4. Confidence intervals

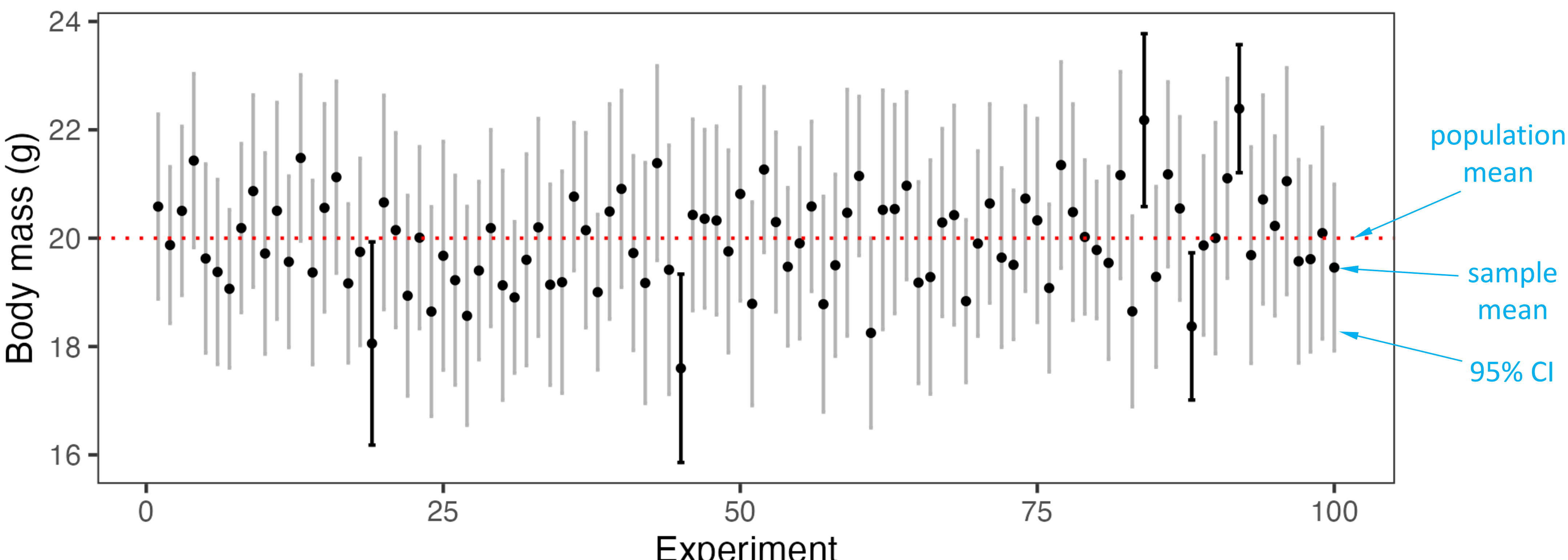
"95% of statistics is made up on the spot"

Anonymous

Reminder: 95% confidence interval

- There is a 95% probability that the random interval includes the true mean

- If you were to repeat the entire experiment many times
  - 95% of cases the true mean would be within the calculated interval
  - 5% of cases (1 in 20) it would be outside it (false result)



Confidence interval for count data

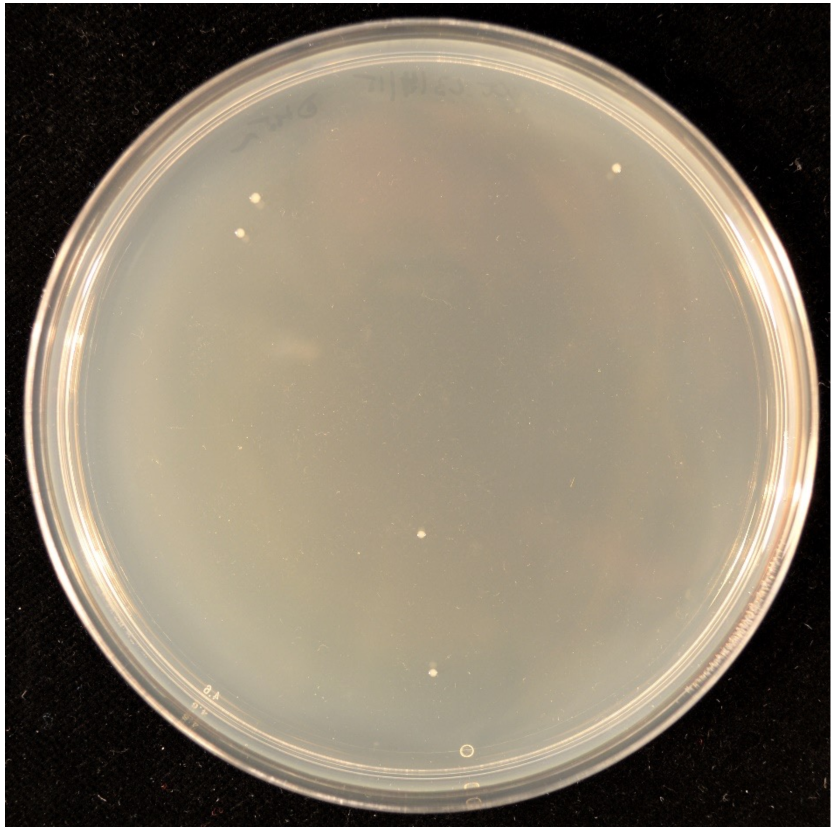
Confidence interval for count data

- Standard error of a count, C, is

  $SE = \sqrt{C}$

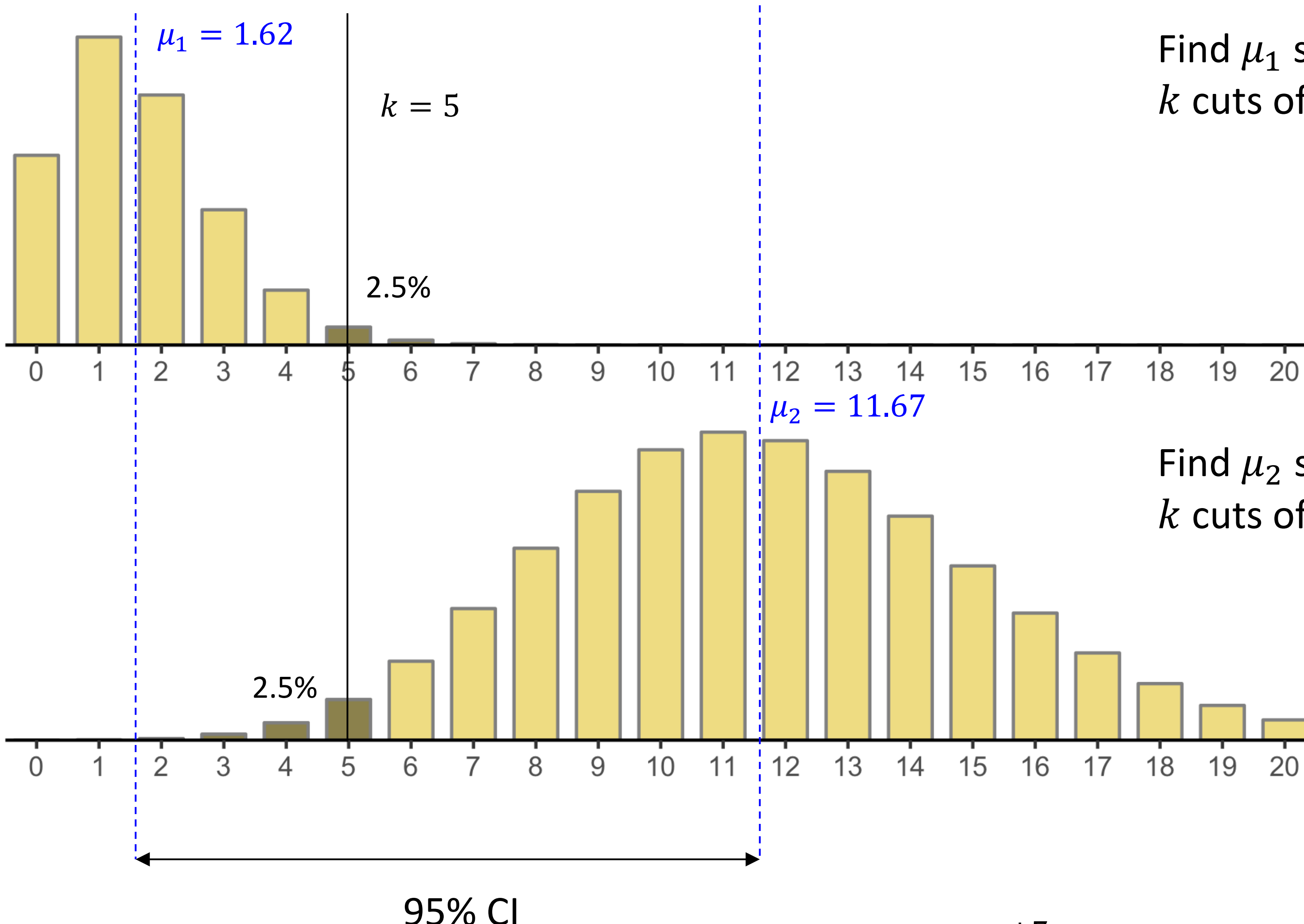
- For example, 5 ± 2 (after rounding up)

