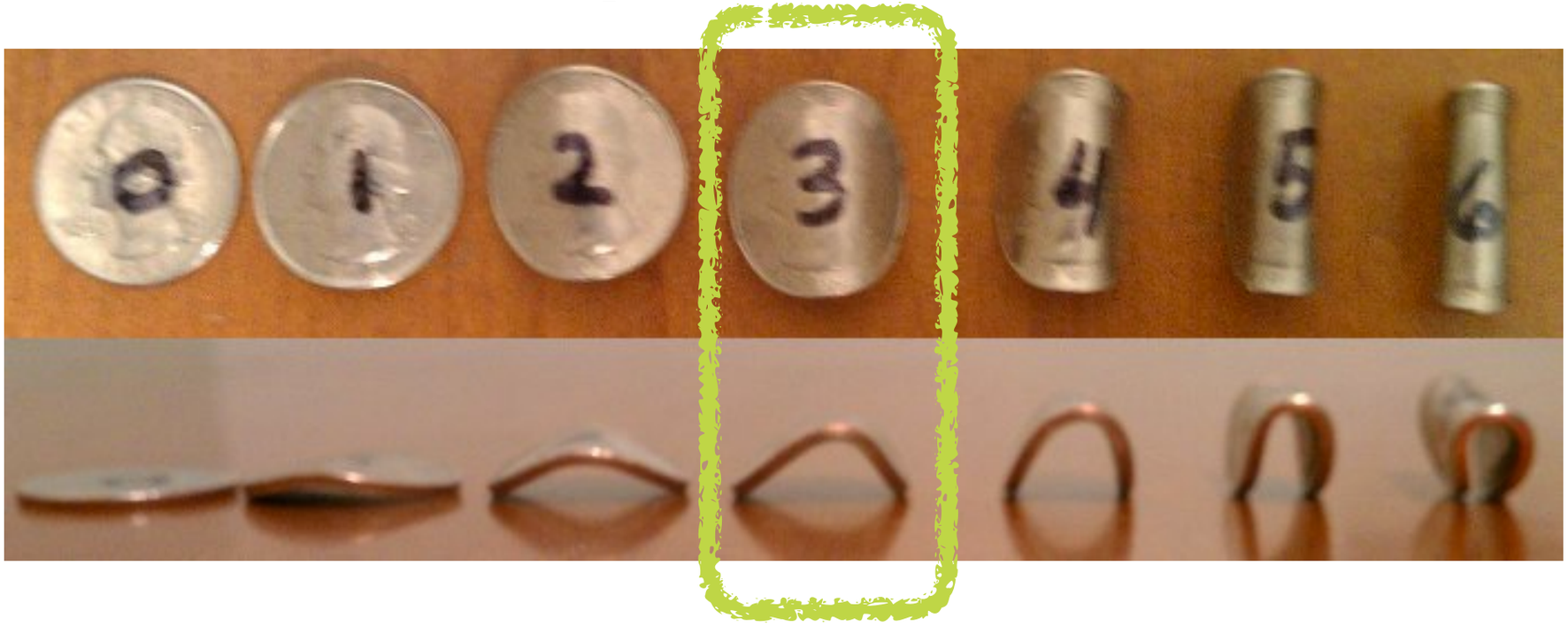
Example 2: A biased coin

Biased coins are modeled using a Bernoulli distribution, which describes probabilities for a binary variable



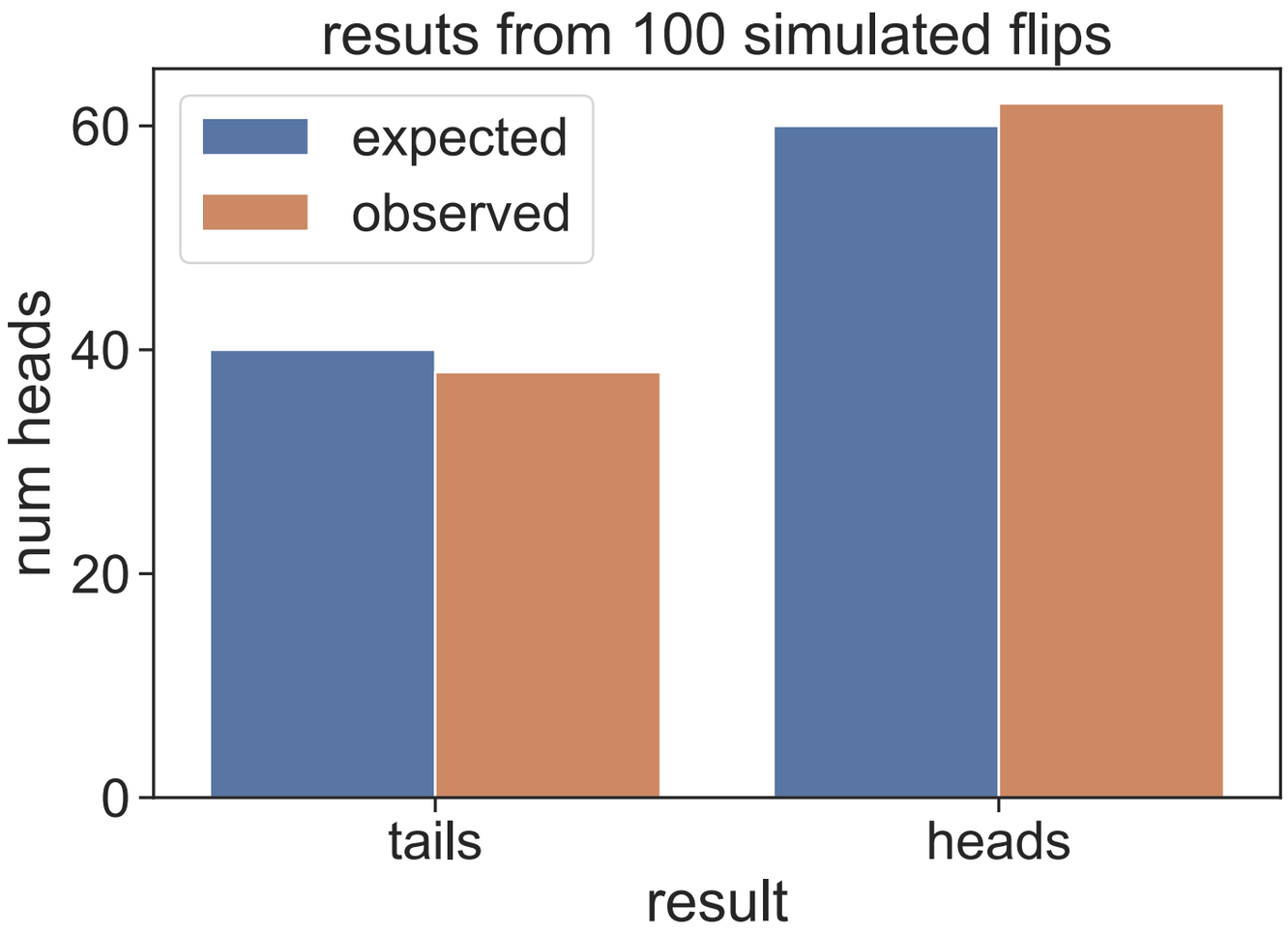
Making a biased coin

$$p(\text{heads}) \approx 60\,\%$$



Mike Izbicki (Claremont McKenna College)
https://izbicki.me/blog/how-to-create-an-unfair-coin-and-prove-it-with-math.html

The number of heads after 100 flips of the biased coin will resemble the underlying probabilities, but will not match exactly



