

I CAN'T BELIEVE SCHOOLS
ARE STILL TEACHING KIDS
ABOUT THE NULL HYPOTHESIS.

|

I REMEMBER READING A BIG
STUDY THAT CONCLUSIVELY
DISPROVED IT YEARS AGO.



Lecture 07

10.14.21

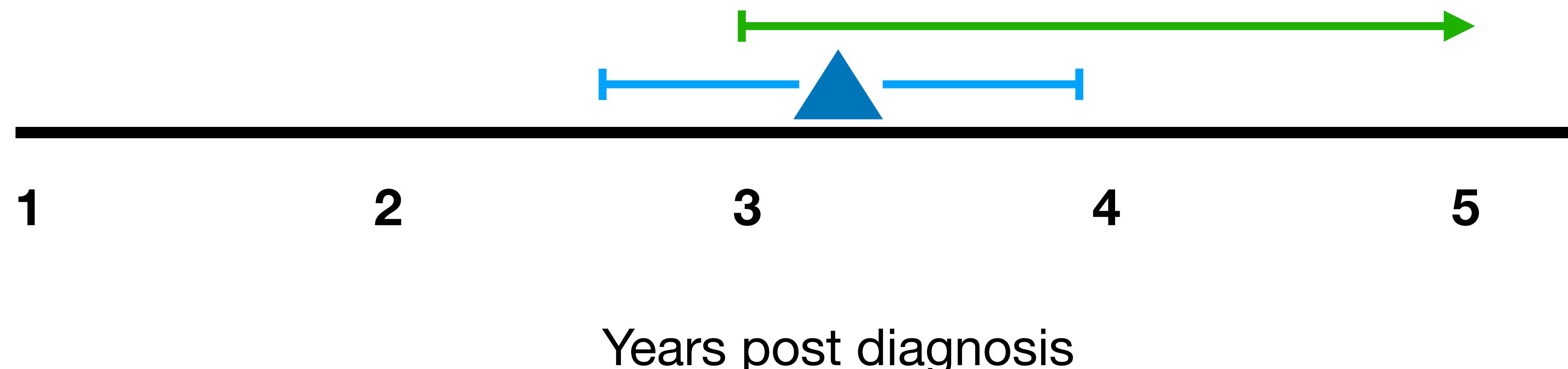
<u>P-VALUE</u>	<u>INTERPRETATION</u>
0.001	HIGHLY SIGNIFICANT
0.01	
0.02	
0.03	
0.04	SIGNIFICANT
0.049	
0.050	OH CRAP. REDO CALCULATIONS.
0.051	
0.06	ON THE EDGE OF SIGNIFICANCE
0.07	HIGHLY SUGGESTIVE, SIGNIFICANT AT THE P<0.10 LEVEL
0.08	
0.09	
0.099	
≥0.1	HEY, LOOK AT THIS INTERESTING SUBGROUP ANALYSIS

Refresher Quiz

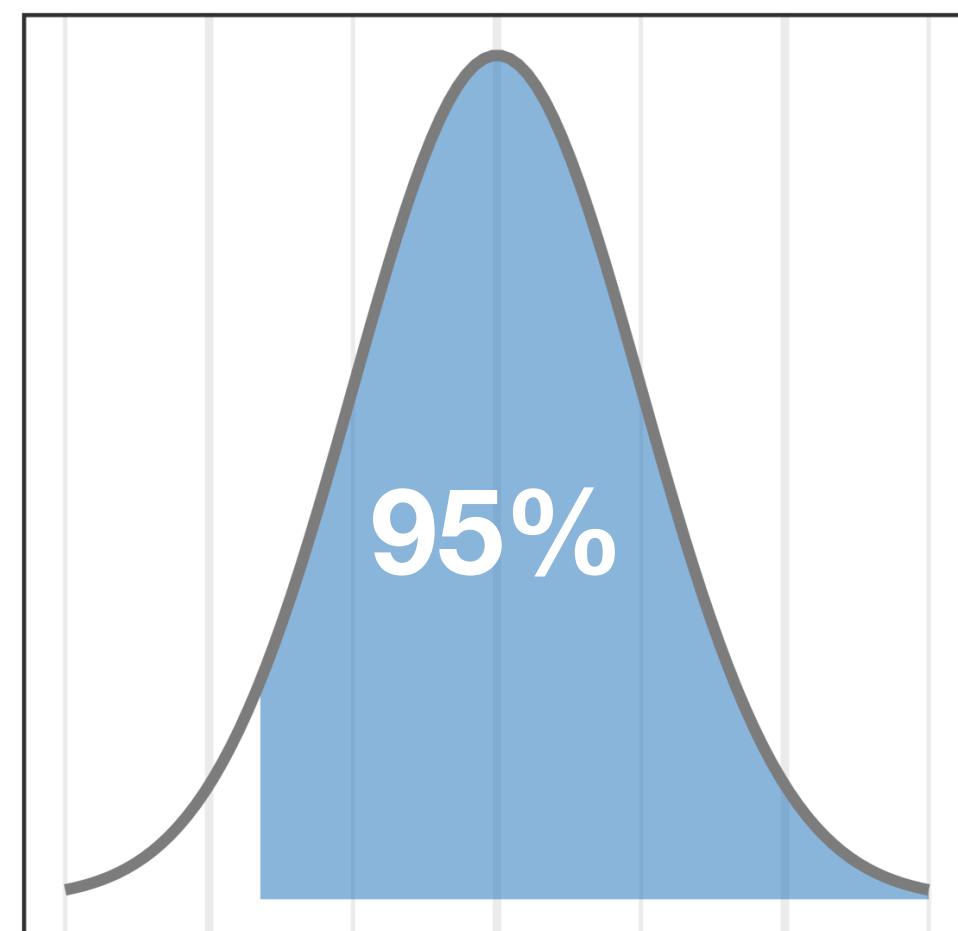
A drug manufacturer would like to make a claim that, on average, their drug improves lifespan of people with cancer by *at least* some length of time. (No one will complain if they survive longer). In a clinical trial, 67 individuals survived an average of 3.2 years after initial diagnosis (with a standard deviation of 1.3 years). Give a 95% confidence lower bound for the mean survival time with this drug.

A drug manufacturer would like to make a claim that, on average, their drug improves lifespan of people with cancer by ***at least some length of time.*** (No one will complain if they survive longer). In a clinical trial, 67 individuals survived an average of 3.2 years after initial diagnosis (with a standard deviation of 1.3 years). Give a 95% confidence lower bound for the mean survival time with this drug.

One-sided confidence interval with a lower bound (upper bound = infinity)



A drug manufacturer would like to make a claim that, on average, their drug improves lifespan of people with cancer by ***at least some length of time***. (No one will complain if they survive longer). In a clinical trial, 67 individuals survived an average of 3.2 years after initial diagnosis (with a standard deviation of 1.3 years). Give a 95% confidence lower bound for the mean survival time with this drug.



\bar{y}

$$\begin{aligned} & (\bar{y} - t_{0.05} \frac{s}{\sqrt{n}}, \infty) \\ & (3.2 - 1.66 \frac{1.3}{\sqrt{67}}, \infty) \\ & (2.935, \infty) \end{aligned}$$