- How to find a confidence interval on μ?
- Exact method: a bit complicated



$C = 5 \pm 2$ (SE)

Confidence interval for count data: hand waving



Find μ_1 such that
k cuts off 2.5% at right

Find μ_2 such that
k cuts off 2.5% at left

$C = 5^{+7}_{-3}$ (95% CI)

Confidence interval for count data: exact method

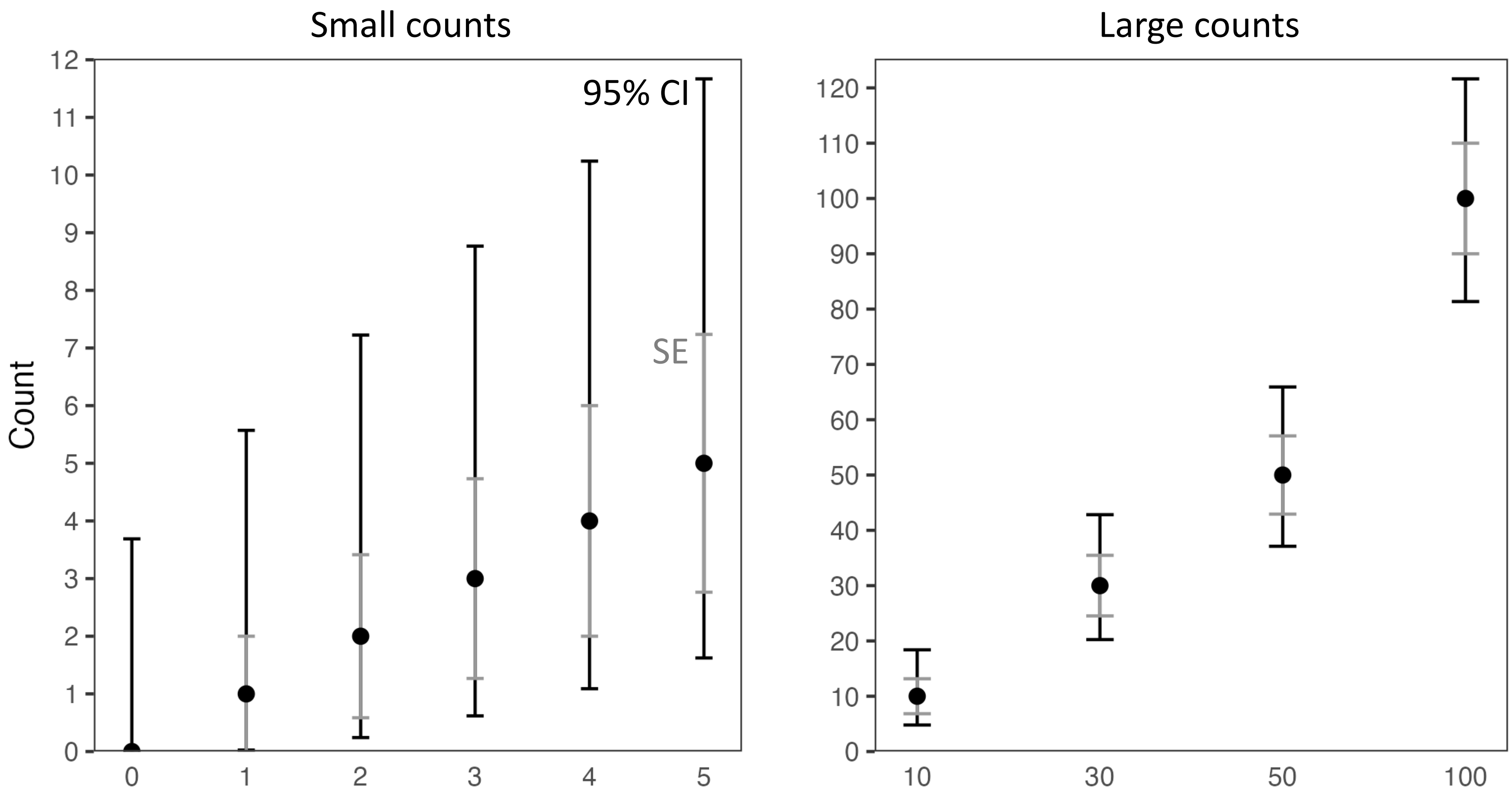
- Solving equations for Poisson cumulative distribution

```
> poisson.test(5, conf.level = 0.95)

        Exact Poisson test

data:  5 time base: 1
number of events = 5, time base = 1, p-value = 0.00366
alternative hypothesis: true event rate is not equal to 1
95 percent confidence interval:
  1.623486 11.668332
sample estimates:
event rate
         5
```

Count errors: example

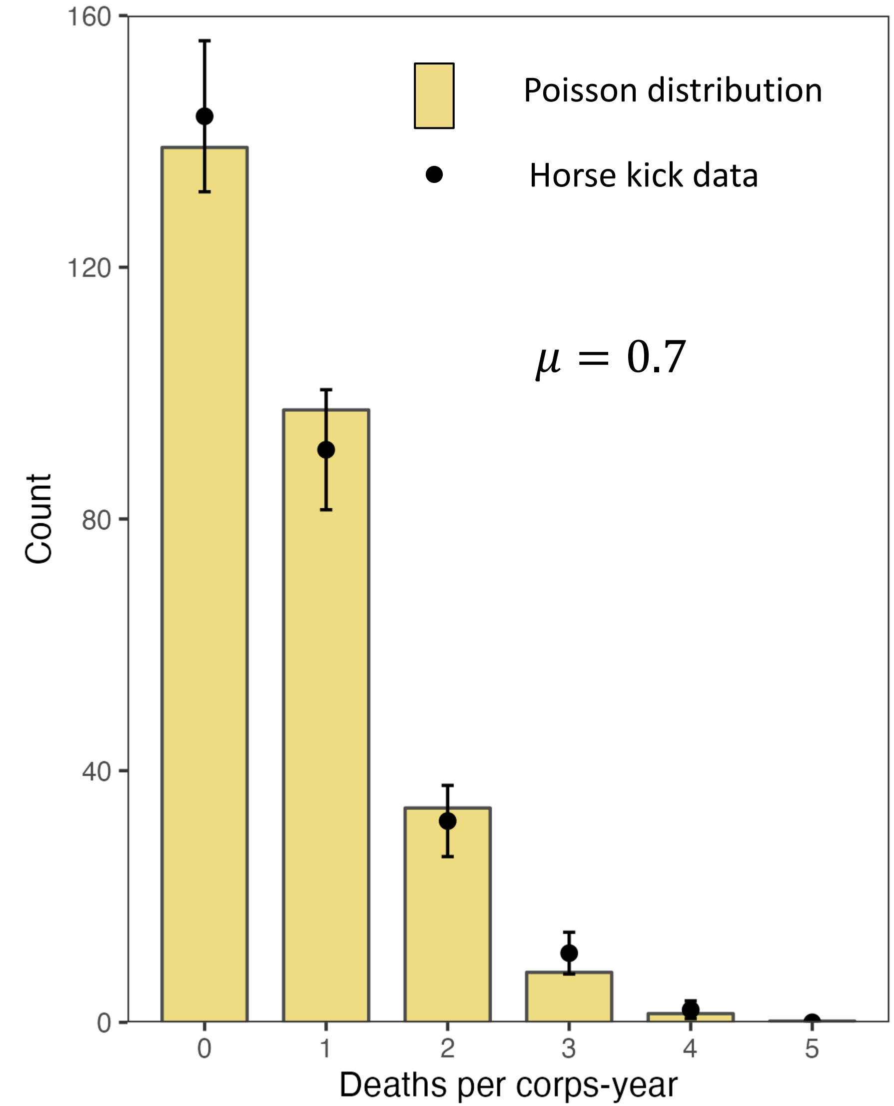


Confidence intervals for count data are not integer

- 95% CI for $C = 5$ is $[1.6, 11.8]$
- Shouldn't the confidence interval be exactly integer?