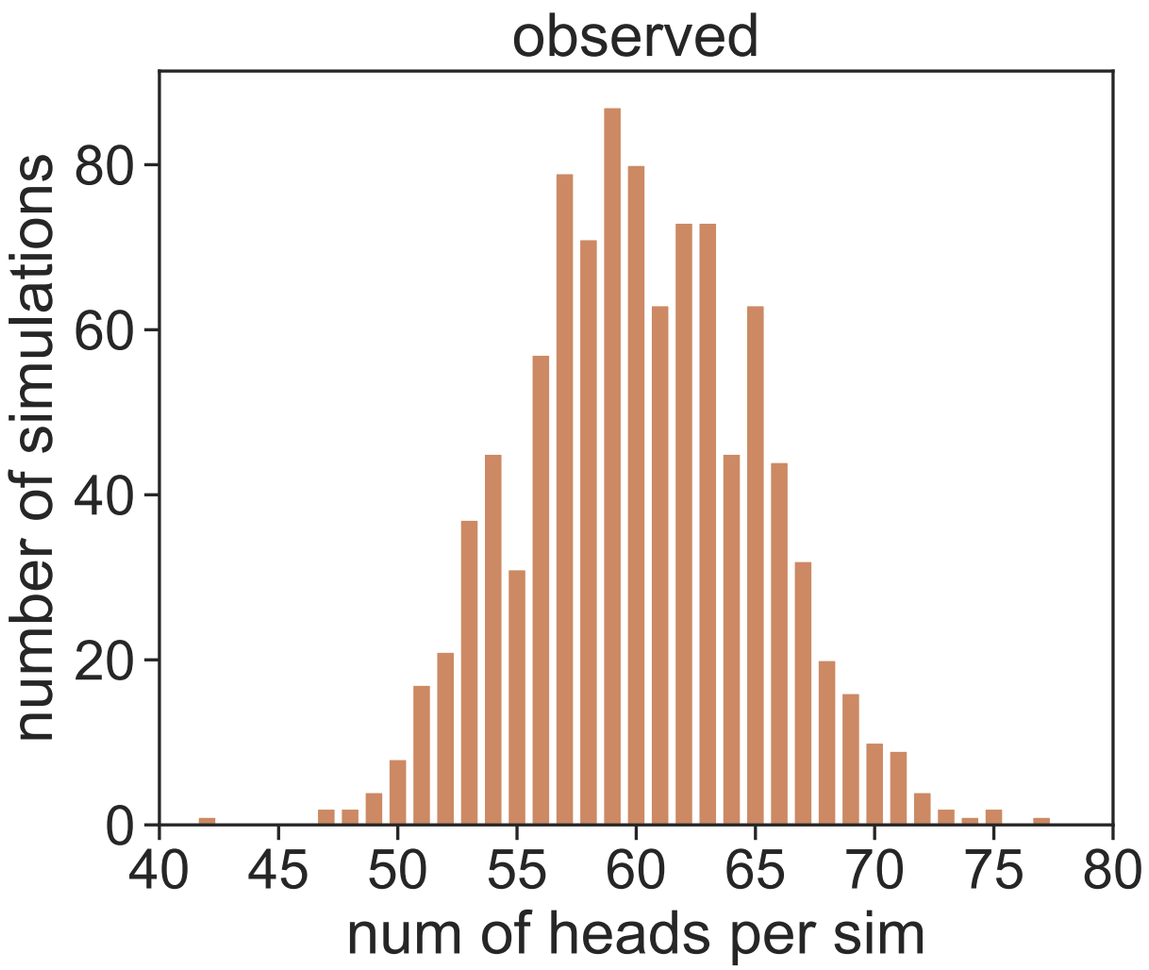
expected: 60 heads, 40 tails

observed: 62 heads, 38 tails

How much deviation from the expected values do we expect?

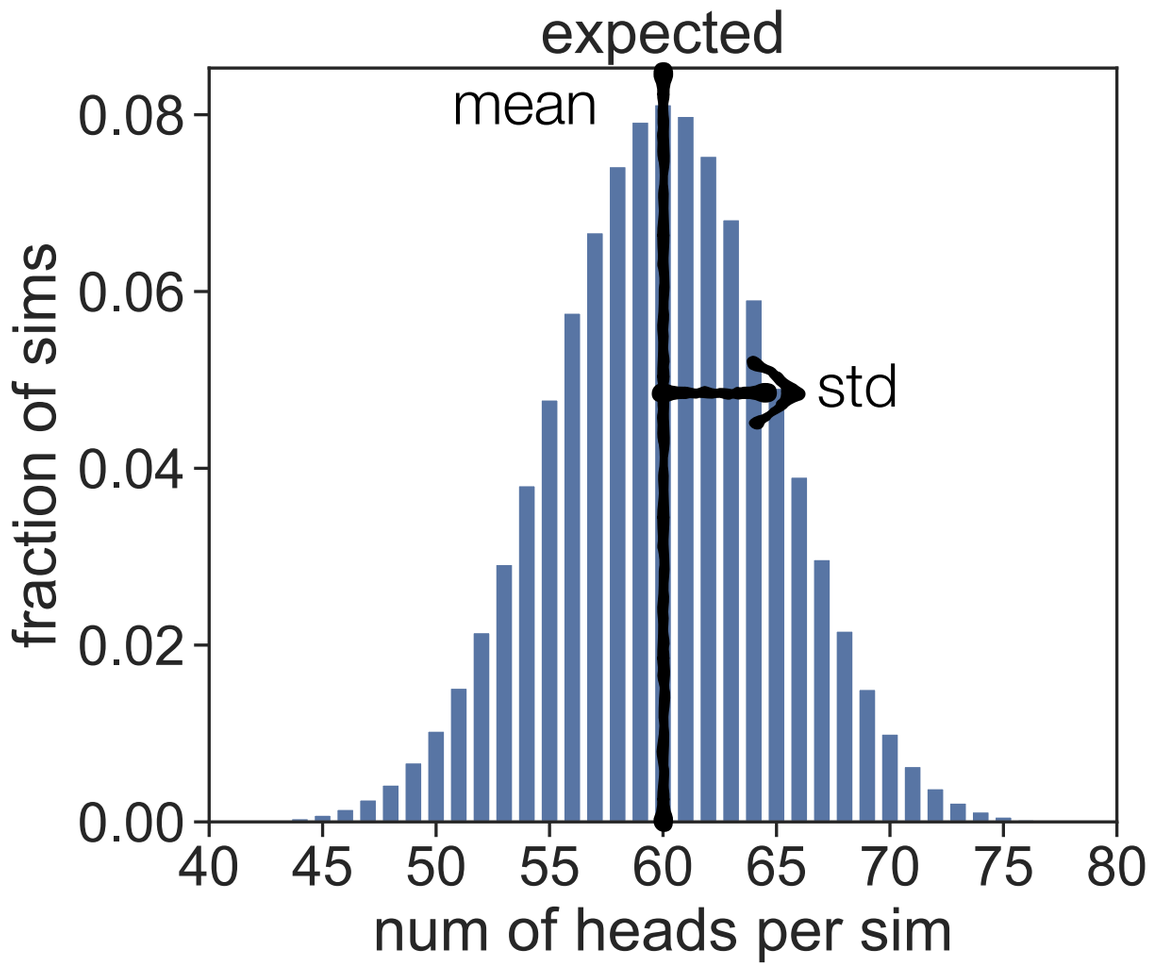
There is substantial variation across replicates. This is to be expected.

Results from 1000 simulations, 100 flips per simulation



The variation in the number of heads from replicate to replicate is described by a binomial distribution

Results from 1000 simulations, 100 flips per simulation



mean = 60

standard deviation (std) = 4.9

Can we determine whether or not a coin is biased by flipping it 100 times?

Suppose we flip a coin 100 times and observe **62 heads** (and 38 tails).

Null hypothesis: heads and tails are equally likely, i.e.

$$p(\text{heads}) = 50\,\%$$

Alternative hypothesis: heads and tails are not equally likely, i.e.

$$p(\text{heads}) \neq 50\,\%$$

Our observation (62 heads) may or may not allow us to reject the null hypothesis and thus accept the alternative hypothesis.