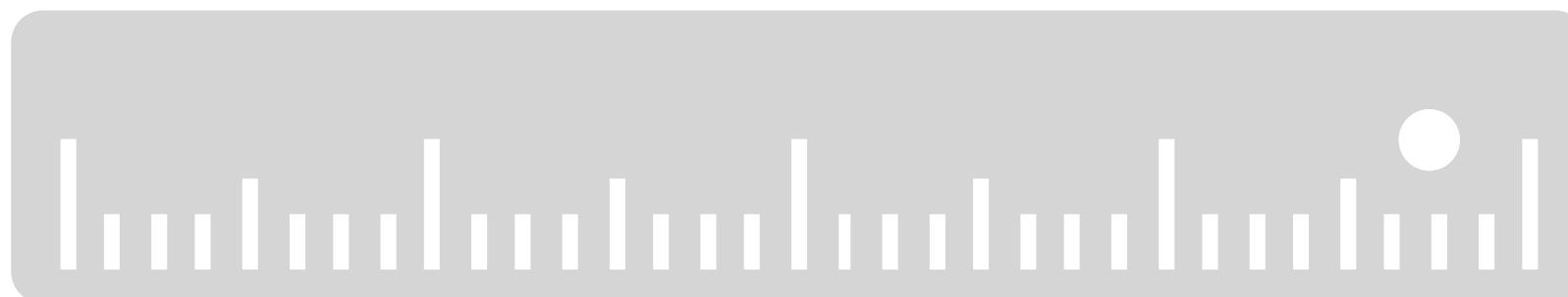
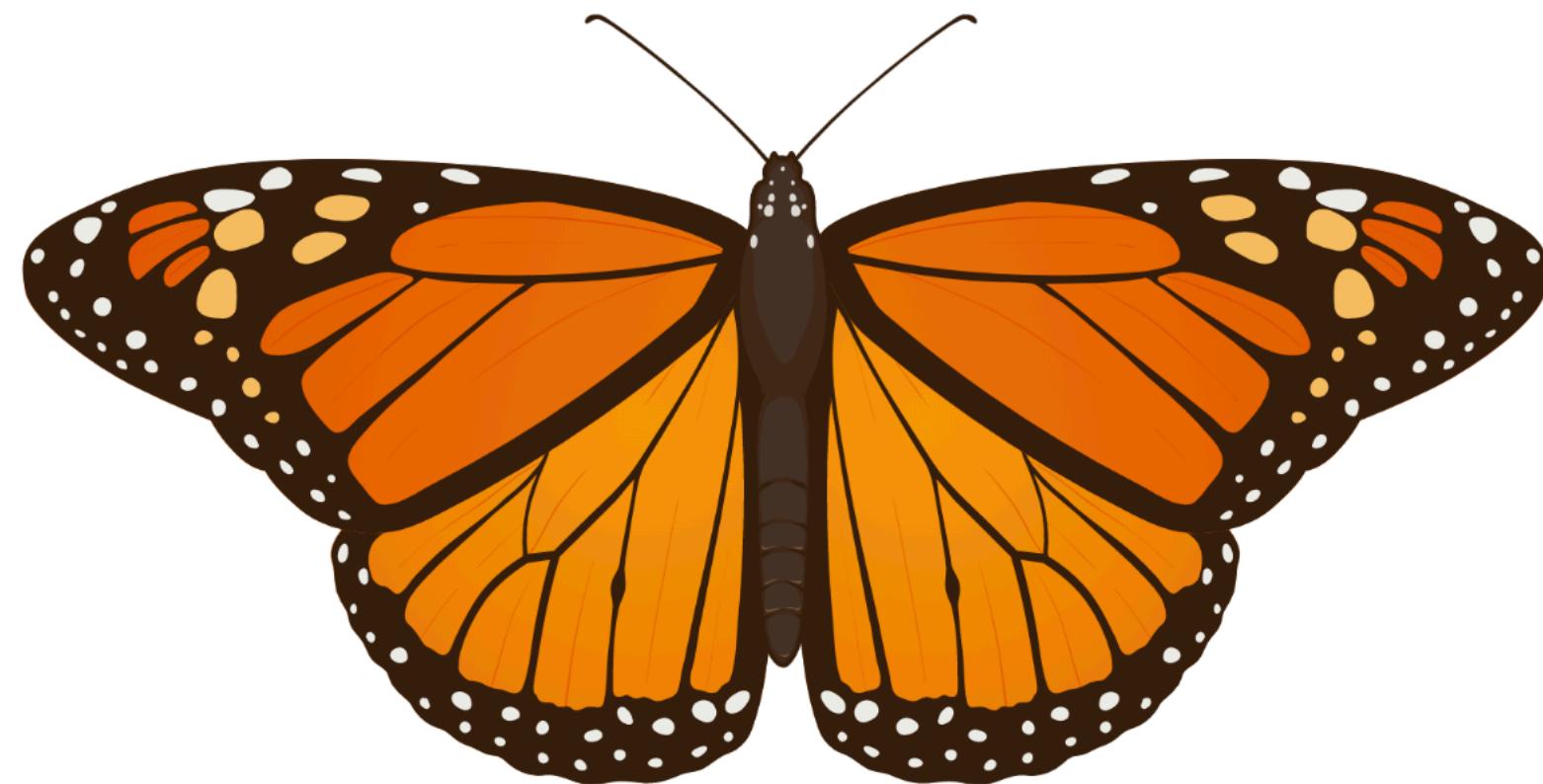
$> qt(0.95, 66)$

(Or we could use a table, but maybe not for $n = 67$)*

↑

In a pinch, a normal distribution could estimate this value because n is large ($qnorm(0.05)$)

Calculating the confidence interval



`qt(t, df)`

`qt(0.975, 13)`

$$n = 14$$

$$df = 13$$

$$\bar{y} = 32.81 \text{ cm}^2$$

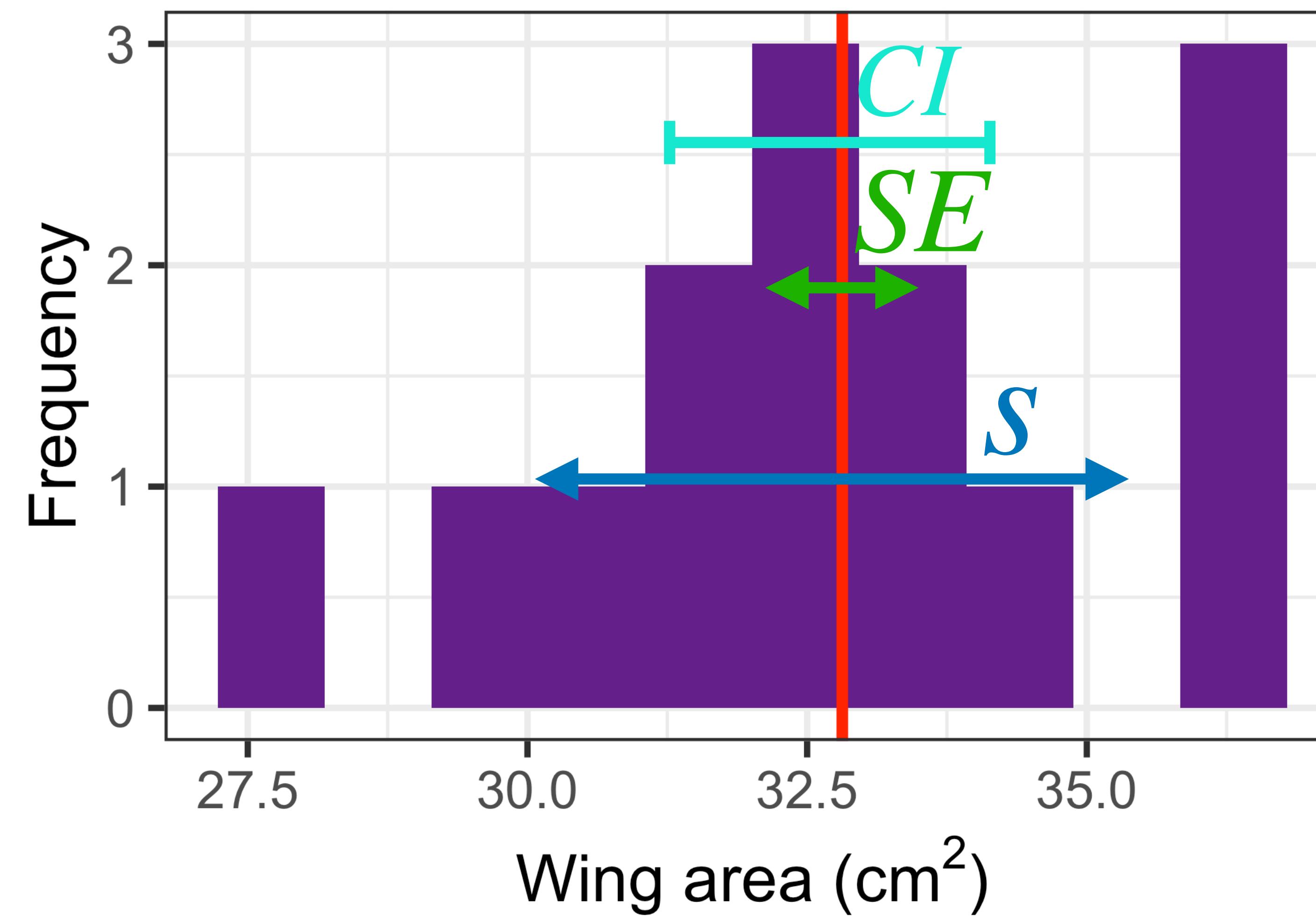
$$s = 2.48 \text{ cm}^2$$

$$\bar{y} \pm t_{0.025} \frac{s}{\sqrt{n}}$$

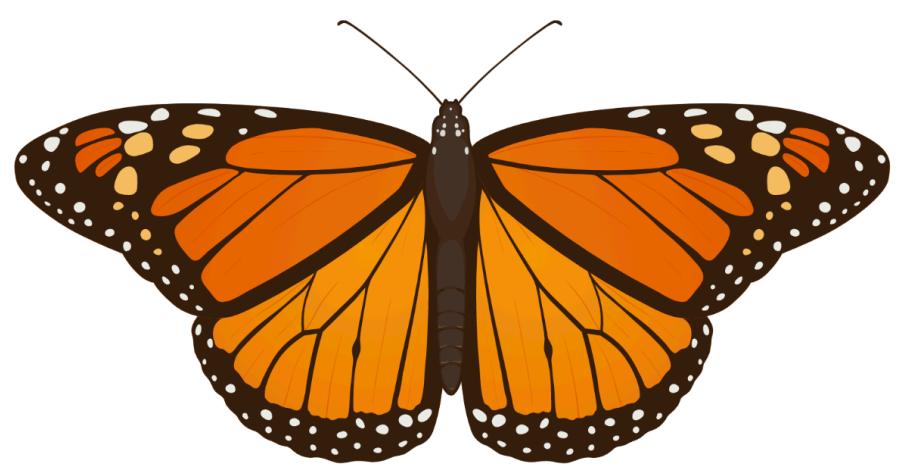
$$32.81 \pm 2.16 \frac{2.48}{\sqrt{14}}$$

$$32.81 \pm 1.43$$

Calculating the confidence interval



An introduction to hypothesis testing



The null hypothesis:

$$H_0 : \bar{y} = \mu$$

$$\begin{aligned}\bar{y} &= 32.81\text{cm}^2 \\ \mu &= 30\text{cm}^2\end{aligned}$$

The alternative hypothesis:

$$H_A : \bar{y} \neq \mu$$

An introduction to hypothesis testing

The null hypothesis:

$$H_0 : \bar{y} = \mu \longrightarrow H_0 : \underline{\bar{y} - \mu} = 0$$

The alternative hypothesis:

$$H_A : \bar{y} \neq \mu \longrightarrow H_A : \underline{\bar{y} - \mu} \neq 0$$

How do we choose between these two hypotheses?