- Confidence interval is not for the sample count!
- We expect the *true mean* to be within $[1.6, 11.8]$ with a certain confidence

- The mean in a Poisson process is **not** integer
- Confidence intervals are for the true mean and are not integer



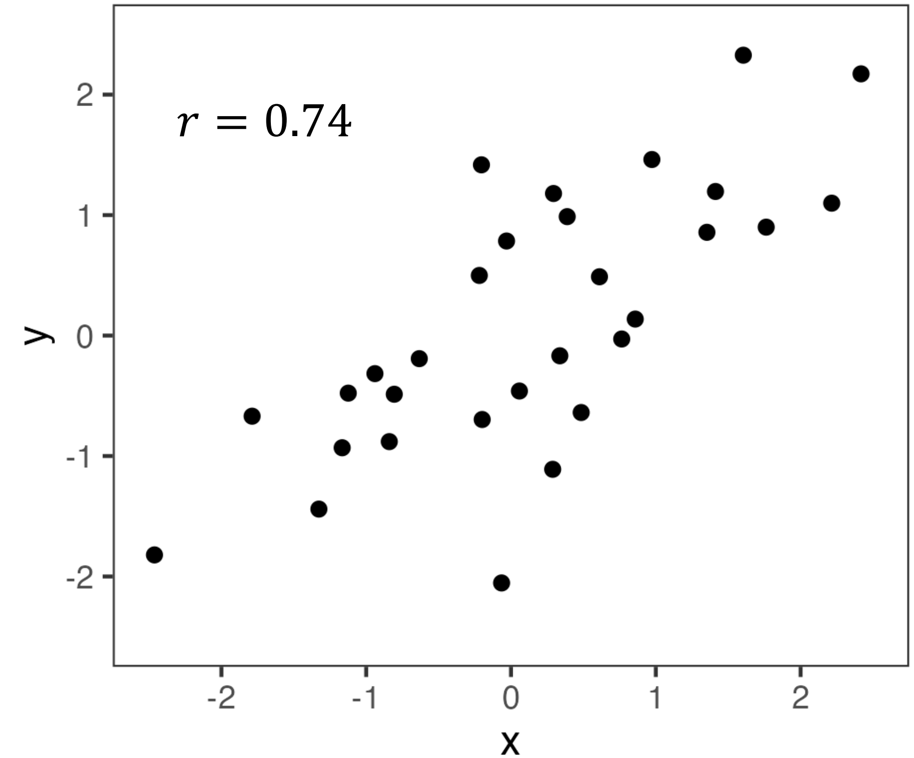
Confidence interval of the correlation coefficient

Confidence interval of the correlation coefficient

- Pearson's correlation coefficient r for a sample of pairs (x_i, y_i)

- It is not enough to say "we find $r = 0.82$, therefore our samples are correlated"

- Confidence limits on r **or** significance of correlation

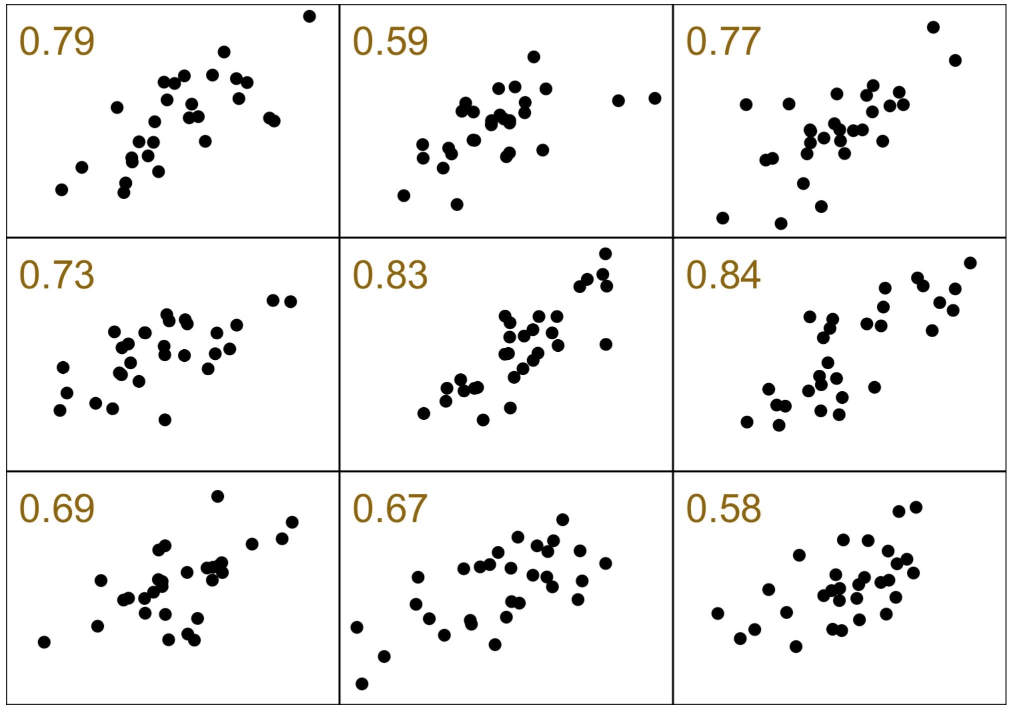


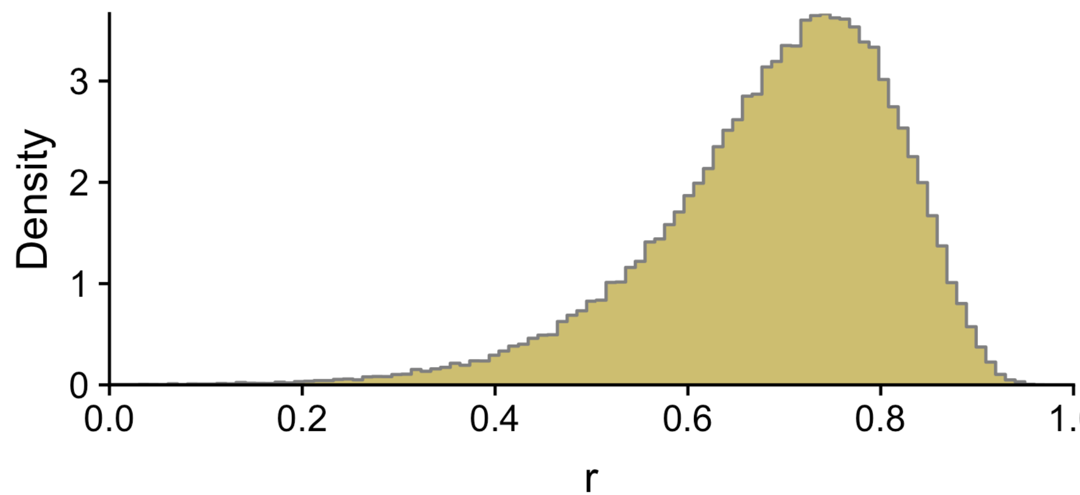
Sampling distribution of the correlation coefficient

- *Gedankenexperiment*
- Consider a population of pairs of numbers (x_i, y_i)
- The (unknown) population correlation coefficient, $\rho = 0.7$

- Draw lots of samples of pairs, size n
- Calculate the correlation coefficient for each sample

- Build a sampling distribution of the correlation coefficient





Sampling distribution of the correlation coefficient

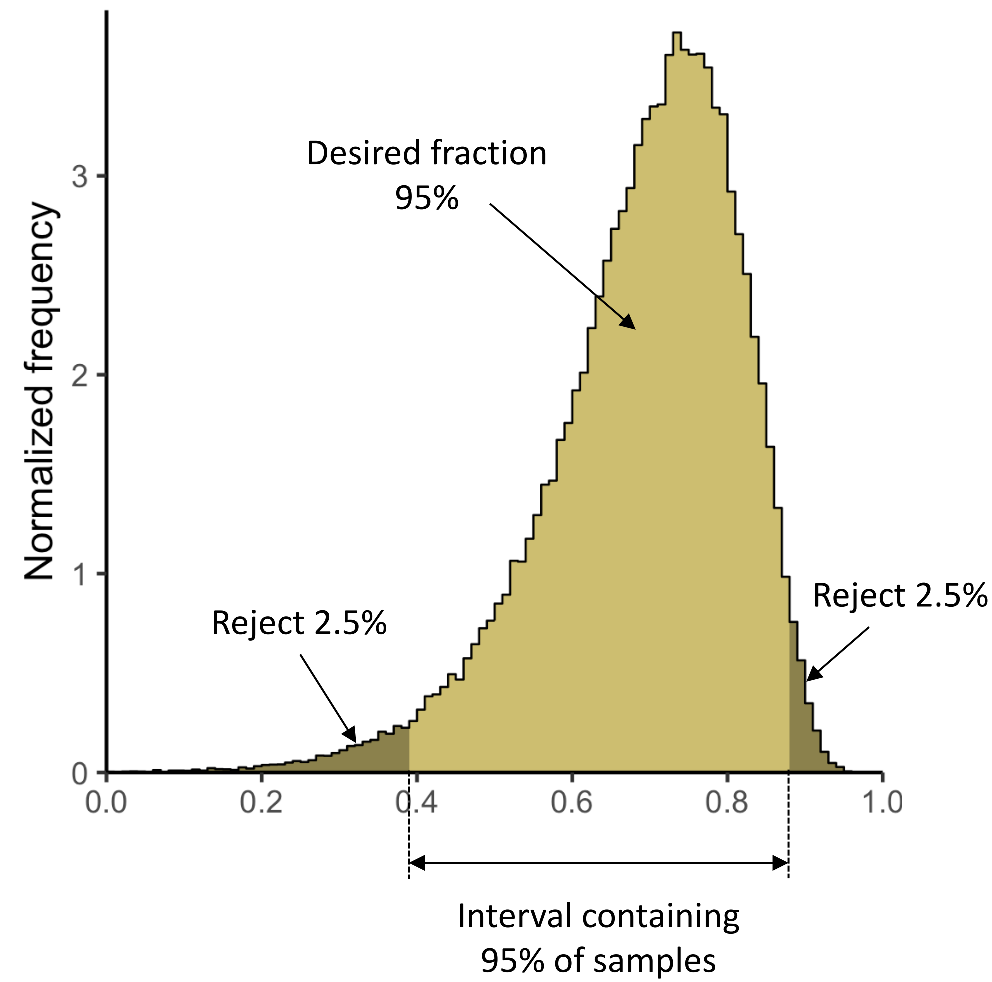
- Sampling distribution of r
- Unknown in analytical form