No amount of data, however, can cause us to accept the null hypothesis.

flips.pzfx — Edited

Search

- Data Tables
  - **Data 1**
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  - **Data 1**
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- Layouts
  - *New Layout...*

Family

- **Data 1**
- **Data 1**

Table format: Parts of whole

		A	B	C	D	E	F	G	H	I
		flips	Title	Title	Title	Title	Title	Title	Title	Title
		Y	Y	Y	Y	Y	Y	Y	Y	Y
1	heads	62								
2	tails	38								
3	Title									
4	Title									
5	Title									
6	Title									
7	Title									
8	Title									
9	Title									
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22	Title									
23	Title									
24	Title									
25	Title									

Data 1 | Row 6, Column C

Create New Analysis

Data to analyze

Table: Data 1

Type of analysis

Which analysis?

- ▼ **Transform, Normalize...**
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  - Transform concentrations (X)
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  - Compare observed distribution with ex...
- ▶ **Multiple variable analyses**
- ▶ **Nested analyses**
- ▶ **Generate curve**
- ▶ **Simulate data**
- ▶ **Recently used**

Analyze which data sets?

☑ A:flips

When you analyze tables or graphs with more than one data set, use this space to select which data set(s) to analyze.

Select All | Deselect All

?

Cancel | OK

Parameters: Compare observed distribution with expected

This analysis expects that each value in the data table is an actual number of events or items, and is not normalized in any way.

Data set to analyze

A: flips

Enter expected values as

- Actual numbers of objects or events
- Percentages

With two rows, perform

- Binomial test (recommended)
- Chi-square test for goodness of fit

Expected distribution

Row	Outcome	Observed %	Expected %
1	heads	62	50
2	tails	38	50

Output

Method to calculate CI: Wilson/Brown (recommended)

Show this many significant digits (for everything except P values): 4

P value style: GP: 0.1234 (ns), 0.0332 (*), 0.0021 (**), 0.000... N= 6

?

Cancel

OK

flips.pzfx — Edited

Search

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- Results
  - **O vs. E of Data 1**
  - *New Analysis...*
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  - Data 1
  - *New Graph...*
- Layouts
  - *New Layout...*

Family

- Data 1
  - O vs. E

O vs. E

1	Table analyzed	Data 1				
2	Column analyzed	Column A				
3						
4	**Binomial test**					
5	P (one-tailed)	0.0105				
6	P (two-tailed)	0.0210				
7	P value summary	*				
8	Is discrepancy significant (P < 0.05)?	Yes				
9						
10	**Outcome**	**Expected #**	**Observed #**	**Expected %**	**Observed %**	**95% CI of Observed %**
11	heads	50.00	62	50.00	62.00	52.21 to 70.90
12	tails	50.00	38	50.00	38.00	29.10 to 47.79
13	TOTAL	100.0	100.0	100.0	100.00	
14						
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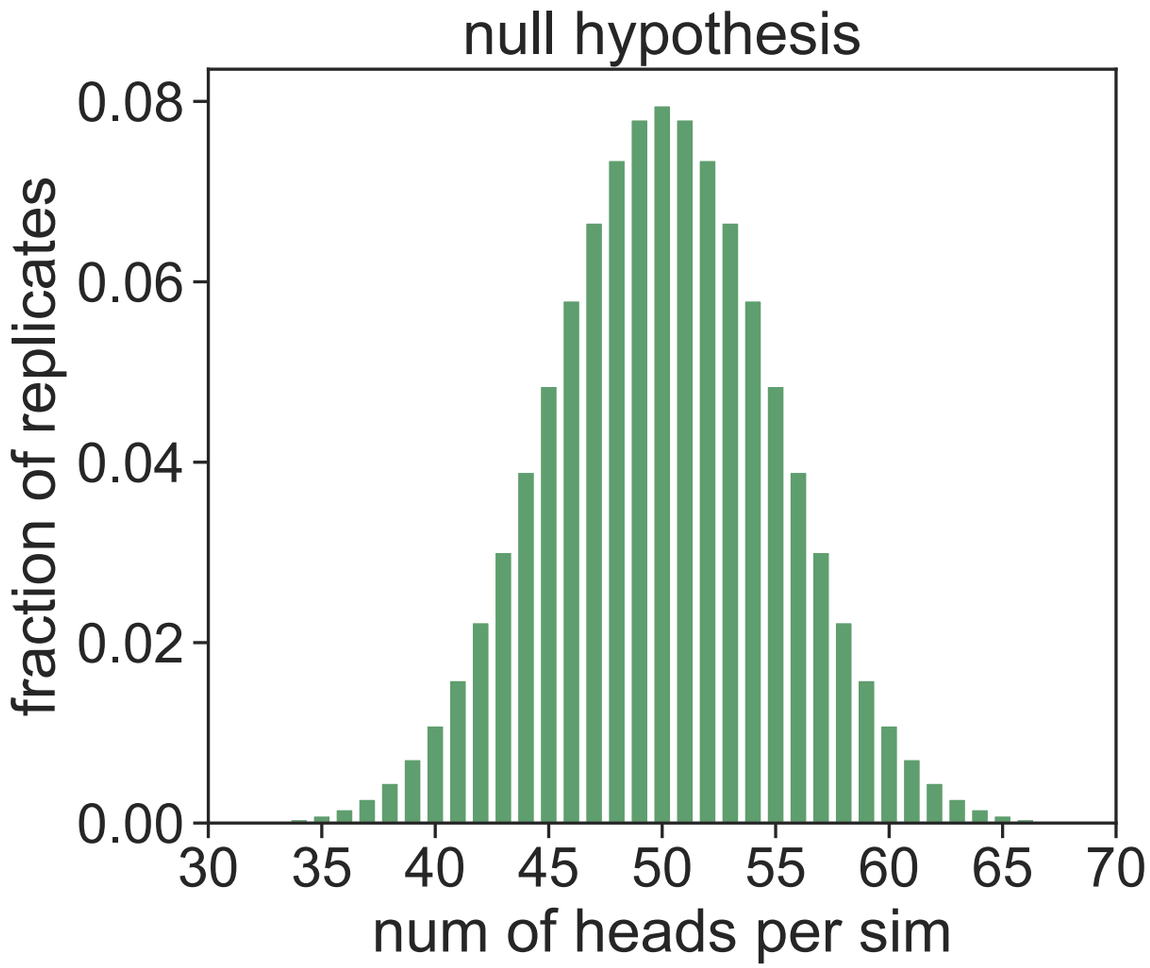
25						