The t statistic for hypothesis testing

The t test is a standard method of choosing between these hypotheses

$$H_0 : \bar{y} = \mu$$

$$H_A : \bar{y} \neq \mu$$

t is in units of SE

Test statistic:

$$t_s = \frac{\bar{y} - \mu}{SE_{\bar{Y}}}$$

Variation in differences of
means from random samples

How far the difference
between the two means
are from 0 (null hypothesis)

The t statistic for hypothesis testing



$$H_0 : \bar{y} = \mu$$

$$H_A : \bar{y} \neq \mu$$

$$\bar{y} = 32.81 \text{ cm}^2$$

$$s = 2.48 \text{ cm}^2$$

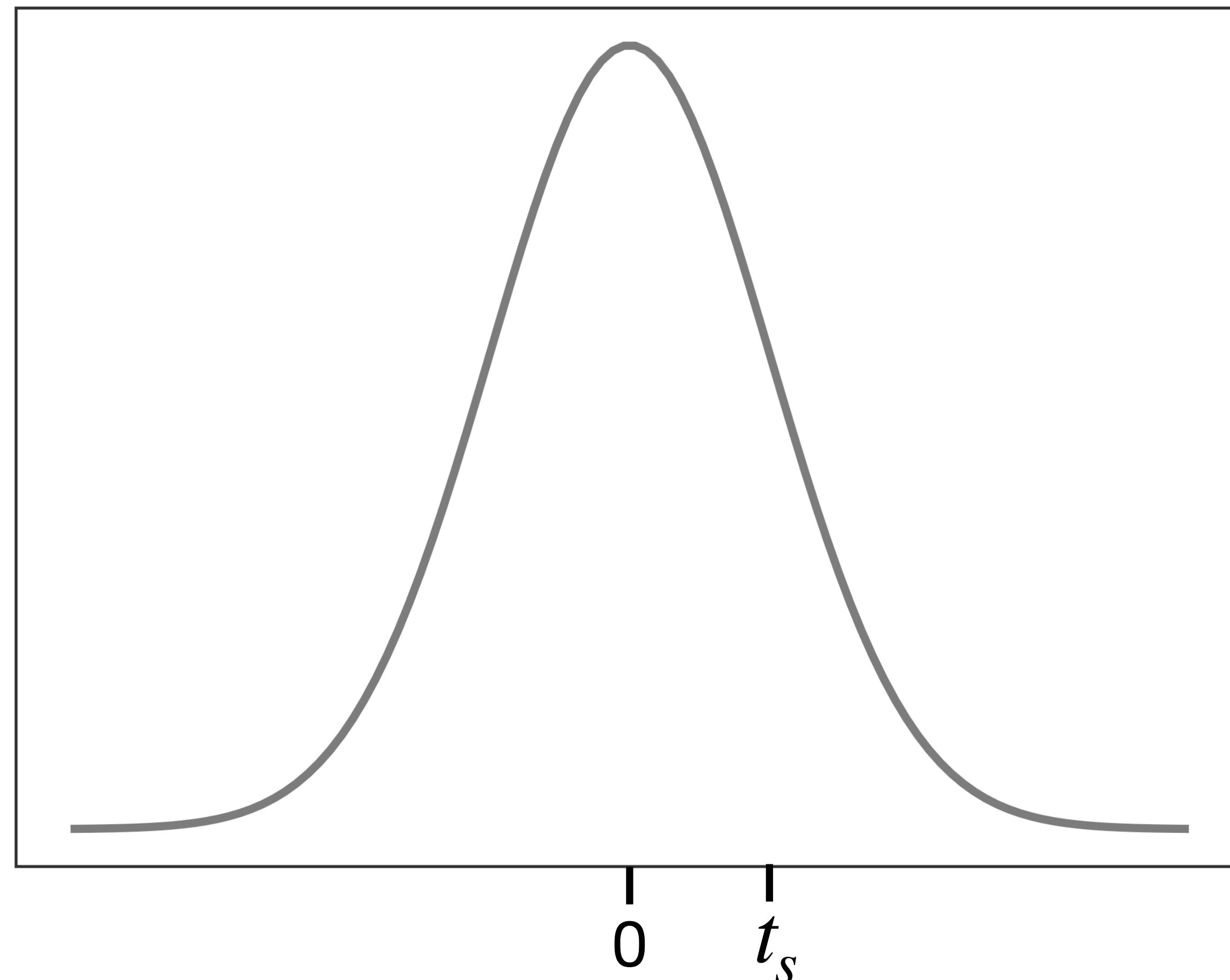
$$\mu = 30 \text{ cm}^2$$

$$t_s = \frac{\bar{y} - \mu}{SE_{\bar{Y}}}$$

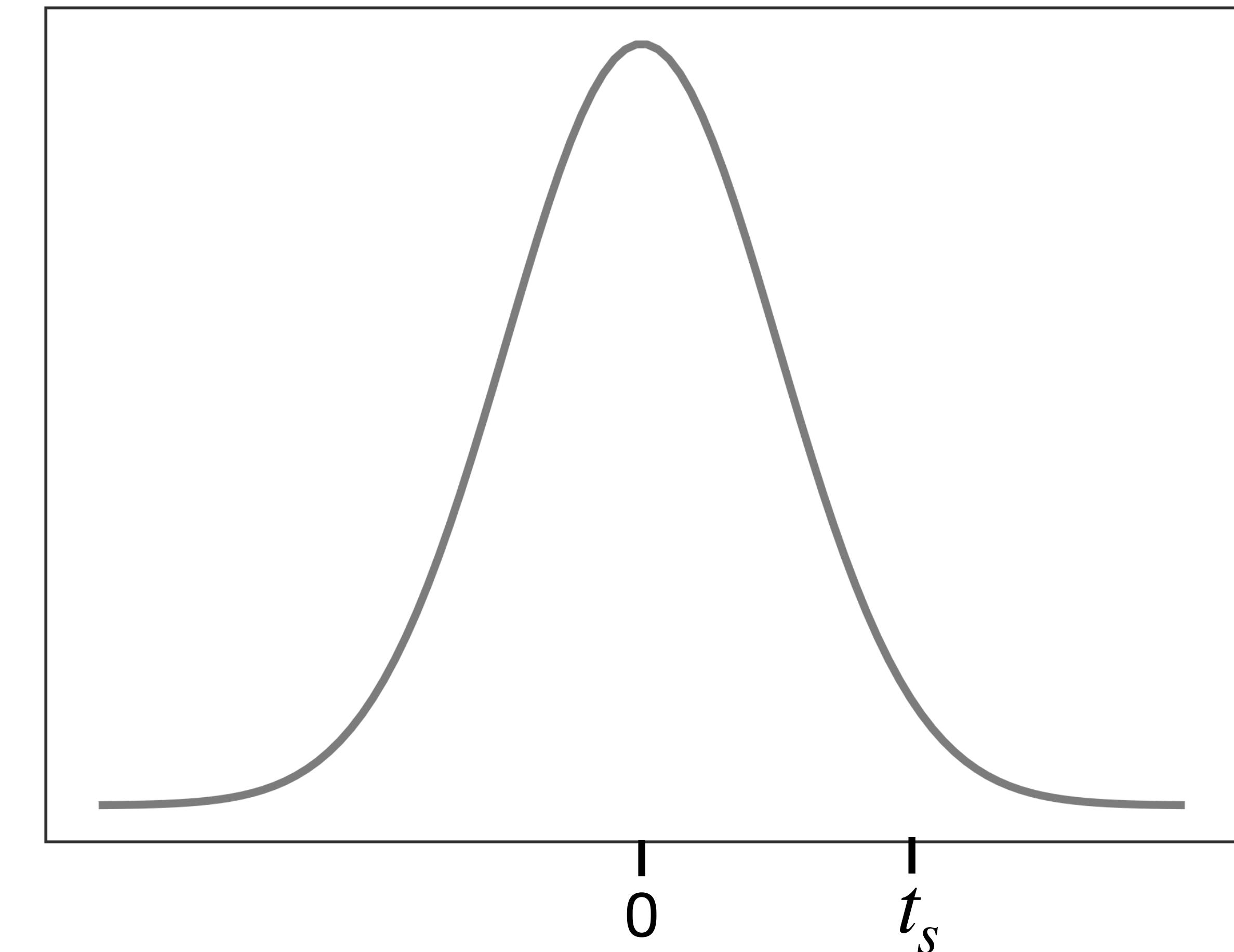
$$t_s = \frac{32.81 - 30}{2.48/\sqrt{14}}$$