- Let us transform it into a known distribution

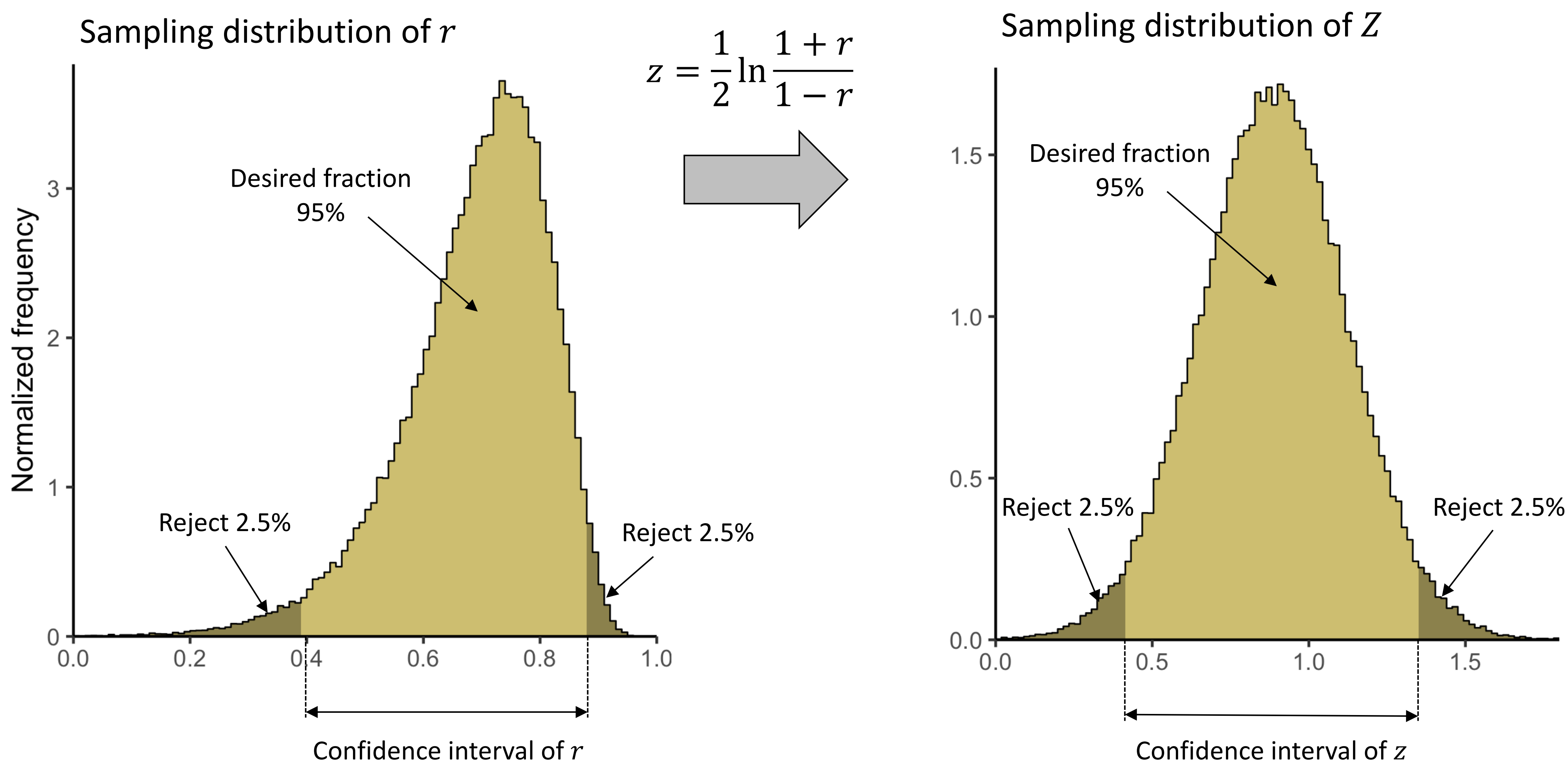
- Fisher's transformation:

$$z = \frac{1}{2} \ln \frac{1+r}{1-r}$$

- Build a sampling distribution of z



Confidence interval of the correlation coefficient



$$\mu = Z, \qquad \sigma = \frac{1}{\sqrt{n-3}}$$

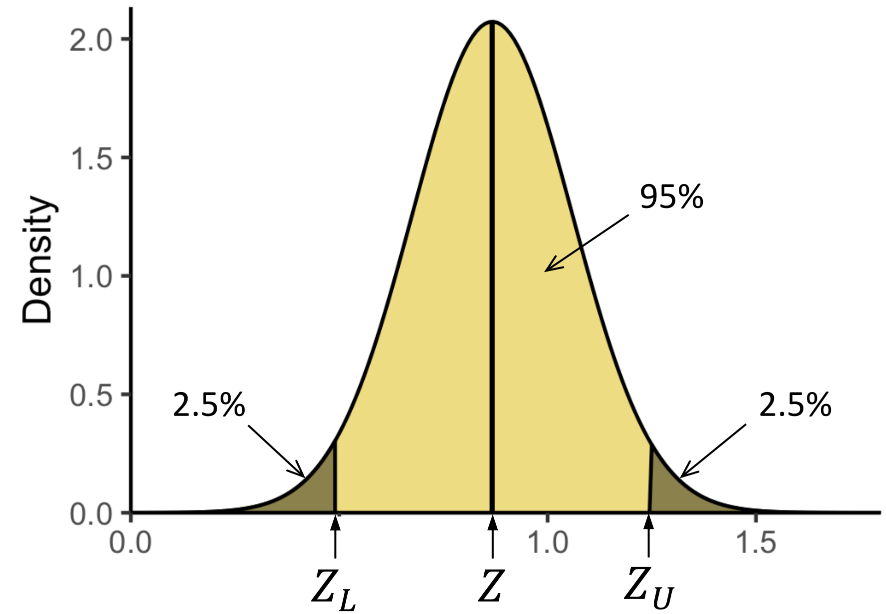
Example: 95% confidence limits on r

- $n = 30$ and $r = 0.7$
- First, find

$$Z = \frac{1}{2}\ln\frac{1+r}{1-r} = 0.867$$

$$\sigma = \frac{1}{\sqrt{n-3}} = 0.192$$

- Z is normally distributed
- 95% CI corresponds to $Z \pm 1.96\sigma$:
  - $Z_L = Z - 1.96\sigma = 0.490$
  - $Z_U = Z + 1.96\sigma = 1.24$