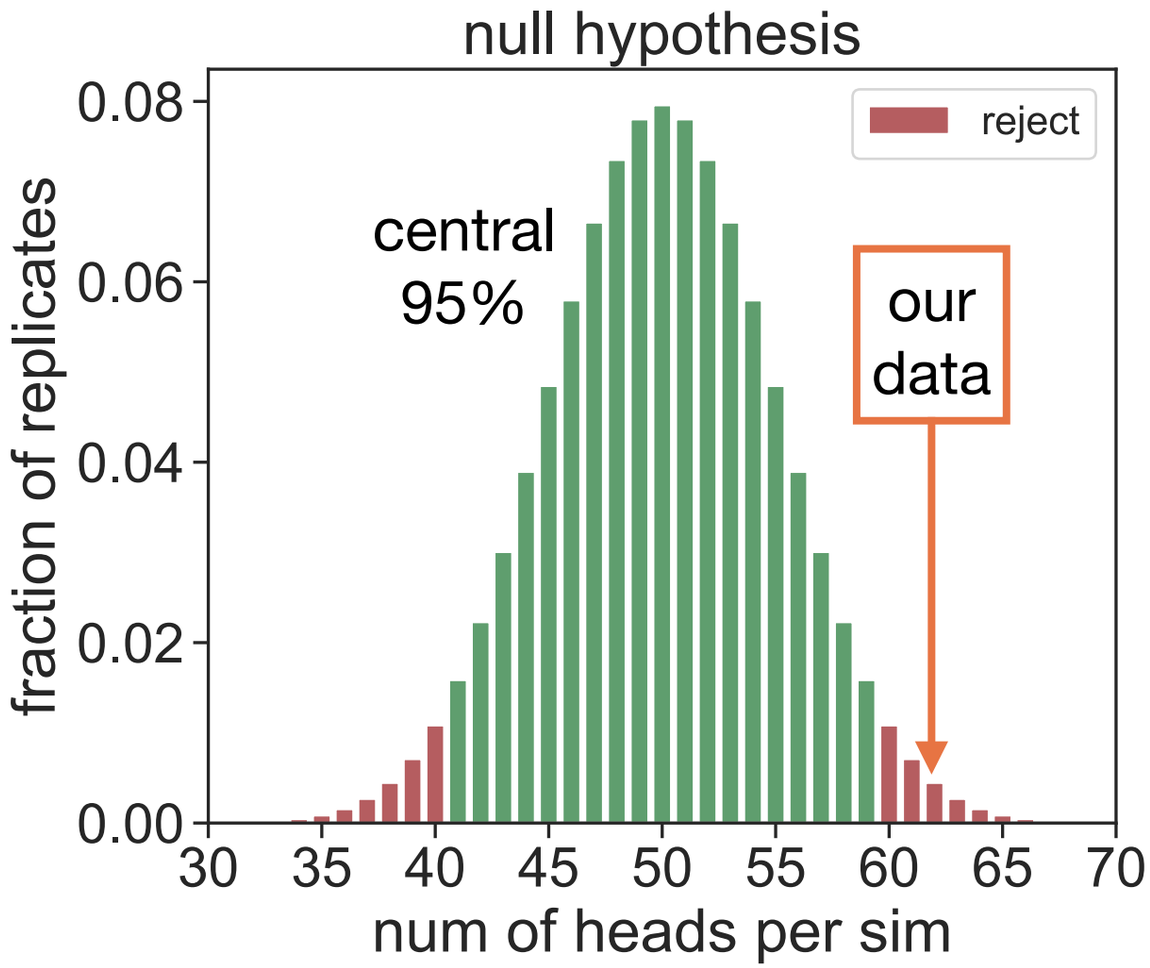
O vs. E of Data 1 | Row 1, Column A

The null hypothesis is assessed by where the data fall within the null distribution



We reject the null hypothesis of the data fall too far away from the bulk of the distribution

If the null hypothesis is true, data should fall within the green region 95% of the time, and within the red “reject” region 5% of the time.

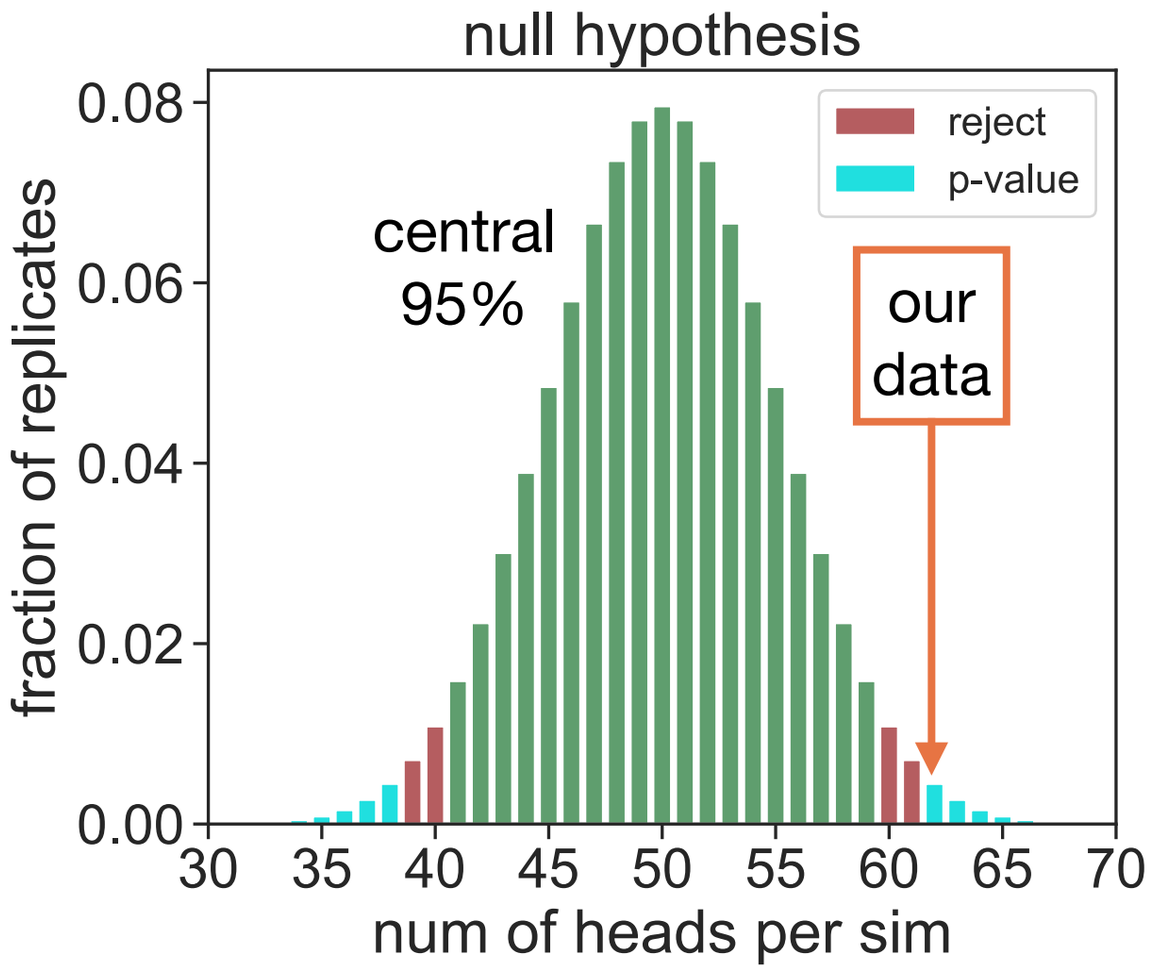


Our assumed dataset (62 heads) lies outside the central 95%.

We can therefore reject the null hypothesis with 95% confidence.

P-values quantify the probability of data being as or more extreme than the data in hand were the null hypothesis true.

The P-value threshold of 0.05 comes from adopting a confidence threshold of 95%.