$$t_s = 4.23$$

The t statistic for hypothesis testing

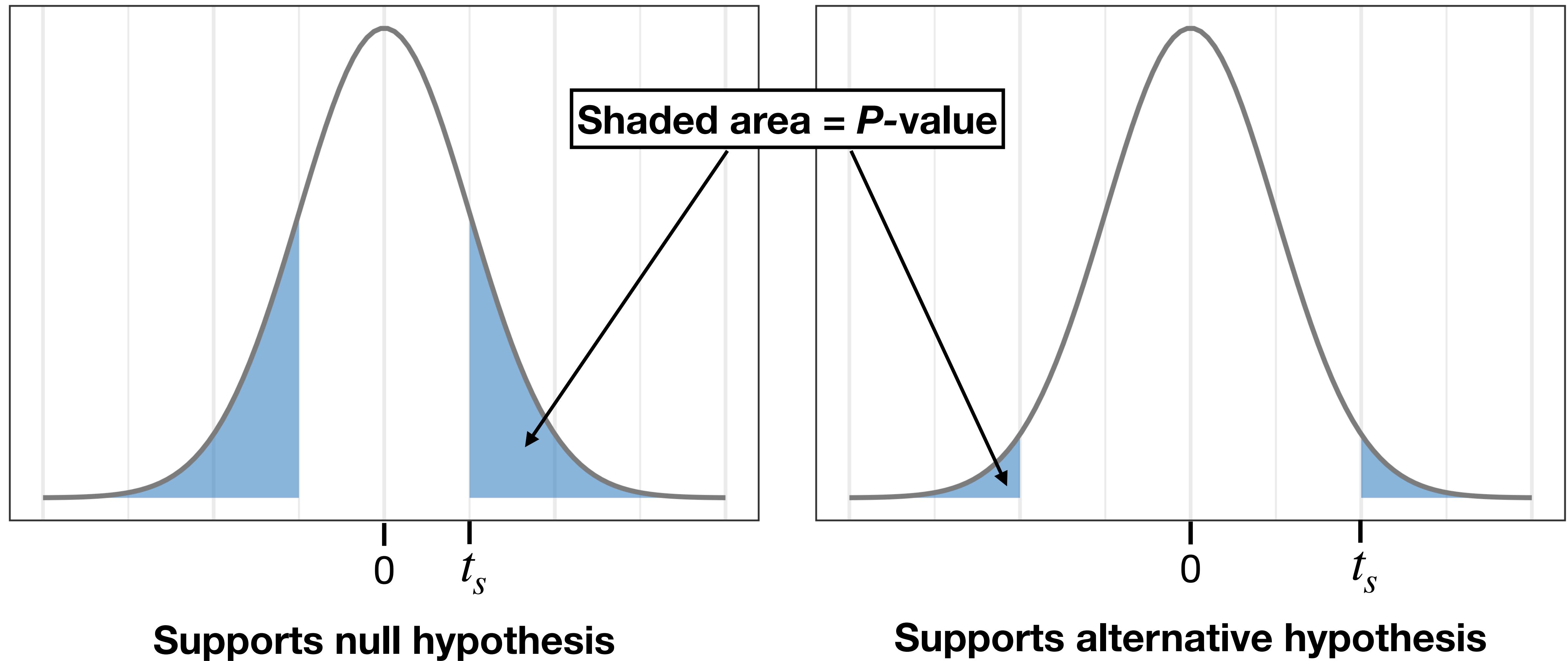


Supports null hypothesis



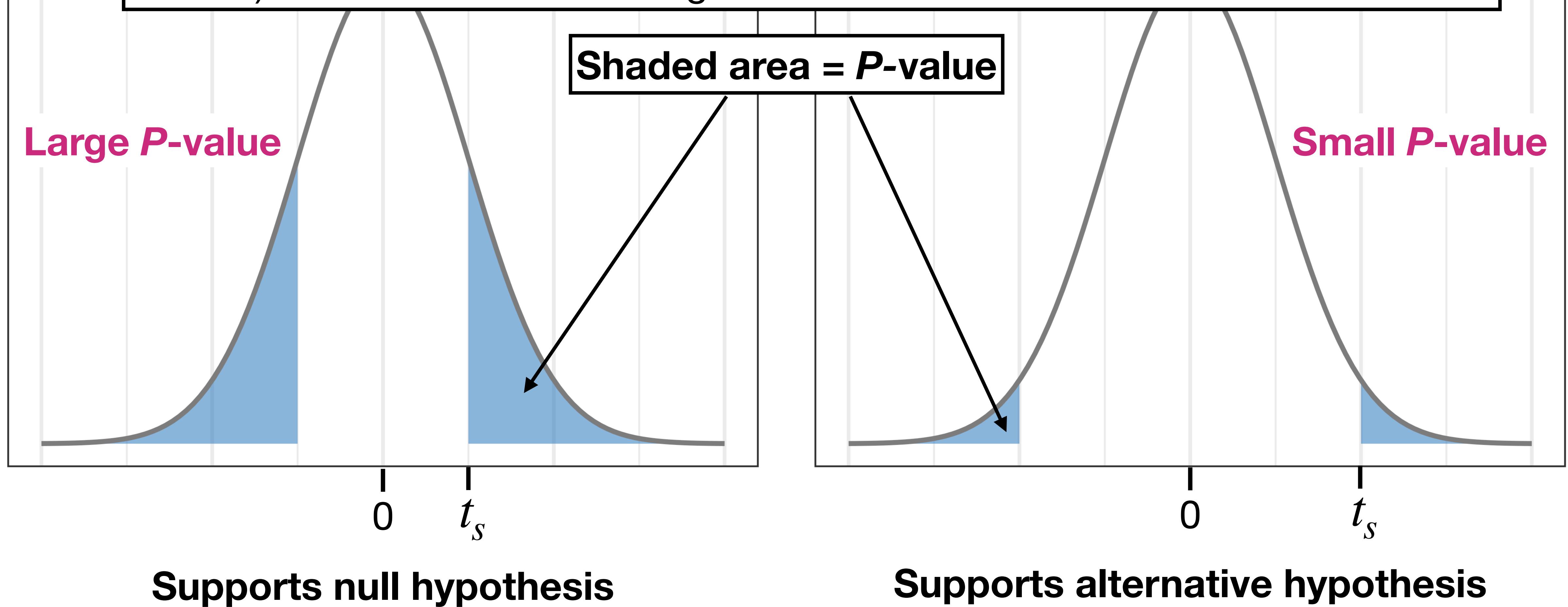
Supports alternative hypothesis

The t statistic for hypothesis testing



The t statistic for hypothesis testing

P-value is the probability (under the assumption that the null hypothesis is true) of the test statistic being at least as extreme as the value obtained