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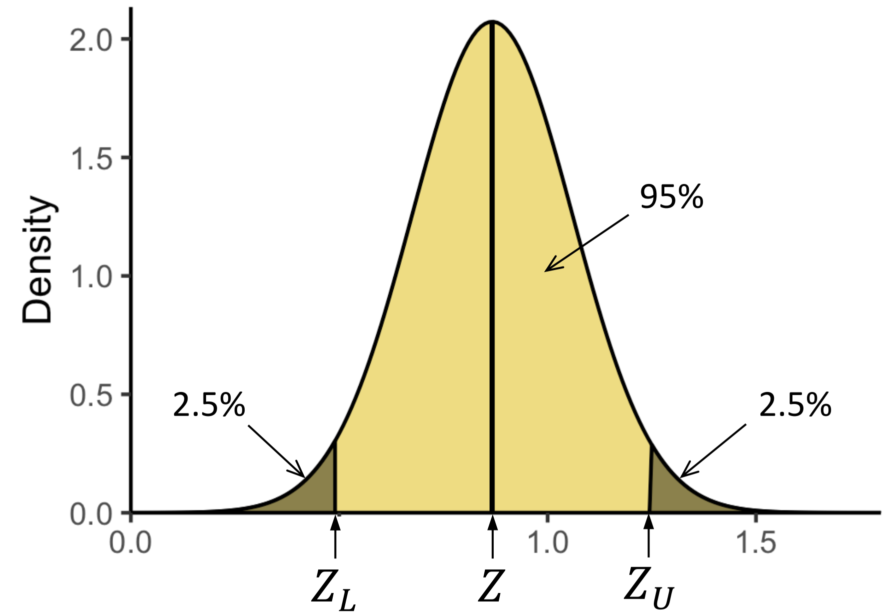
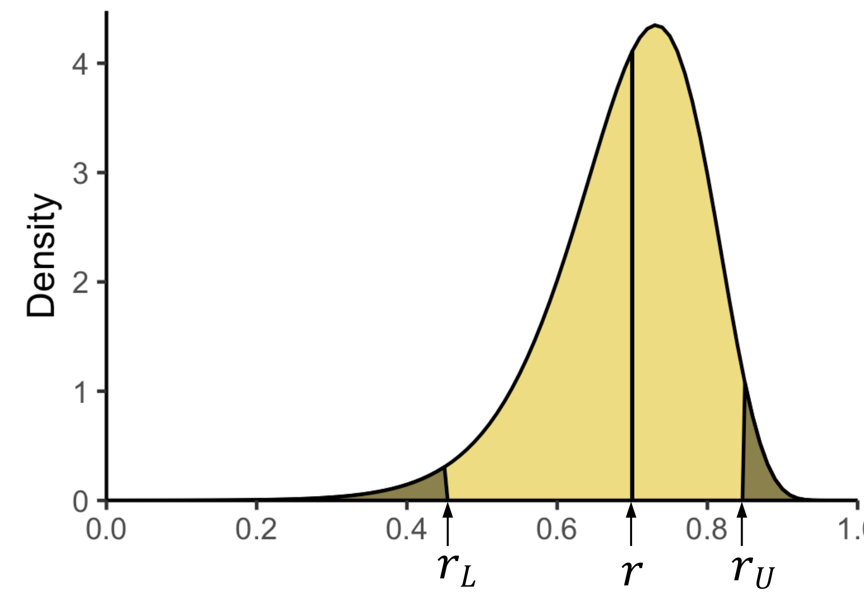
- Now we find the corresponding limits on r

$$r = \frac{e^{2Z} - 1}{e^{2Z} + 1}$$

  - $r_L = 0.454$
  - $r_U = 0.847$
- Hence, with 95% confidence, $r = 0.7^{+0.15}_{-0.25}$





How to do this in R

Need to know r and n

```
> r <- 0.7
> n <- 30
> Z <- 0.5 * log((1+r) / (1-r))
> Z
[1] 0.8673005
> sigma <- 1 / sqrt(n - 3)
> sigma
[1] 0.1924501
> Z95 <- qnorm(0.975)
> Z95
[1] 1.959964
> Z.limits <- c(Z - Z95 * sigma, Z + Z95 * sigma)
> Z.limits
[1] 0.4901053 1.2444958
> r.limits <- (exp(2*Z.limits) - 1) / (exp(2*Z.limits) + 1)
> r.limits
[1] 0.4543000 0.8467329
```

How to do this in R: the easy way

Need to know all data

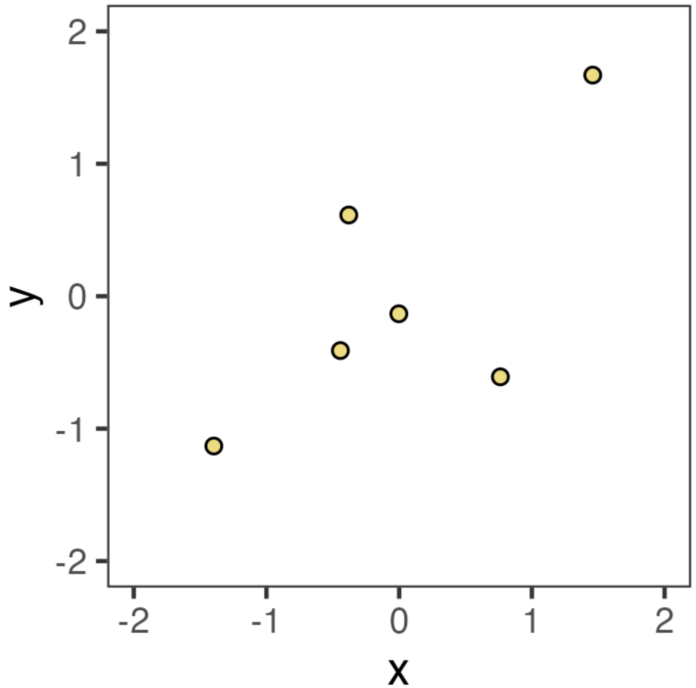
```
# generate random data (in reproducible way)
> set.seed(47)
> x <- 1:30
> y <- x + rnorm(30, 0, 7)
# correlation test to find CI
> cor.test(x, y)

        Pearson's product-moment correlation

data:  x and y
t = 5.1419, df = 28, p-value = 1.882e-05
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 0.4494788 0.8450094
sample estimates:
      cor
0.6968971
```

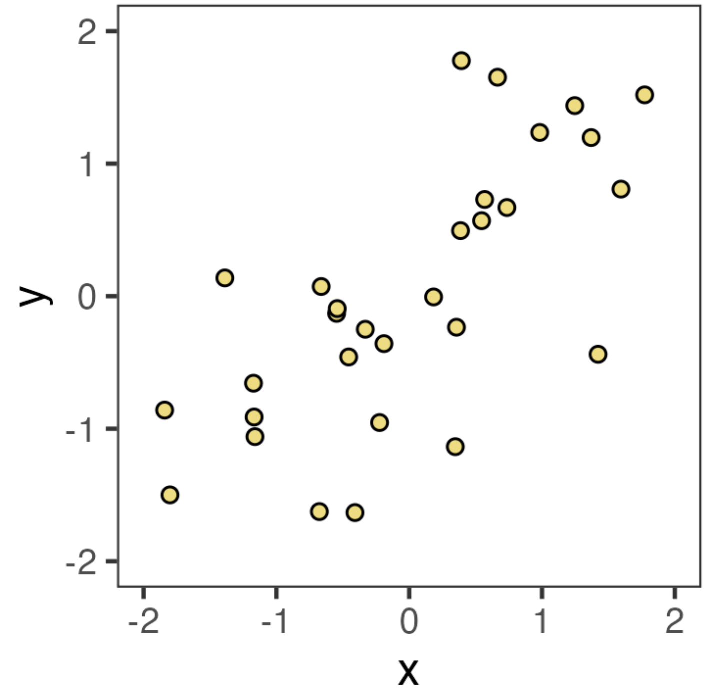
Example: 95% CI for correlation with $n = 6$ and $n = 30$

$$r = 0.7$$

$CI = [-0.26, 0.96]$
$p = 0.12$

$CI = [0.45, 0.85]$
$p = 2\times10^{-5}$





Confidence interval of a proportion

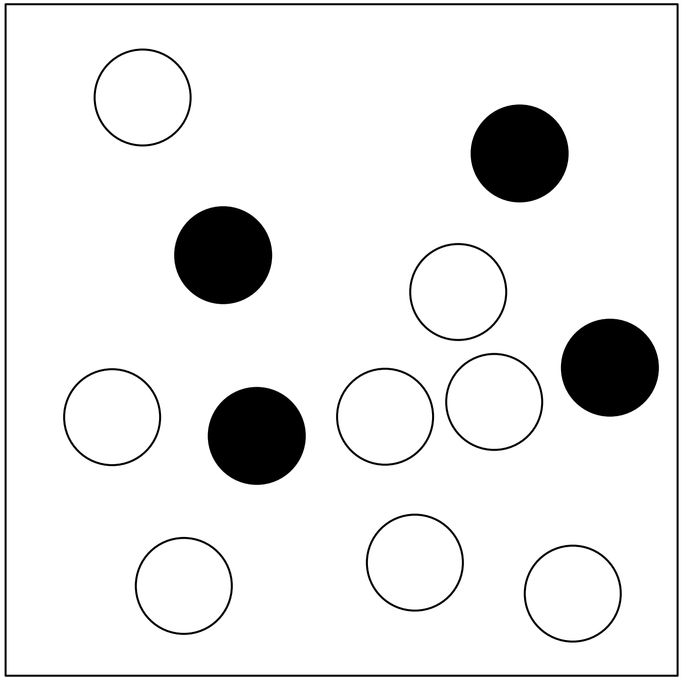
Confidence interval of a proportion

- Proportion:

$$\hat{p} = \frac{\hat{S}}{n} = \frac{\text{number of successes}}{\text{sample size}}$$

- Examples:
  - poll results
  - survival experiments
  - counting cells with a property

- Sample proportion, $\hat{p}$, is an estimator of the (unknown) population proportion, p