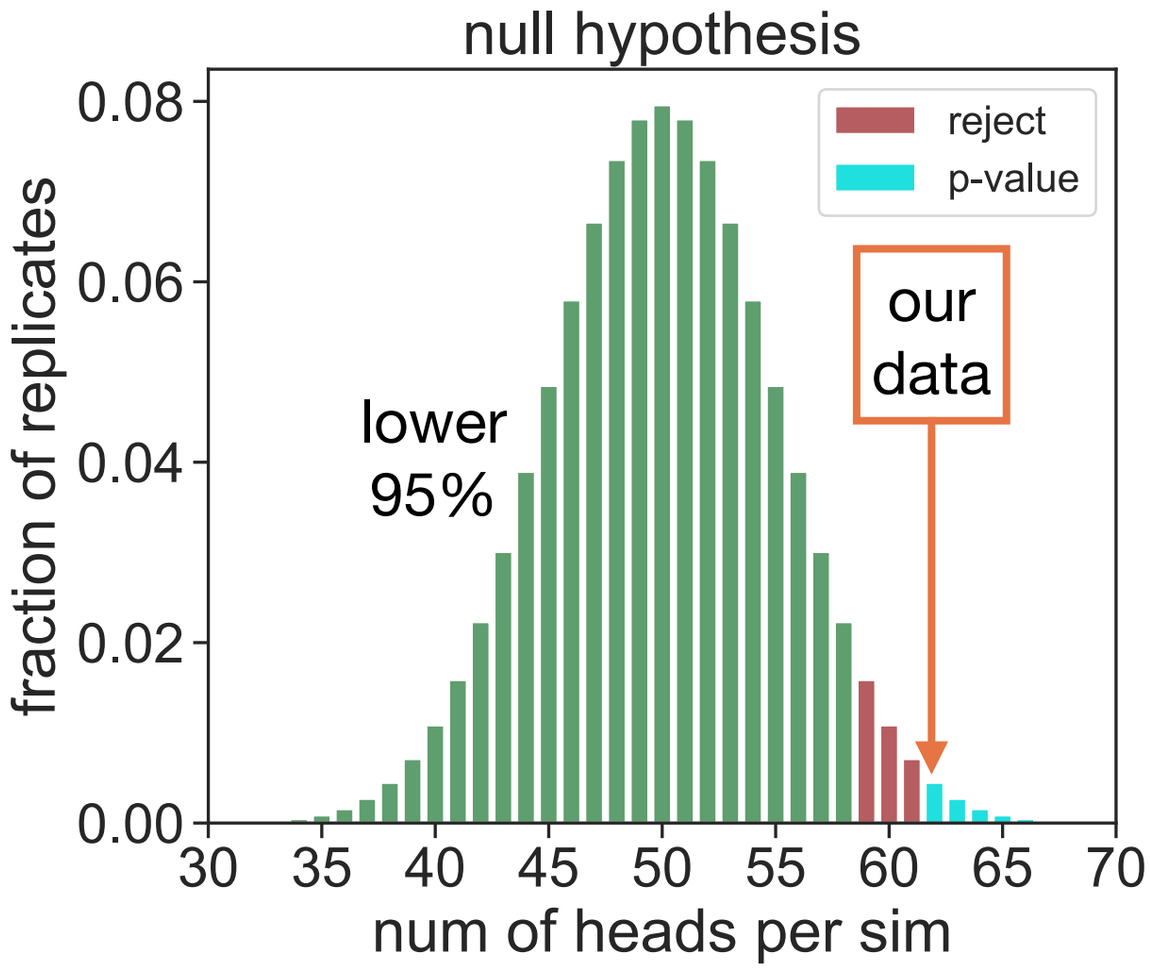


We find that **p=0.0210** for the two-sided test.

We therefore say that our result is "statistically significant"

P-values quantify the probability of data being as or more extreme than the data in hand were the null hypothesis true.

A one-sided hypothesis test only considers one side of the distribution.

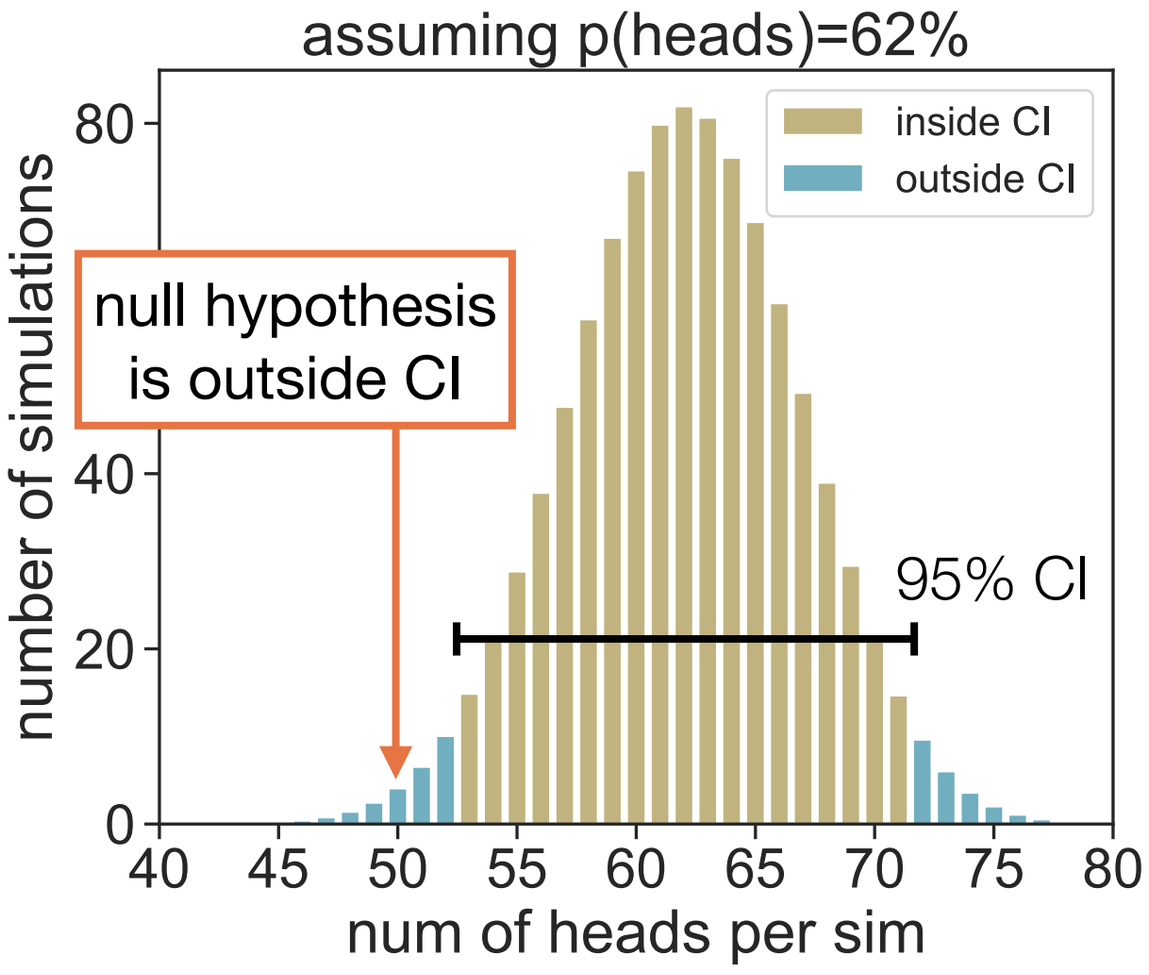


We find that **p=0.0105** for the one-sided test.

In general, two-sided tests are more conservative than one-sided tests.

Unless you have good reason to do otherwise, use two-sided tests.

Confidence intervals (CIs) are more informative than P-values



We conclude that $p(\text{heads})$ lies within [52.5%, 71.5%] with 95% confidence.

We can reject the null hypothesis because it lies outside this confidence interval.

P-values have multiple pitfalls

- “Statistically significant” does not actually mean “significant” in the normal sense. At best, it means “detectable”.
- P-values do not say how big an observed effect is.
- P-values do not say how important that observed effect is.
- P-values calculations rely on assumptions, and violation of any of those assumptions can render P-values meaningless.
- Perhaps most severe is the fact that P-values do not actually quantify you how likely or unlikely your null hypothesis is!

Why are Confidence Intervals better than P-values?

- Like a P-value, a CI communicates statistical significance (i.e. detectability).
- A CI also communicates effect size, as well as the uncertainty in that effect size.
- A 95% CI does not actually mean that the true value of a parameter lies within that interval with 95% probability. Still, this (extremely common) misinterpretation is largely benign compared to the misinterpretation of P-values.
- However, P-values are more commonly reported than confidence intervals.

The perils of null hypothesis testing

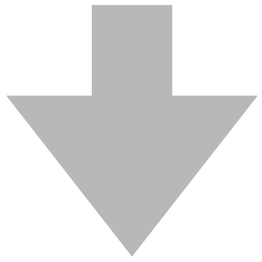
Summary of null hypothesis testing

Step 1: Specify a null hypothesis.

Step 2: Specify a confidence level (usually 95%)

Step 3: Identify the appropriate statistical test

Then:
evaluate on data



Result: P-value summarizing how unlikely the data is compared to null hypothesis expectations.