The t statistic for hypothesis testing



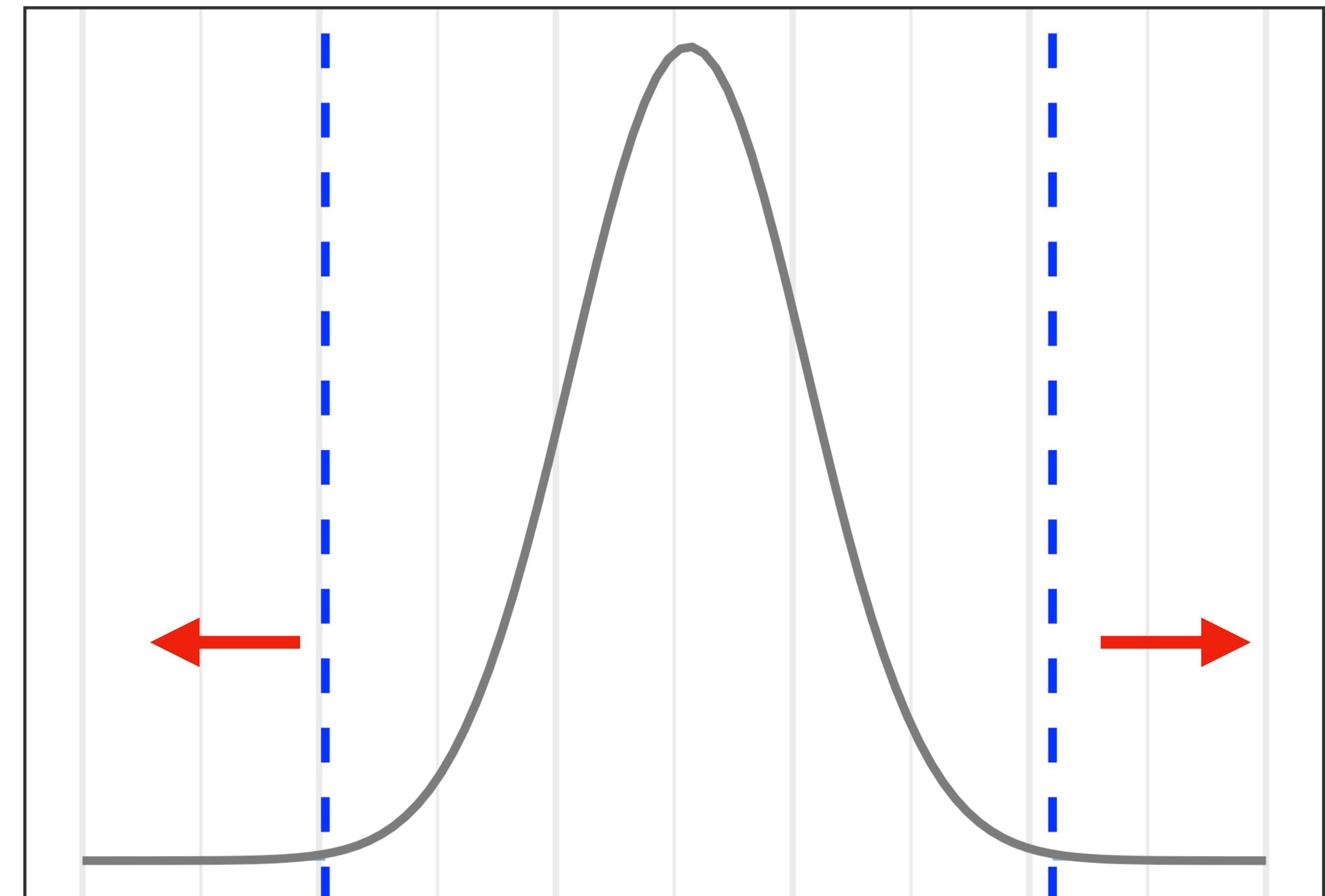
$$\bar{y} = 32.81 \text{ cm}^2$$

$$s = 2.48 \text{ cm}^2$$

$$\mu = 30 \text{ cm}^2$$

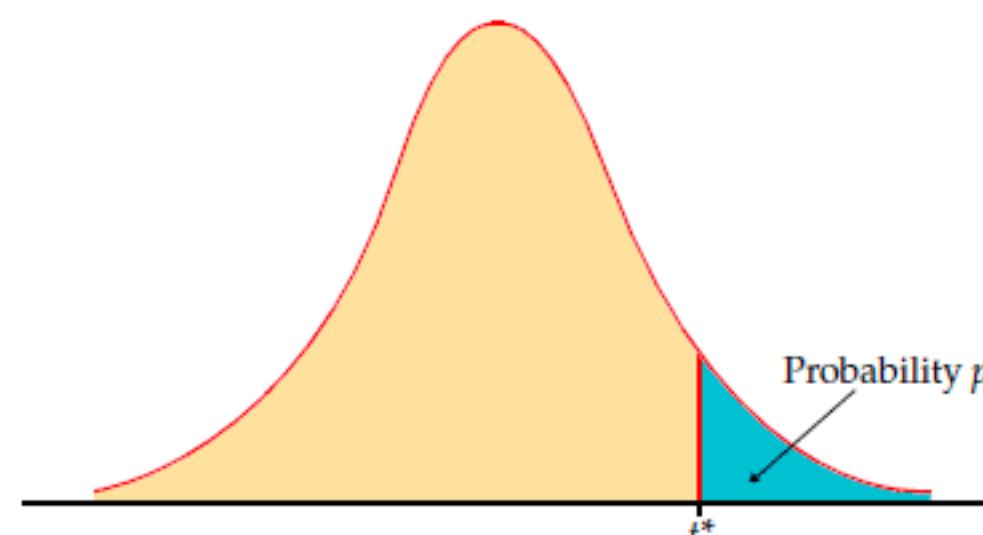
$$H_0 : \bar{y} = \mu$$

$$H_A : \bar{y} \neq \mu$$



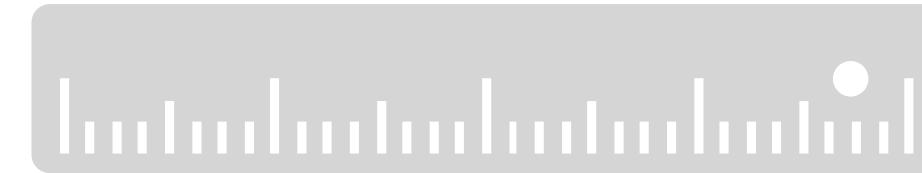
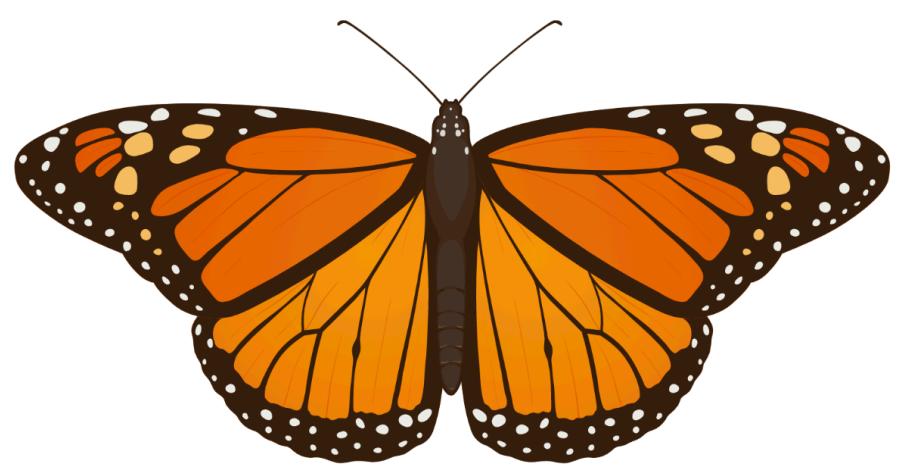
$$t_s = 4.23$$