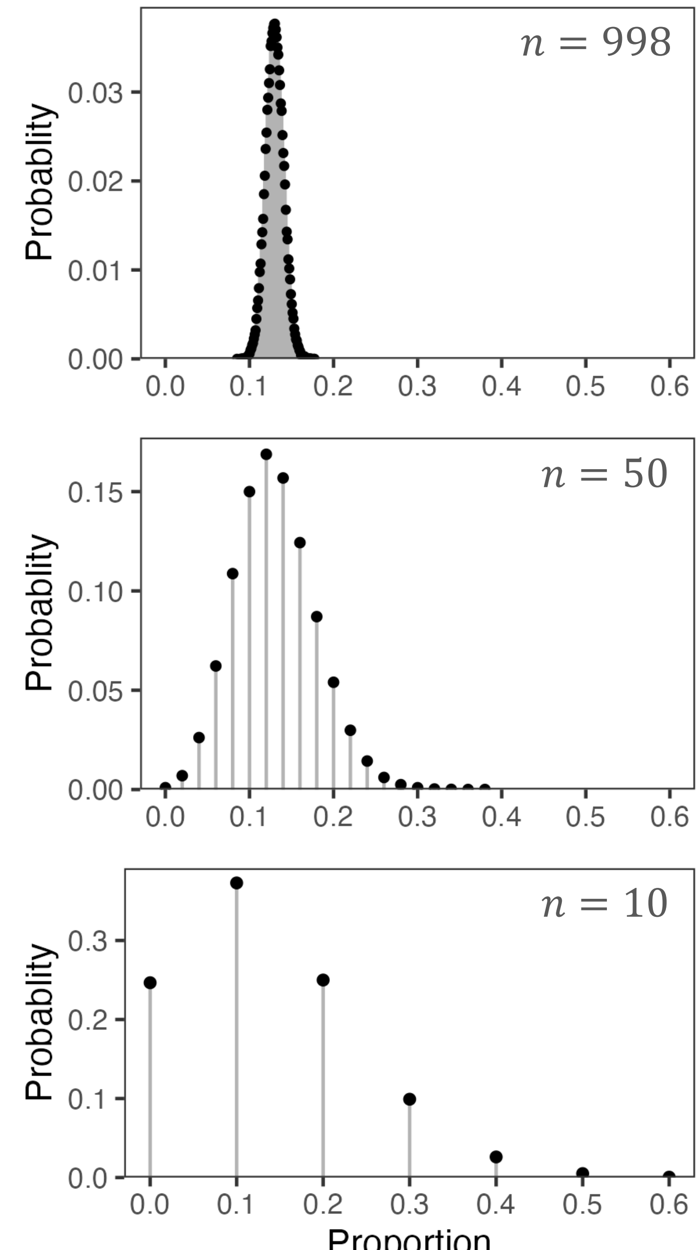
● $\hat{S} = 4$

○ + ● $n = 12$

$$\hat{p} = \frac{4}{12} = 0.33$$

Sampling distribution of a proportion

- *Gedankenexperiment*
- Population of mice where $p = 13\%$ are immune to a certain disease
- Draw a random sample of size n and find the proportion of immune mice, $\hat{p}$, in the sample
- Repeat 100,000 times and plot the distribution of $\hat{p}$
- What kind of distribution is it?
- Hint: every time you select a mouse, it can be either immune or not, with probability p or $1 - p$
- Binomial distribution
  - immune = "success", probability p
  - not immune = "failure", probability $1 - p$
- Good! Sampling distribution is known



Sampling distribution of a proportion: scaled binomial

Absolute numbers

- X – binomial random variable
- Mean and standard deviation

$$\mu = np$$

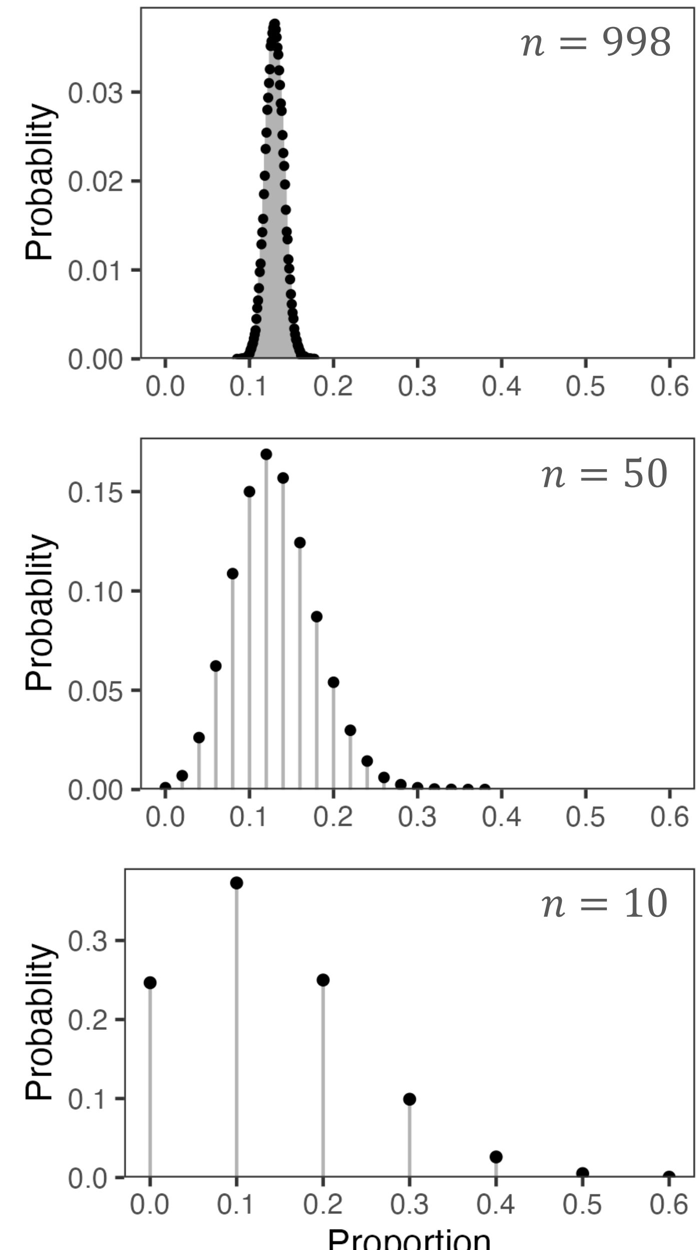
$$\sigma = \sqrt{np(1-p)}$$

Proportion

- $R = X/n$ – scaled binomial random variable
- Mean and standard deviation scaled by n:

$$\mu_R = p$$

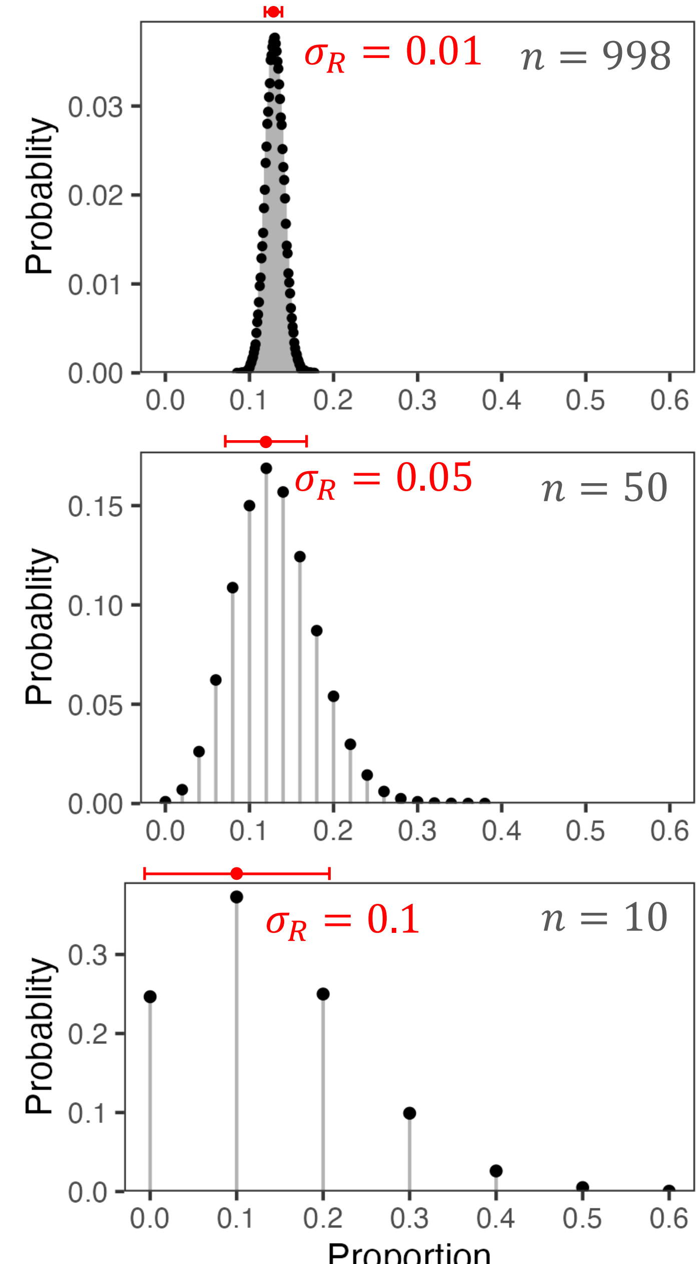
$$\sigma_R = \sqrt{\frac{p(1-p)}{n}}$$



Sampling distribution of a proportion

- Width of the sampling distribution of a proportion

$$\sigma_R = \sqrt{\frac{p(1-p)}{n}}$$



Reminder from lecture 2

Standard error of the mean

Hypothetical experiment

- 100,000 samples of 30 mice
- Build a distribution of sample means
- Width of this distribution is the true uncertainty of the mean