Perhaps most problematic is how easily P-values are misinterpreted.

Roughly speaking, P-values quantify how likely our data would be if the null hypothesis were true.

$$p(\text{data} \mid \text{null hypothesis})$$

P-values do not quantify the probability of the null hypothesis given our data. Unfortunately, this is the quantity that we actually care about.

$$p(\text{null hypothesis} \mid \text{data})$$

My opinion: the use of P-values to reject hypotheses is predicated on the base rate fallacy

By convention P < 0.05, then one rejects null hypothesis, supposedly because

$$p(\text{null hypothesis} \,|\, \text{data})$$ is small.

For this to make sense, one has to accept the base rate fallacy, i.e.,

$$p(\text{data} \,|\, \text{null hypothesis}) \approx p(\text{null hypothesis} \,|\, \text{data})$$

Whether or not this is true in a specific case depends on the prior odds,

$$p(\text{null hypothesis}),$$

which Frequentist statistics refuses to consider.

The misinterpretation of P-values reflects the Frequentist / Bayesian divide

Frequentist statistics (a.k.a. classical statistics) focuses on likelihood:

$$p(\text{data} \mid \text{hypothesis}).$$

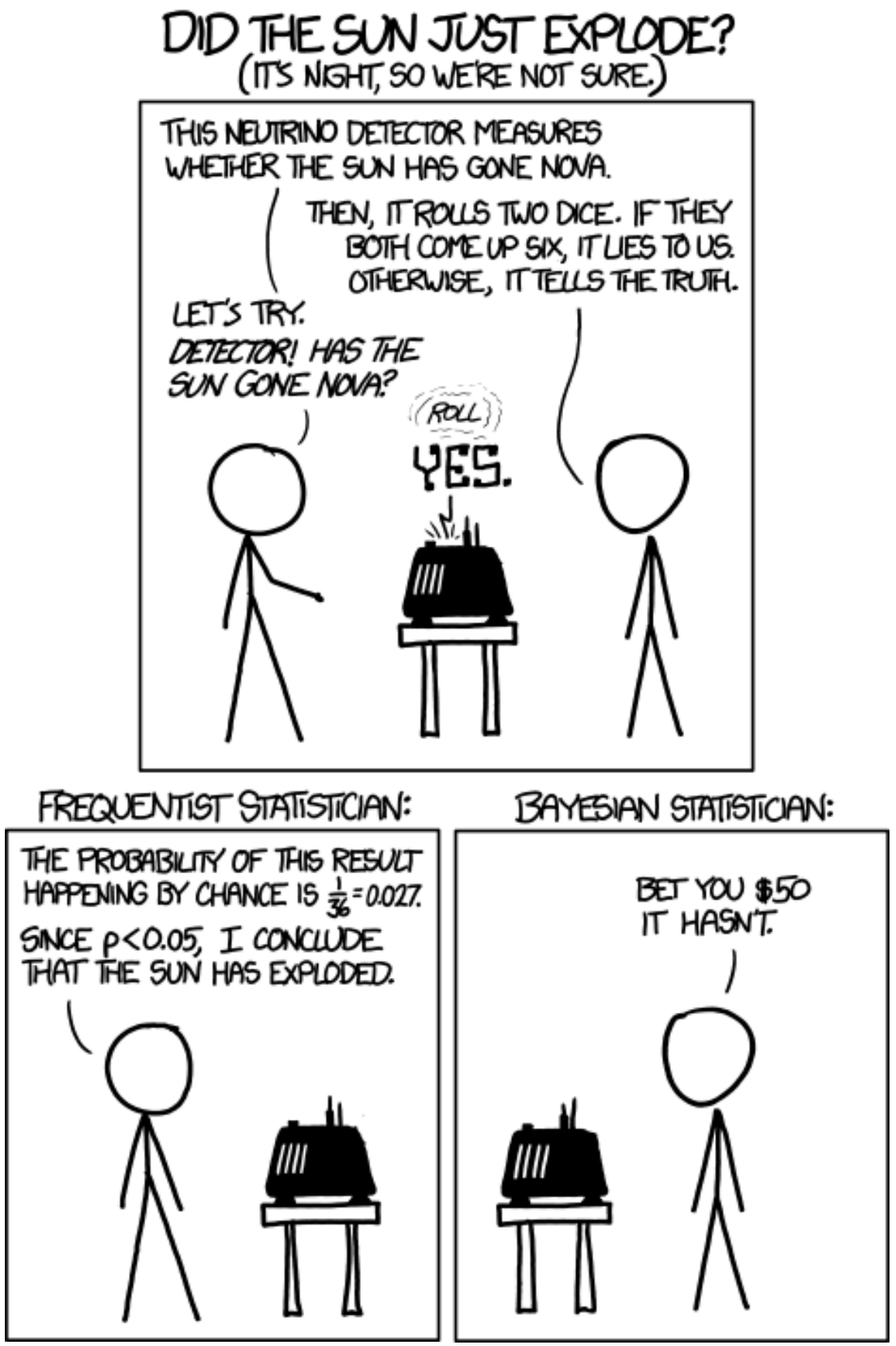
Iron Law of Frequentist Statistics:
Never compute the probability of a hypothesis.

Bayesian statistics focuses on computing posterior probabilities:

$$p(\text{hypothesis} \mid \text{data}).$$

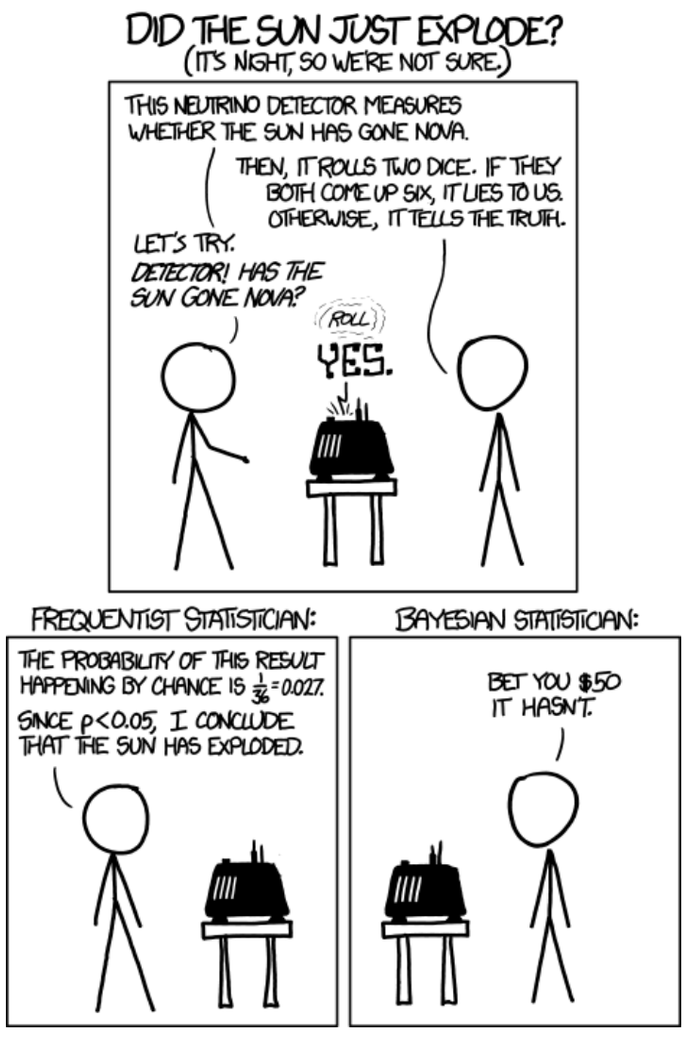
Example 3: Supernova detection machine

Exercise: supernova



https://xkcd.com/1132/

Exercise: supernova



https://xkcd.com/1132/

Bayes's theorem (from yesterday):

$$\frac{p(\text{nova}^+ \,|\, \text{detector}^+)}{p(\text{nova}^- \,|\, \text{detector}^+)} = \frac{p(\text{detector}^+ \,|\, \text{nova}^+)}{p(\text{detector}^+ \,|\, \text{nova}^-)} \times \frac{p(\text{nova}^+)}{p(\text{nova}^-)}$$

$$\left[\frac{35/36}{1/36} = 35\right]$$

If our prior belief is that a supernova is very unlikely, i.e.

$$\frac{p(\text{nova}^+)}{p(\text{nova}^-)} \ll \frac{1}{35},$$

then we still shouldn't believe the sun has gone nova.