$$t_s = 4.23$$



$$P = 0.0005^*2$$

The t statistic for hypothesis testing



$$\bar{y} = 32.81 \text{ cm}^2$$

$$s = 2.48 \text{ cm}^2$$

$$\mu = 30 \text{ cm}^2$$

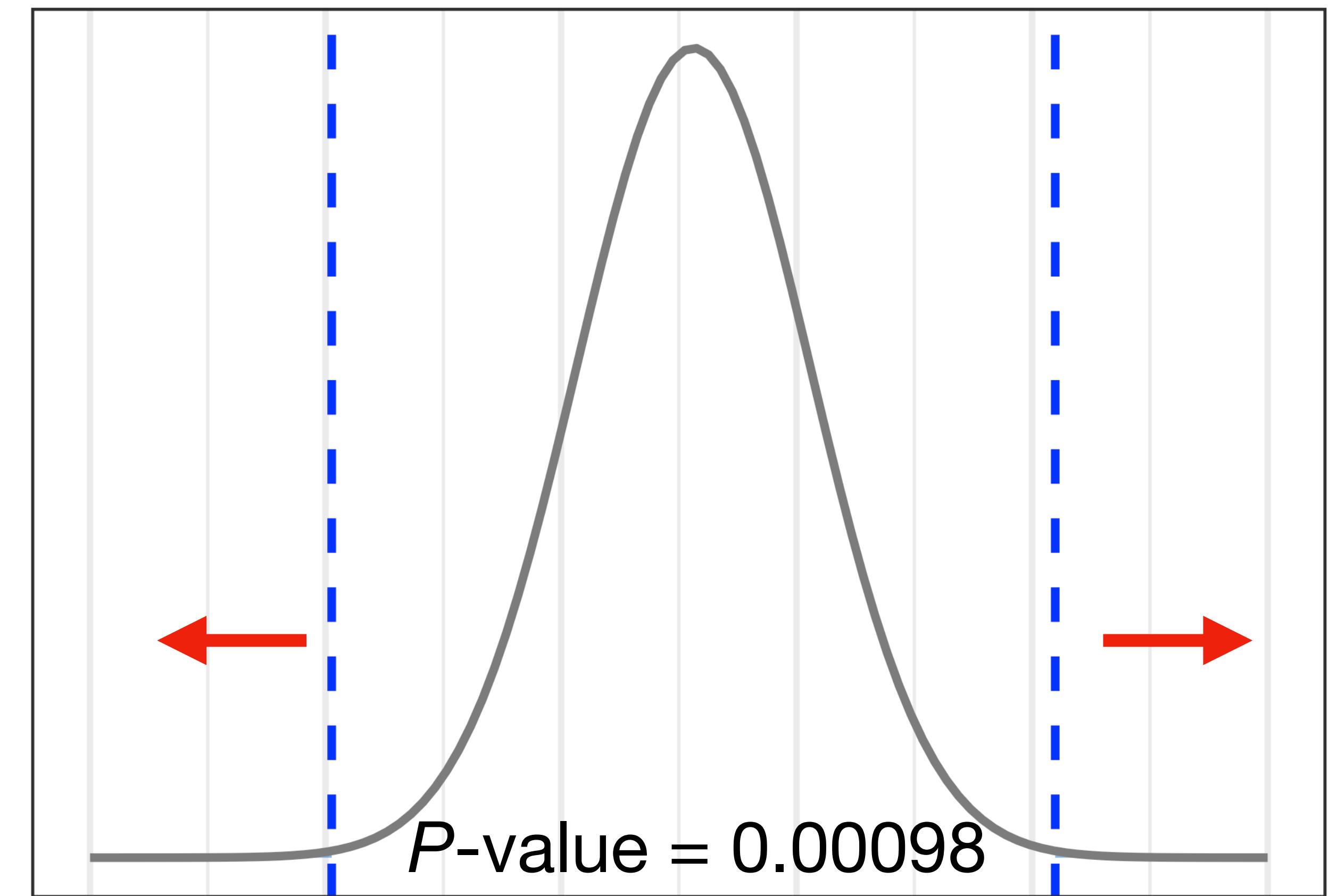
$$H_0 : \bar{y} = \mu$$

$$H_A : \bar{y} \neq \mu$$

```
> 2 * (1 - pt(4.23, 13))
```

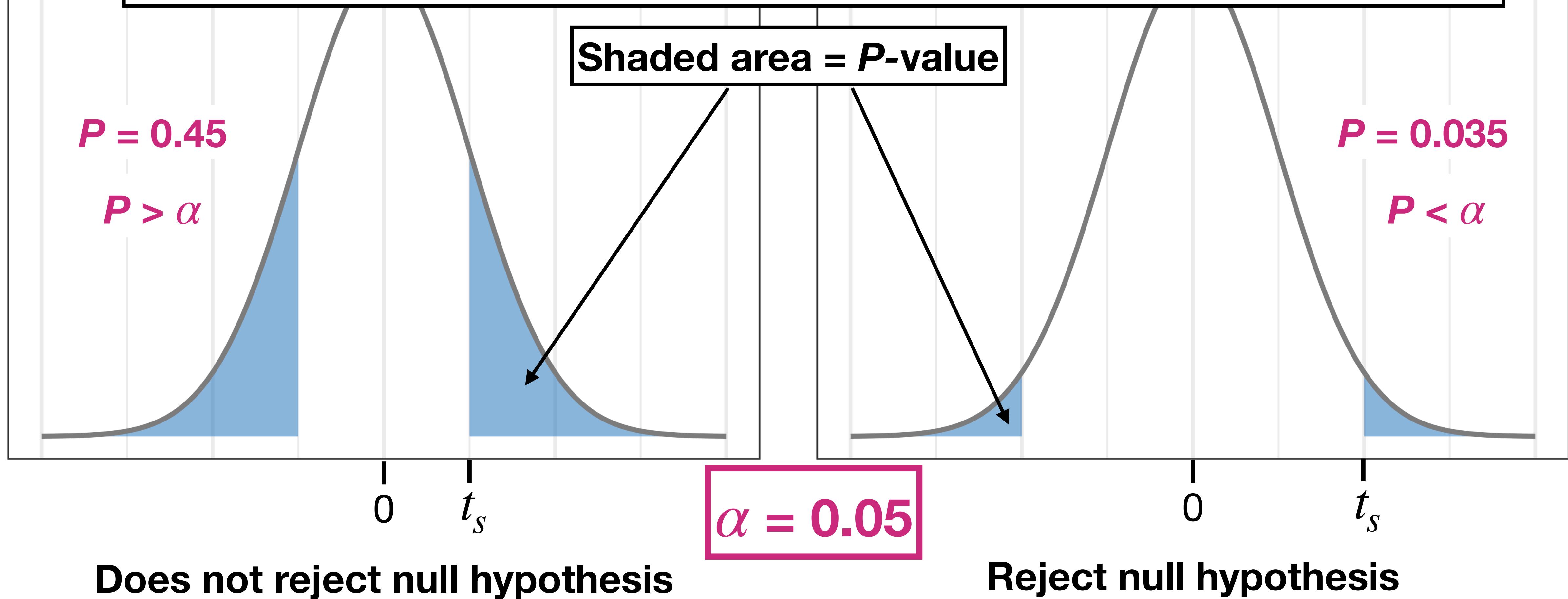
```
> 2 * pt(4.23, 13, lower.tail = F)
```

$$t_s = 4.23$$



Drawing conclusions from a t test

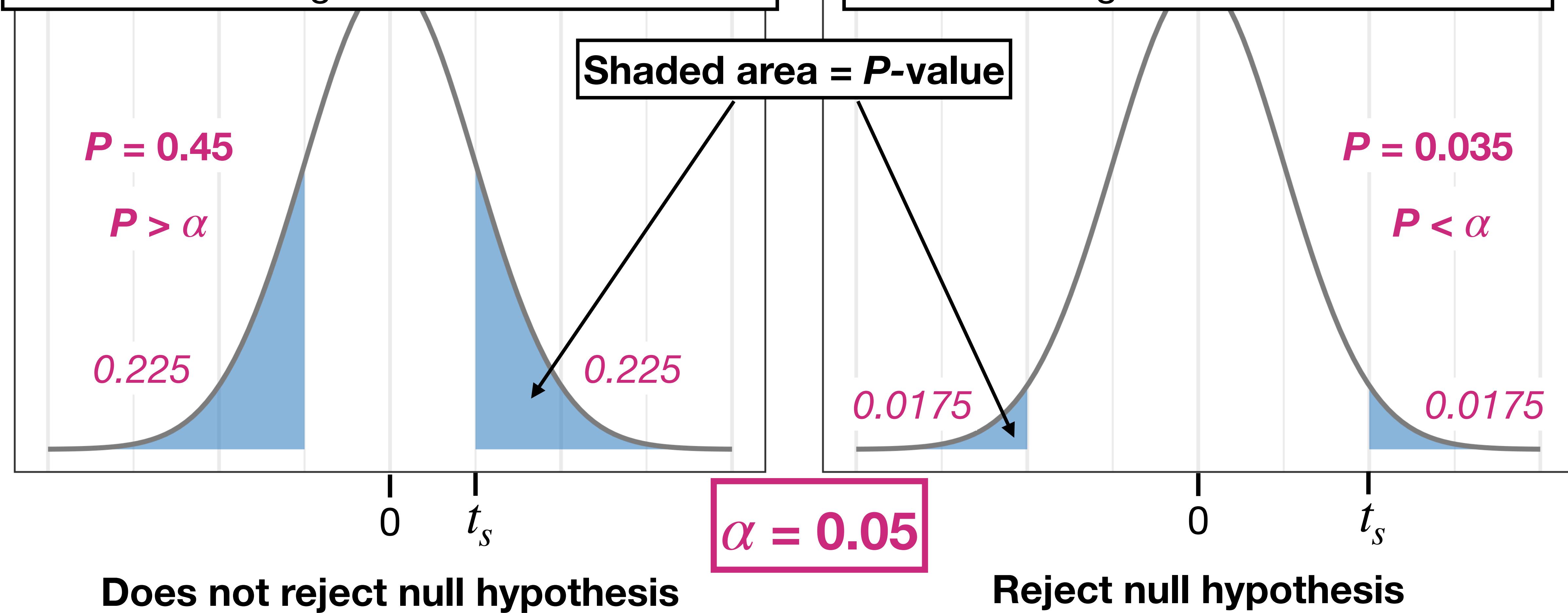
Significance level α is a threshold for determining what is sufficient vs. insufficient evidence to support the alternative hypothesis



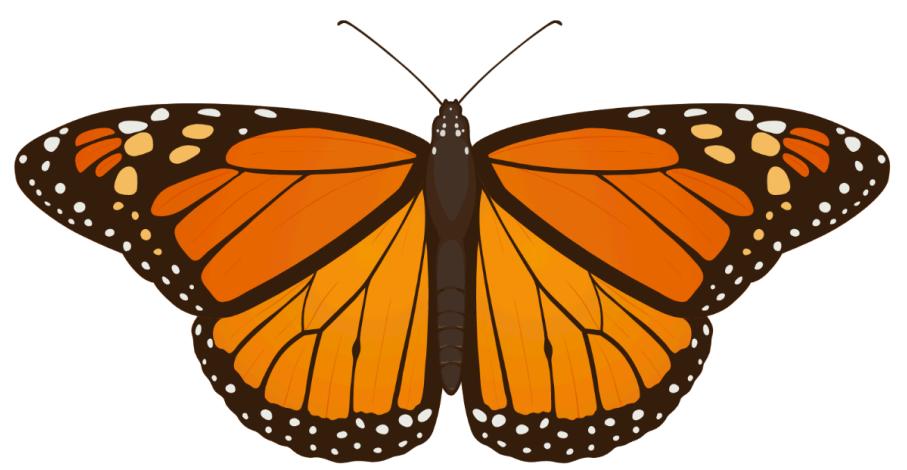
Drawing conclusions from a t test

The data do not provide sufficient evidence at the 0.05 significance level that...

The data provide sufficient evidence at the 0.05 significance level that...