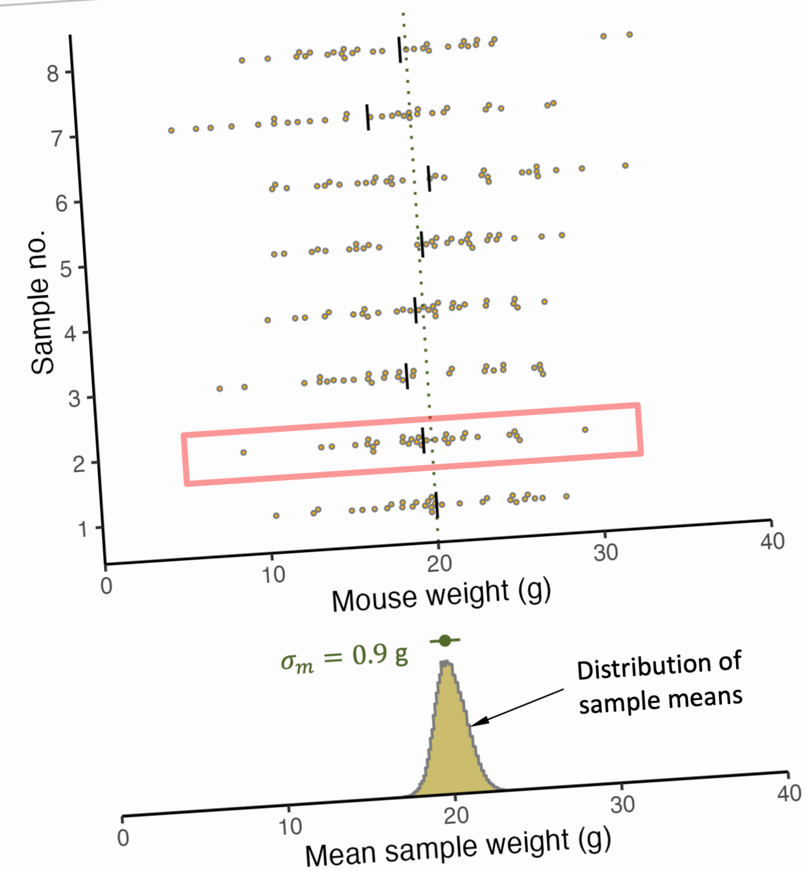
$$\sigma_m = \frac{\sigma}{\sqrt{n}} = 0.9 \text{ g}$$

Real experiment

- 30 mice
- Measure body mass:
  8.7, 13.4, ..., 29.2 g
- Find standard error

$$SE = \frac{SD}{\sqrt{n}} = 0.76 \text{ g}$$

***SE* is an approximation of σ_m**



Sampling distribution of a proportion

- Width of the sampling distribution of a proportion

$$\sigma_R = \sqrt{\frac{p(1-p)}{n}}$$

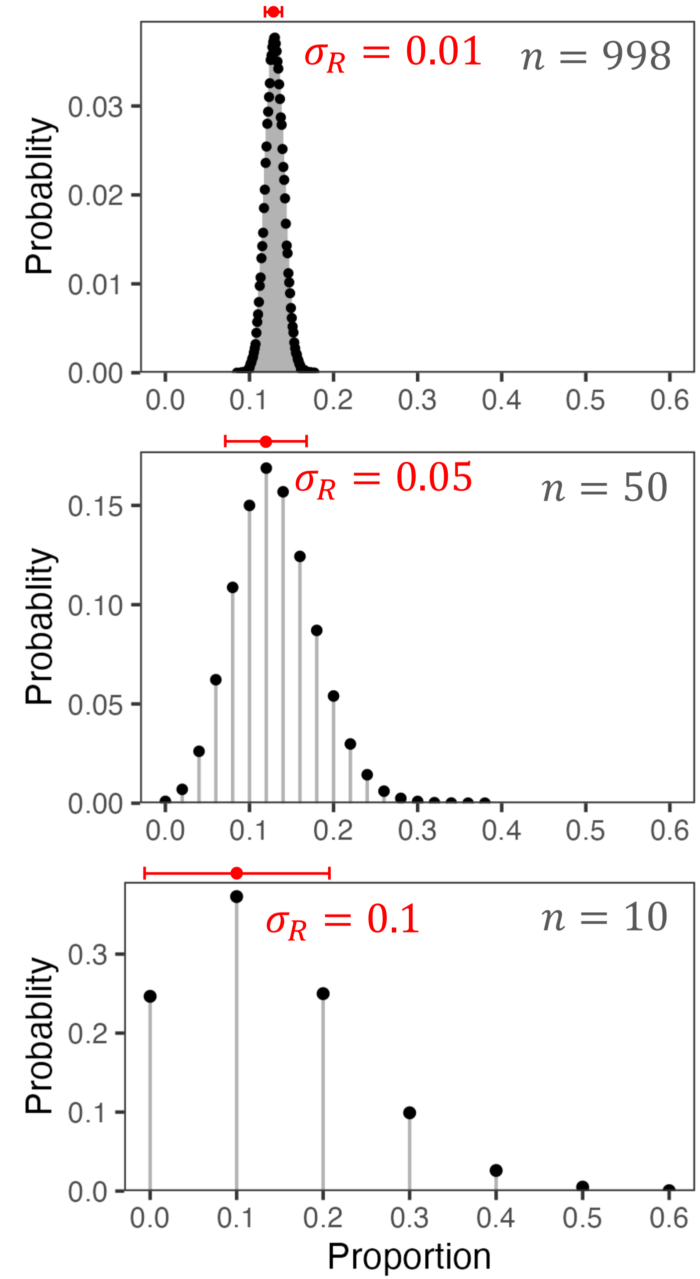
- Replace an unknown population parameter, p, with the observed estimator, $\hat{p}$

$$SE_R = \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

- Standard error of a proportion
- SE_R **estimates** the width of the sampling distribution

- Approximate 95% CI is $1.96 \times SE_R$

- However, this doesn't work for small n, or when proportion is close to 0 or 1



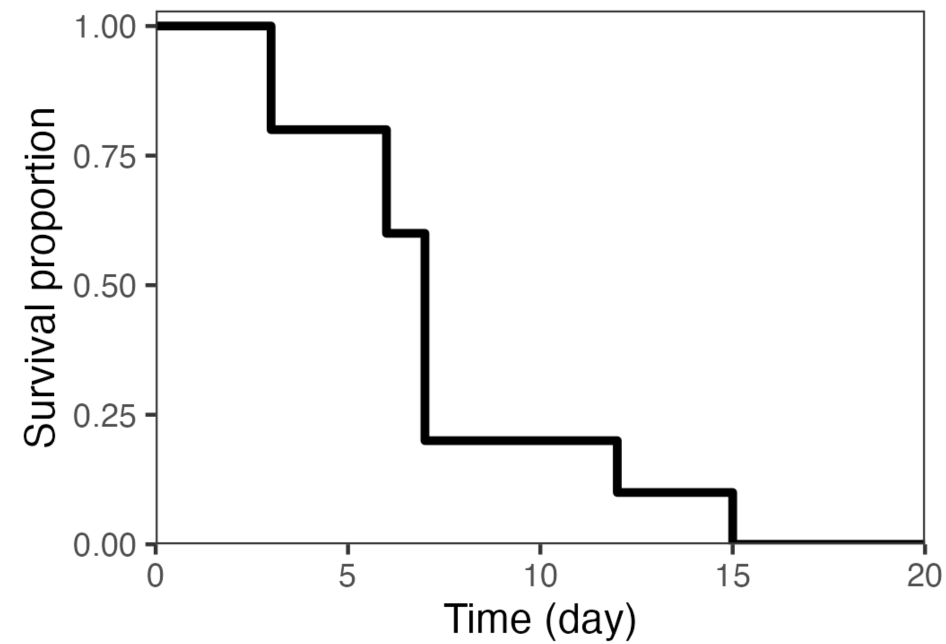
Example in R using prop.test

Method provided by Wilson (1927). The interval is asymmetric.

```
> prop.test(1, 10)

        1-sample proportions test with continuity correction

data:  1 out of 10, null probability 0.5
X-squared = 4.9, df = 1, p-value = 0.02686
alternative hypothesis: true p is not equal to 0.5
95 percent confidence interval:
 0.005242302 0.458846016
sample estimates:
  p
0.1
```

Confidence intervals of a proportion

- Consider survival experiment
  - take 10 mice
  - infect with something nasty
  - apply treatment
  - count survival proportion over time
- We need errors of proportion!