Even though, with a null hypothesis of nova^-,

$$\text{P value} = p(\text{detector}^+ \,|\, \text{nova}^-) = \frac{1}{36} = 0.028 < 0.05$$

Example 4: Mendel's Peas

	Flower Colour	Plant Height	Seed Color	Seed Shape	Pod Colour	Pod Shape	Flower Position
Dominant Trait	 Purple	 Tall	3/4  Yellow	3/4  Round	 Green	 Inflated (full)	 Axial
Recessive Trait	 White	 Short	1/4  Green	1/4  Wrinkled	 Yellow	 Constricted (flat)	 Terminal

https://ib.bioninja.com.au/standard-level/topic-3-genetics/34-inheritance/mendels-laws.html

Chi square test (known proportions)

Example: Mendel's peas

	observed	expected proportion	expected counts
Round & yellow	315	9/16	312.75
Round & green	108	3/16	104.25
Angular & yellow	101	3/16	104.25
Angular & green	32	1/16	34.75
Total	556	16/16	556.00

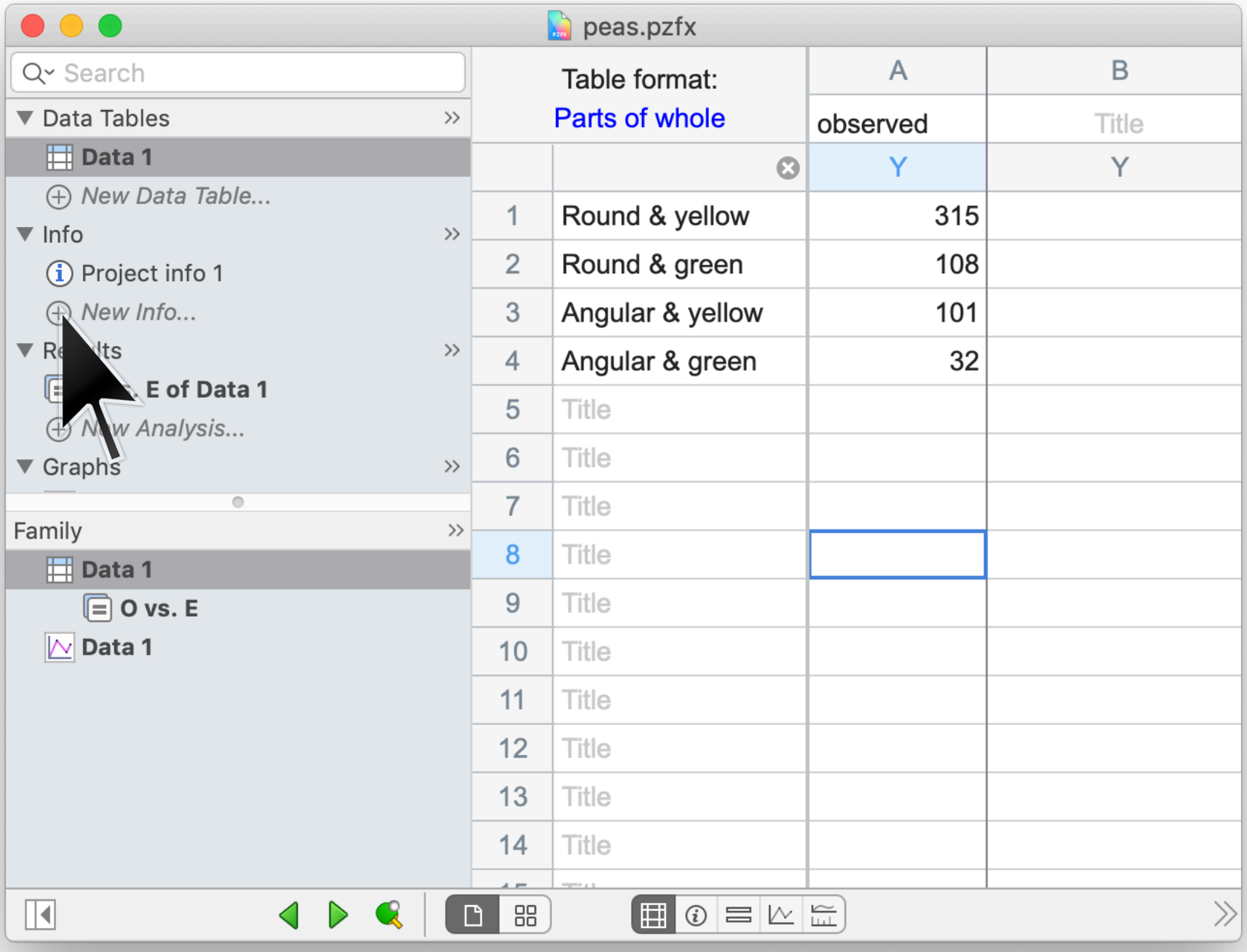
Null Hypothesis:

observations in $K = 4$ different categories occur in the expected proportions

Data: number of observations in each category

Statistic: $\chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$

Null distribution: Chi square distribution with $K - 1 = 3$ degrees of freedom (DOF)


peas.pzfx
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Data 1
Table format:
Parts of whole
A
observed
Y
B
Title
Y
1 Round & yellow 315
2 Round & green 108
3 Angular & yellow 101
4 Angular & green 32
5 Title
6 Title
7 Title
8 Title
9 Title
10 Title
11 Title
12 Title
13 Title
14 Title

Parameters: Compare observed distribution with expected

This analysis expects that each value in the data table is an actual number of events or items, and is not normalized in any way.

Data set to analyze

A: observed

Enter expected values as

- ○ Actual numbers of objects or events
- ◉ Percentages

With two rows, perform

- ○ Binomial test (recommended)
- ◉ Chi-square test for goodness of fit

Expected distribution

Row	Outcome	Observed %	Expected %
1	Round & yellow!	56.65	56.25
2	Round & green	19.42	18.75
3	Angular & yellow!	18.17	18.75
4	Angular & green!	5.76	6.25

enter manually

Output

Method to calculate CI: Wilson/Brown (recommended)

Show this many significant digits (for everything except P values): 4

P value style: GP: 0.1234 (ns), 0.0332 (*), 0.0021 (**), 0.000... N= 6

?