The t statistic for hypothesis testing



$$\bar{y} = 32.81 \text{ cm}^2$$

$$s = 2.48 \text{ cm}^2$$

$$\mu = 30 \text{ cm}^2$$

$$\alpha = 0.05$$

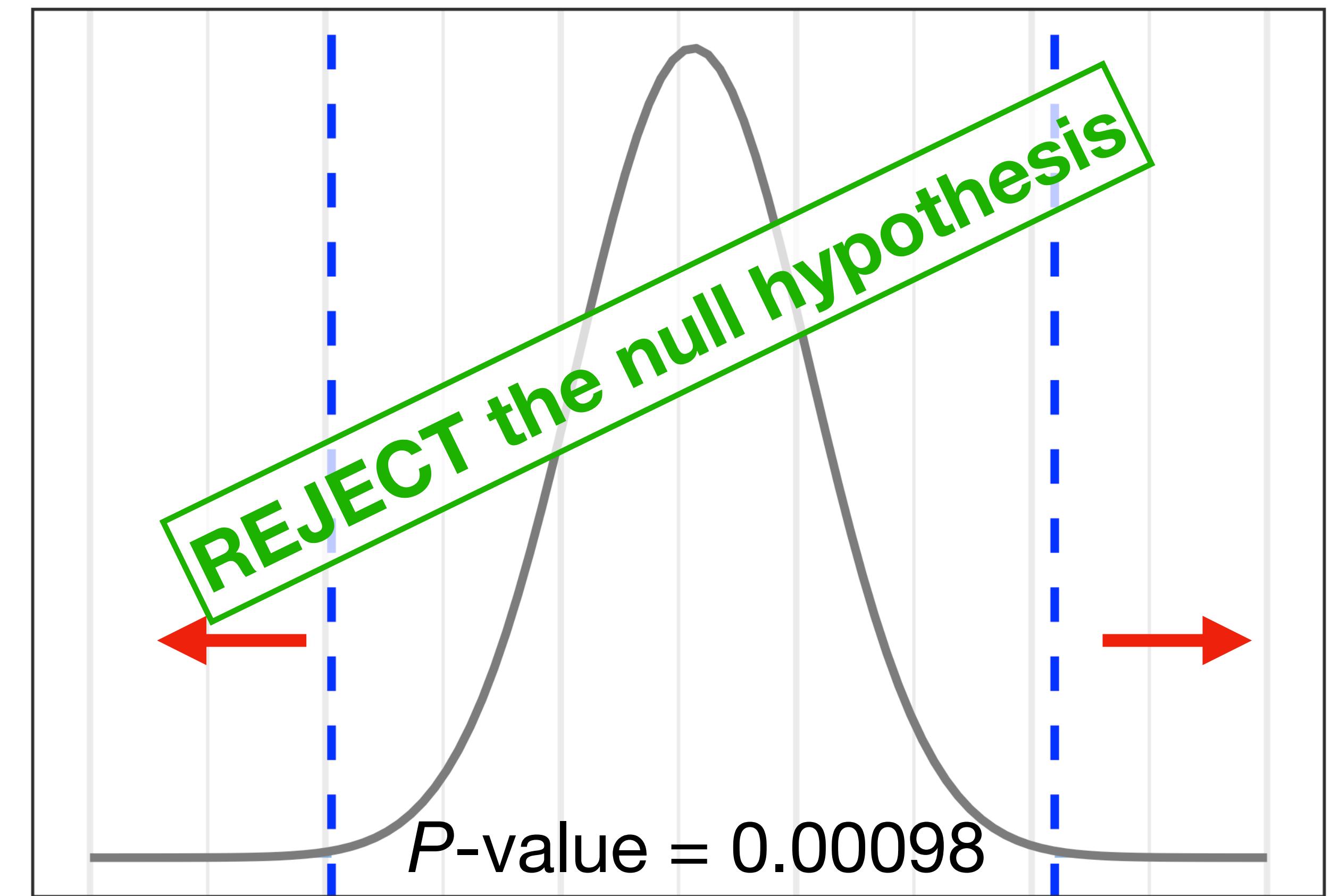
$$H_0 : \bar{y} = \mu$$

$$H_A : \bar{y} \neq \mu$$

```
> 2 * (1 - pt(4.23, 13))
```

```
> 2 * pt(4.23, 13, lower.tail = F)
```

$$t_s = 4.23$$



Drawing conclusions from a t test

- We generally do not say there is evidence for the null hypothesis, rather that there is insufficient evidence against it
- “Absence of evidence is not evidence of absence” - Carl Sagan
- Start with assumption that null hypothesis is true then ask whether data contradict that assumption
- Usually a significance level of 0.05 is chosen, but there is nothing special about this value
- Be careful with the wording of your statement and always provide the P -value to let others decide “significance” at their own α

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

1. Generate a hypothesis and choose a significance level

$$H_0 : \bar{y} = 1300 \quad H_A : \bar{y} \neq 1300 \quad \alpha = 0.05$$

2. Calculate test statistic

$$t_s = \frac{\bar{y} - \mu}{SE_{\bar{Y}}}$$

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

1. Generate a hypothesis and choose a significance level

$$H_0 : \bar{y} = 1300 \quad H_A : \bar{y} \neq 1300 \quad \alpha = 0.05$$

2. Calculate test statistic

$$t_s = \frac{\bar{y} - \mu}{s/\sqrt{n}}$$

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

1. Generate a hypothesis and choose a significance level

$$H_0 : \bar{y} = 1300 \quad H_A : \bar{y} \neq 1300 \quad \alpha = 0.05$$

2. Calculate test statistic

$$t_s = \frac{\bar{y} - \mu}{s/\sqrt{n}} = \frac{1269 - 1300}{145/\sqrt{8}} = -0.605$$

3. Calculate the *P*-value

$$df = n - 1 = 7$$

A pharmacologist measured the heart rate of eight rats. The mean difference from the expected value was 14 beats/min with a standard deviation was 14 beats/min. The null hypothesis was that there was no difference from the expected value.

$$df = 7$$

$$t_S = -0.605$$

$$\alpha = 0.05$$

$$P > 0.2$$

	P							
one-tail	0.1	0.05	0.025	0.01	0.005	0.001	0.0005	
two-tails	0.2	0.1	0.05	0.02	0.01	0.002	0.001	
DF								
1	3.078	6.314	12.706	31.821	63.656	318.289	636.578	
2	1.886	2.92	4.303	6.965	9.925	22.328	31.6	
3	1.638	2.353	3.182	4.541	5.841	10.214	12.924	
4	1.533	2.132	2.776	3.747	4.604	7.173	8.61	
5	1.476	2.015	2.571	3.365	4.032	5.894	6.869	
6	1.44	1.943	2.447	3.143	3.707	5.208	5.959	
7	1.415	1.895	2.365	2.998	3.499	4.785	5.408	
8	1.397	1.86	2.306	2.896	3.355	4.501	5.041	
9	1.383	1.833	2.262	2.821	3.25	4.297	4.781	
10	1.372	1.812	2.228	2.764	3.169	4.144	4.587	
11	1.363	1.796	2.201	2.718	3.106	4.025	4.437	
12	1.356	1.782	2.179	2.681	3.055	3.93	4.318	
13	1.35	1.771	2.16	2.65	3.012	3.852	4.221	
14	1.345	1.761	2.145	2.624	2.977	3.787	4.14	
15	1.341	1.753	2.131	2.602	2.947	3.733	4.073	
120	1.289	1.658	1.98	2.358	2.617	3.16	3.373	
1000	1.282	1.646	1.962	2.33	2.581	3.098	3.3	
Inf	1.282	1.645	1.96	2.326	2.576	3.091	3.291	

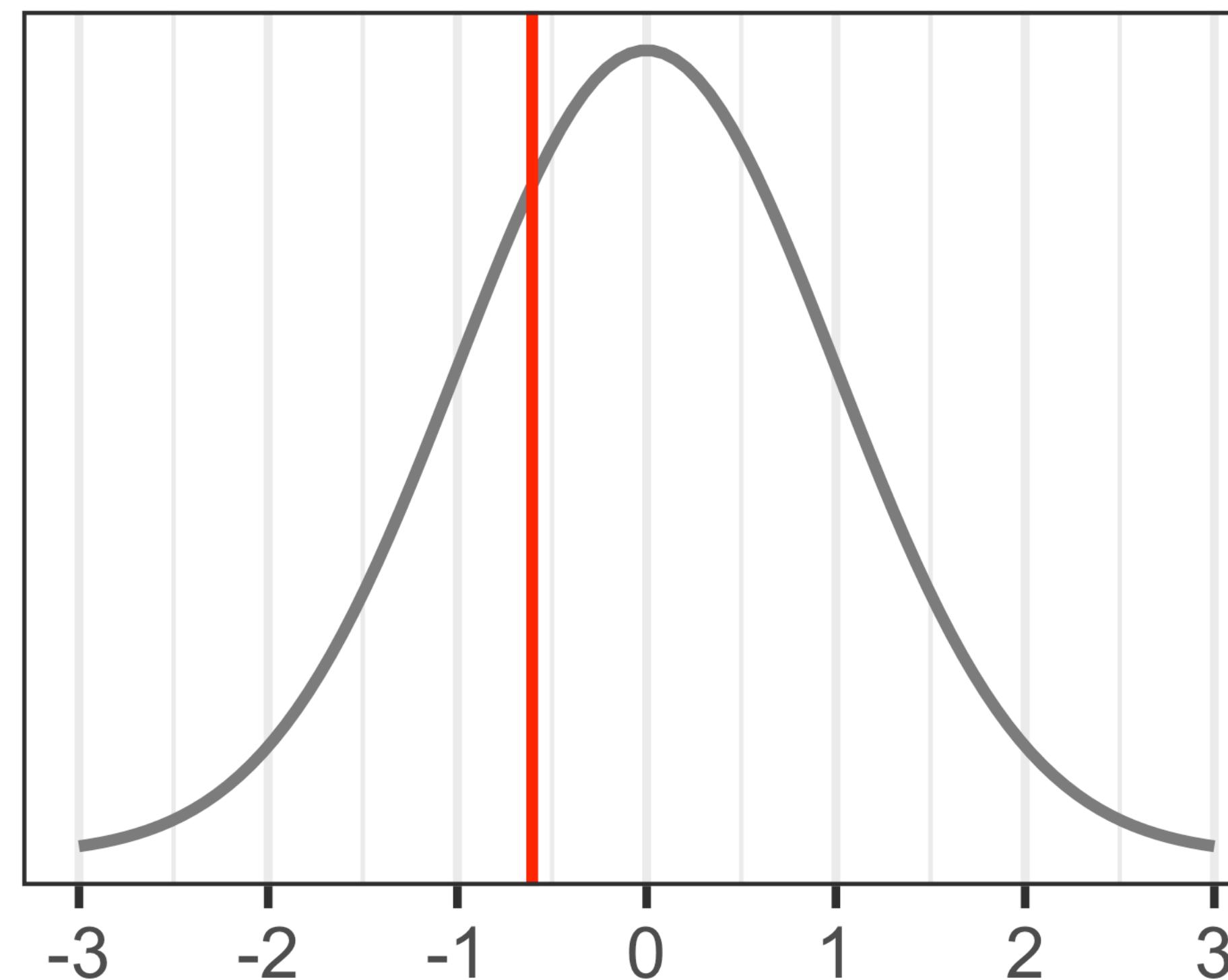
A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