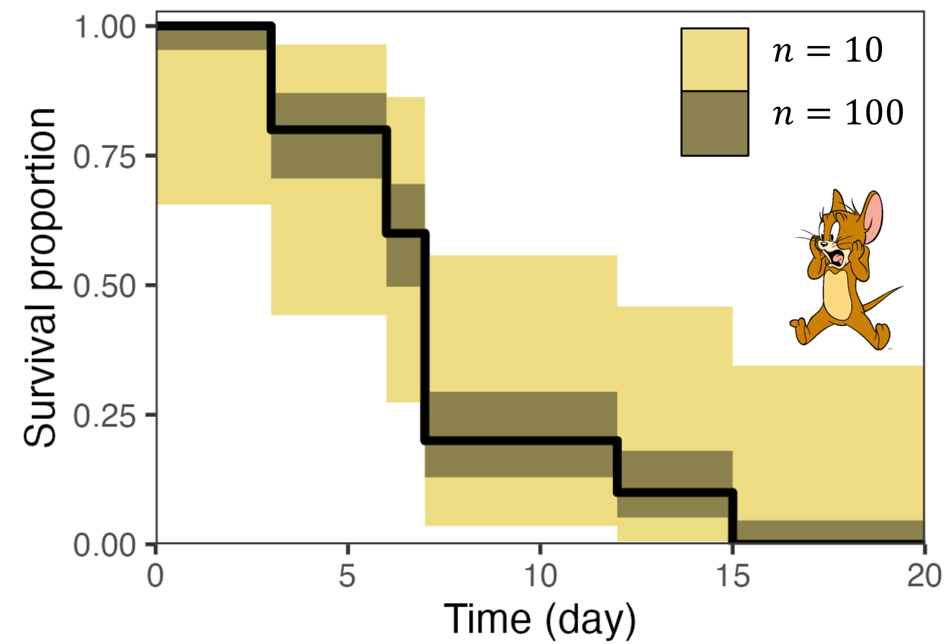


Confidence intervals of a proportion

- Consider survival experiment
  - take 10 mice
  - infect with something nasty
  - apply treatment
  - count survival proportion over time

- 95% CIs
- The bigger sample, the smaller error

- Even when $\hat{p} = 0$, error allows for non-zero proportion
- We have zombie mice!



Beware of small samples!

- When you count things, small samples are not very good
- Consider a small number $n = 10$

	Count $C = 10$	Correlation $r = 0.73$	Proportion $\hat{S} = 3$
95% CI	$[4.8, 18.4]$	$[0.19, 0.93]$	$[0.10, 0.61]$
Half CI as a fraction of the value	68%	51%	71%

- When you do counts, you need $n > 30$

Small and large numbers

	Count, proportion, correlation		Mean, median
Number	Small	Large	Any
Observed variability	Counting statistics	Biology	Biology
Example	5 mice out of 12	120 cells out of 860	Sample of 5
What to use	Low-count statistics	Replicates	Replicates

Bootstrapping

Bootstrapping

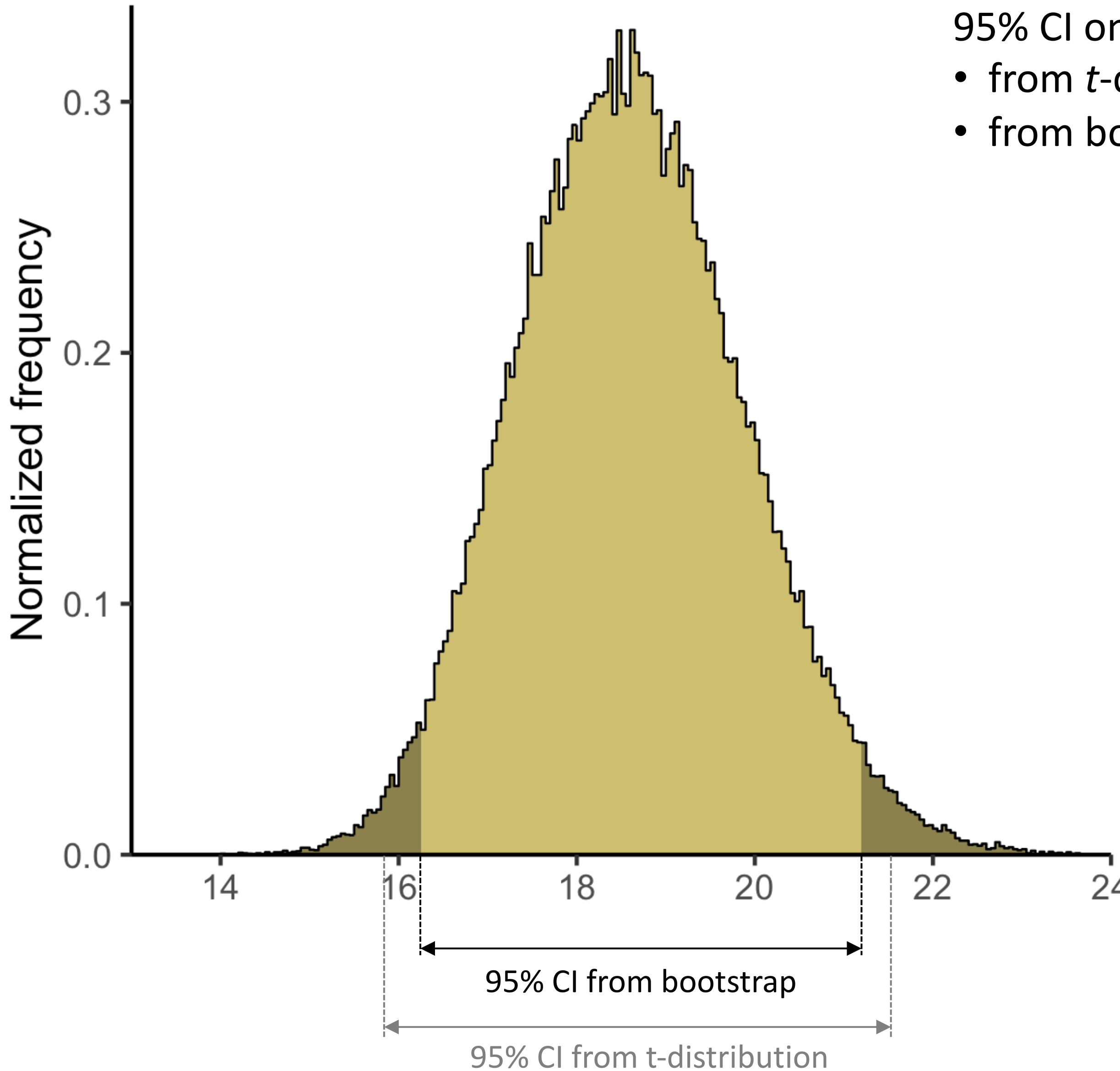
- Versatile technique used when
  - distribution of the estimator is complicated or unknown
  - for power calculations
- Approximate sampling distribution from one sample only
- Use random resampling *with replacement*

19.4	18.2	11.5	17.2	25.7	19.2	21.5	16.7	15.6	27.7	14.3	16.3	$M = 18.6$	original sample
27.7	18.2	18.2	25.7	11.5	17.2	17.2	25.7	21.5	11.5	14.3	17.2	$M = 18.8$	
19.2	14.3	19.2	15.6	14.3	14.3	17.2	16.3	19.2	19.2	16.3	21.5	$M = 17.2$	
14.3	17.2	18.2	18.2	18.2	11.5	14.3	18.2	17.2	19.4	11.5	16.3	$M = 16.2$	resamples
25.7	18.2	15.6	15.6	19.4	19.2	18.2	19.4	21.5	16.7	14.3	18.2	$M = 18.5$	
19.2	21.5	16.7	17.2	21.5	18.2	21.5	17.2	21.5	15.6	21.5	21.5	$M = 19.4$	

…

- Repeat this many times (e.g. 10^5) and collect all means
- Build the bootstrap distribution of the mean

Bootstrapping



95% CI on the population mean

- from *t*-distribution [15.7, 21.5]
- from bootstrapping [16.3, 21.2]

This is not a sampling distribution, it only approximates it

Confidence intervals in R

Most statistical *test* functions in R provide with confidence intervals.

Quantity	R function
Mean	`t.test`
Median	`wilcox.test`
Count	`poisson.test`
Correlation	`cor.test`
Proportion	`prop.test`

How to extract CI limits in R

```
> prop.test(12, 87)

        1-sample proportions test with continuity correction

data:  12 out of 87, null probability 0.5
X-squared = 44.184, df = 1, p-value = 2.989e-11
alternative hypothesis: true p is not equal to 0.5
95 percent confidence interval:
 0.07637419 0.23243382
sample estimates:
       p
0.137931

# store test result in a variable
> p <- prop.test(12, 87)
# extract confidence intervals from object p
> ci <- p$conf.int
# ci is a vector of two elements: lower and upper CI limit
> ci[1]
[1] 0.07637419
> ci[2]
[1] 0.2324338
```

Slides available at
https://dag.compbio.dundee.ac.uk/training/Statistics_lectures.html