Cancel OK

peas.pzfx — Edited

Search

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  - **Data 1**
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  - *New Info...*
- Results
  - **O vs. E of Data 1**
  - *New Analysis...*
- Graphs
  - Data 1
  - *New Graph...*

Family
- **Data 1**
  - **O vs. E**

O vs. E

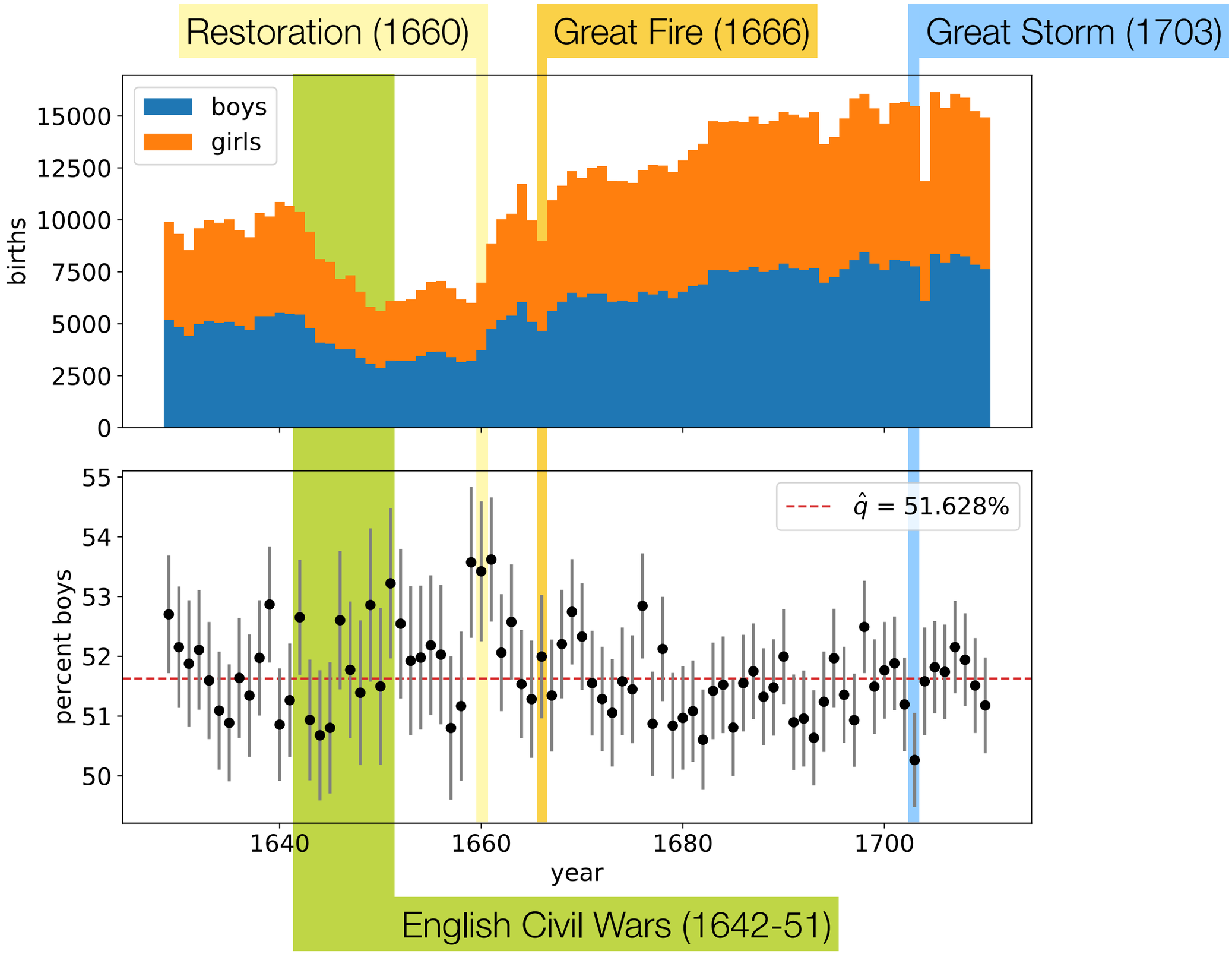
1	Table analyzed	Data 1			
2	Column analyzed	Column A			
3					
4	**Chi-square test**				
5	Chi-square	0.4700			
6	DF	3			
7	P value (two-tailed)	0.9254			
8	P value summary	ns			
9	Is discrepancy significant (P < 0.05)?	No			
10					
11	**Outcome**	**Expected #**	**Observed #**	**Expected %**	**Observed %**
12	Round & yellow	312.8	315	56.25	56.65
13	Round & green	104.3	108	18.75	19.42
14	Angular & yellow	104.3	101	18.75	18.17
15	Angular & green	34.75	32	6.250	5.755
16	TOTAL	556.0	556.0	100.0	100.00
17					

data fits expectations

O vs. E of Data 1 | Row 1, Column

Example 4: Human sex ratio in London over time

Is it possible that the boy/girl ratio changes from year to year?



Chi square test (unknown proportions)

year	sex: male	sex: female
1629	5218	4683
1630	4858	4457
1631	4422	4102
1632	4994	4590
1633	5158	4839
1634	5035	4820
1635	5106	4928
1636	4917	4605
1637	4703	4457
1638	5359	4952

Null Hypothesis:

Two multi-category variables A and B are independent, i.e.,

$$p(A, B) = p(A) \cdot p(B)$$

Statistic:

$$\chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

Null distribution:

Chi square distribution with

$$\text{DOF} = nm - m - n + 1$$

where

m = number of possible values for A

n = number of possible values or B

arbuthnot.pzfx

Search

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Family
- arbuthnot

Table format: Contingency

		Outcome A	Outcome B	Outcome C	Outcome D	Outcome E	Outcome F	Outcome G	Outcome H
		boys	girls	Title	Title	Title	Title	Title	Title
		Y	Y	Y	Y	Y	Y	Y	Y
1	1629	5218	4683						
2	1630	4858	4457						
3	1631	4422	4102						
4	1632	4994	4590						
5	1633	5158	4839						
6	1634	5035	4820						
7	1635	5106	4928						
8	1636	4917	4605						
9	1637	4703	4457						
10	1638	5359	4952						
11	1639	5366	4784						
12	1640	5518	5332						
13	1641	5470	5200						
14	1642	5460	4910						
15	1643	4793	4617						
16	1644	4107	3997						
17	1645	4047	3919						
18	1646	3768	3395						
19	1647	3796	3536						
20	1648	3363	3181						
21	1649	3079	2746						
22	1650	2890	2722						
23	1651	3231	2840						
24	1652	3220	2908						
25	1653	3196	2959						
26	1654	3441	3179						
27	1655	3655	3349						
28	1656	3668	3382						
29	1657	3396	3289						

arbuthnot

Row 6, Column E

Create New Analysis

Data to analyze

Table: arbuthnot

Type of analysis

Which analysis?

- **Transform, Normalize...**
  - Transform
  - Transform concentrations (X)
  - Normalize
  - Prune rows
  - Remove baseline and column math
  - Transpose X and Y
  - Fraction of Total
- **XY analyses**
- **Column analyses**
- **Grouped analyses**
- **Contingency table analyses**
  - Chi-square (and Fisher's exact) test
  - Row means with SD or SEM
  - Fraction of Total
- **Survival analyses**
- **Parts of whole analyses**
- **Multiple variable analyses**
- **Nested analyses**
- **Generate curve**
- **Simulate data**
- **Recently used**

Analyze which data sets?

- [x] A:boys
- [x] B:girls

Select All | Deselect All

?

Cancel | OK

Parameters: Chi-square (and Fisher's exact) test

Main Calculations | Options

Effect sizes to report

- [ ] Relative Risk
  Used for prospective and experimental studies
- [ ] Difference between proportions (attributable risk) and NNT
  Used for prospective and experimental studies
- [ ] Odds ratio
  Used for retrospective case-control studies
- [ ] Sensitivity, specificity and predictive values
  Used for diagnostic tests

Method to compute the P value

- ( ) Fisher's exact test
- ( ) Yates' continuity corrected chi-square test
- (•) Chi-square test
- ( ) Chi-square test for trend

Looking for the z test to compare proportions? Choose the chi-square test (with or without the Yates' correction). The chi-square and z tests are equivalent.

?

Cancel | OK

arbuthnot.pzfx — Edited

Search

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  - New Graph...
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  - New Layout...

Family

- arbuthnot
  - Contingency

Contingency

1	**Table Analyzed**	arbuthnot
2		
3	**P value and statistical significance**	
4	Test	Chi-square
5	Chi-square, df	169.7, 81
6	P value	<0.0001
7	P value summary	****
8	One- or two-sided	NA
9	Statistically significant (P < 0.05)?	Yes
10		
11	**Data analyzed**	
12	Number of rows	82
13	Number of columns	2
14		
15		
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		
29		

Contingency of arbuthnot