$$df = 7$$

$$t_s = -0.605$$

$$\alpha = 0.05$$

$$P > 0.2$$



P-value = area under the curve showing extremes of test statistic

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

$$df = 7$$

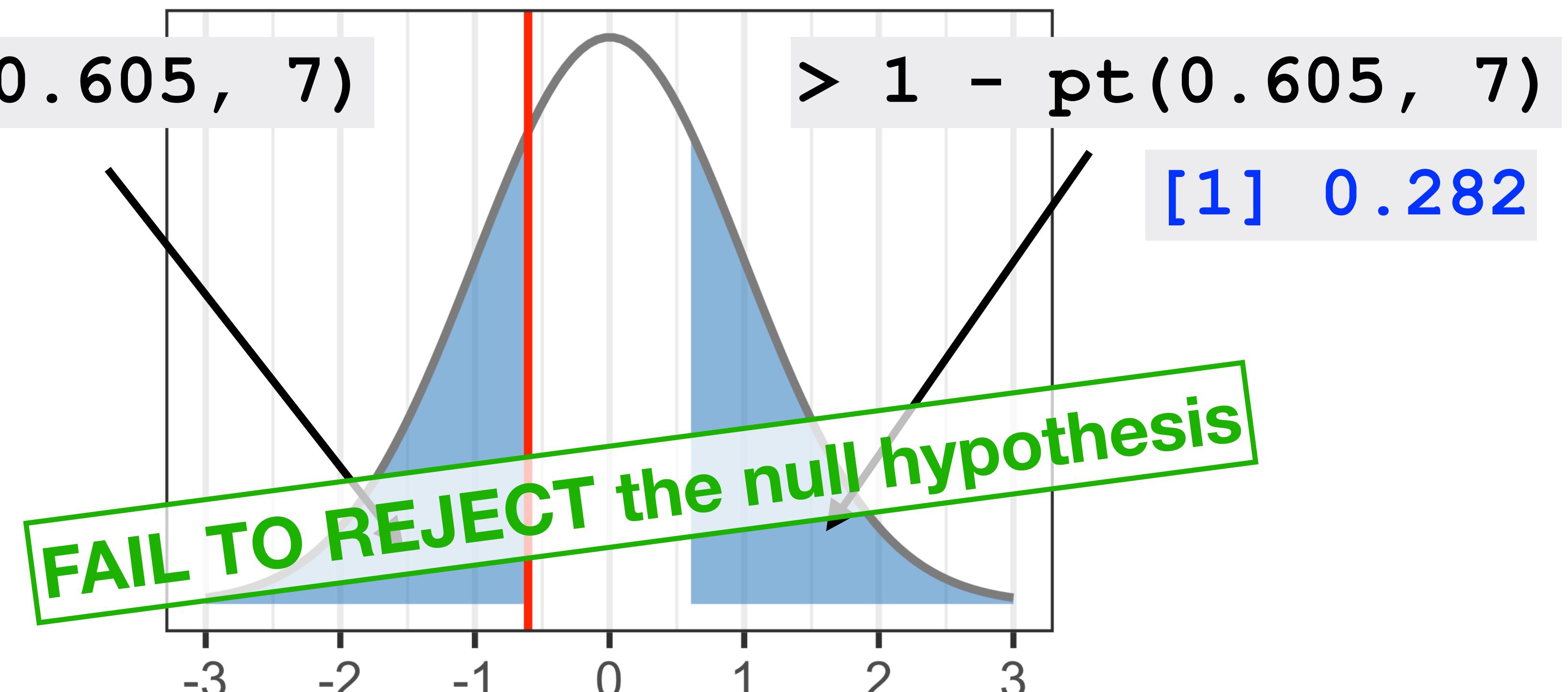
$> \text{pt}(-0.605, 7)$

$$t_s = -0.605$$

$$\alpha = 0.05$$

$$P > 0.2$$

$$P = 0.564$$



P-value = area under the curve showing extremes of test statistic

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

$$df = 7$$

$$> pt(-0.605, 7)$$

$$t_s = -0.605$$

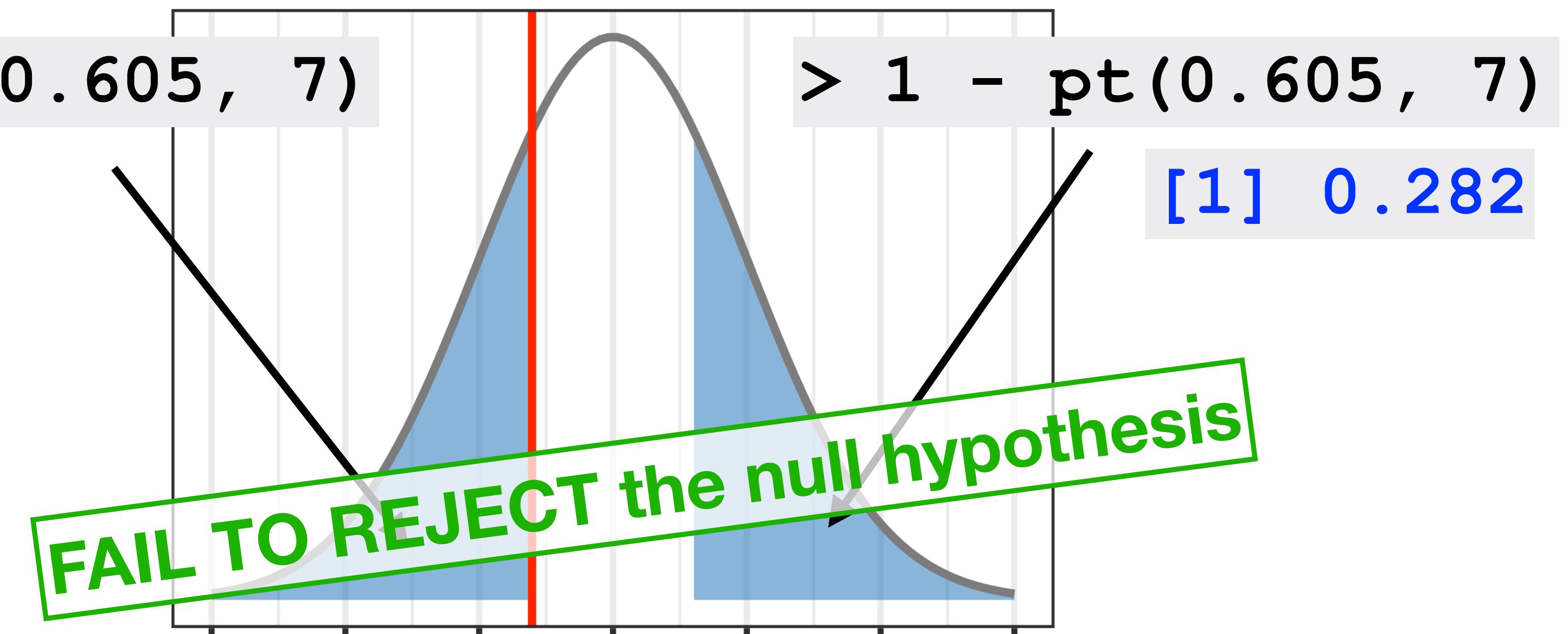
$$\alpha = 0.05$$

$$P > 0.2$$

$$P = 0.564$$

$$> 1 - pt(0.605, 7)$$

[1] 0.282



The data do not provide sufficient evidence at the 0.05 significance level that this sample is significantly different from the expected concentration 1,300 ng/gm ($P = 0.564$)

Confidence intervals vs. t test

- There is a close relationship between the confidence interval approach and the hypothesis testing approach to the comparison of means
 - Both use the same three quantities ($\bar{y} - \mu$, $SE_{\bar{Y}}$, and $t_{0.025}$) but manipulate them in different ways
 - **Confidence intervals** indicate the magnitude of differences
 - **t test** provides a P -value that describes the strength of evidence for the difference
 - If confidence interval **includes zero (or the value you are comparing it to)**, it is consistent with the **null hypothesis**

A pharmacologist measured the concentration of dopamine in the brains of eight rats. The mean concentration was 1,269 ng/gm and the standard deviation was 145 ng/gm. How does this sample compare to the expected dopamine concentration of 1,300 ng/gm?

$$df = 7$$

$$> pt(-0.605, 7)$$

$$t_s = -0.605$$

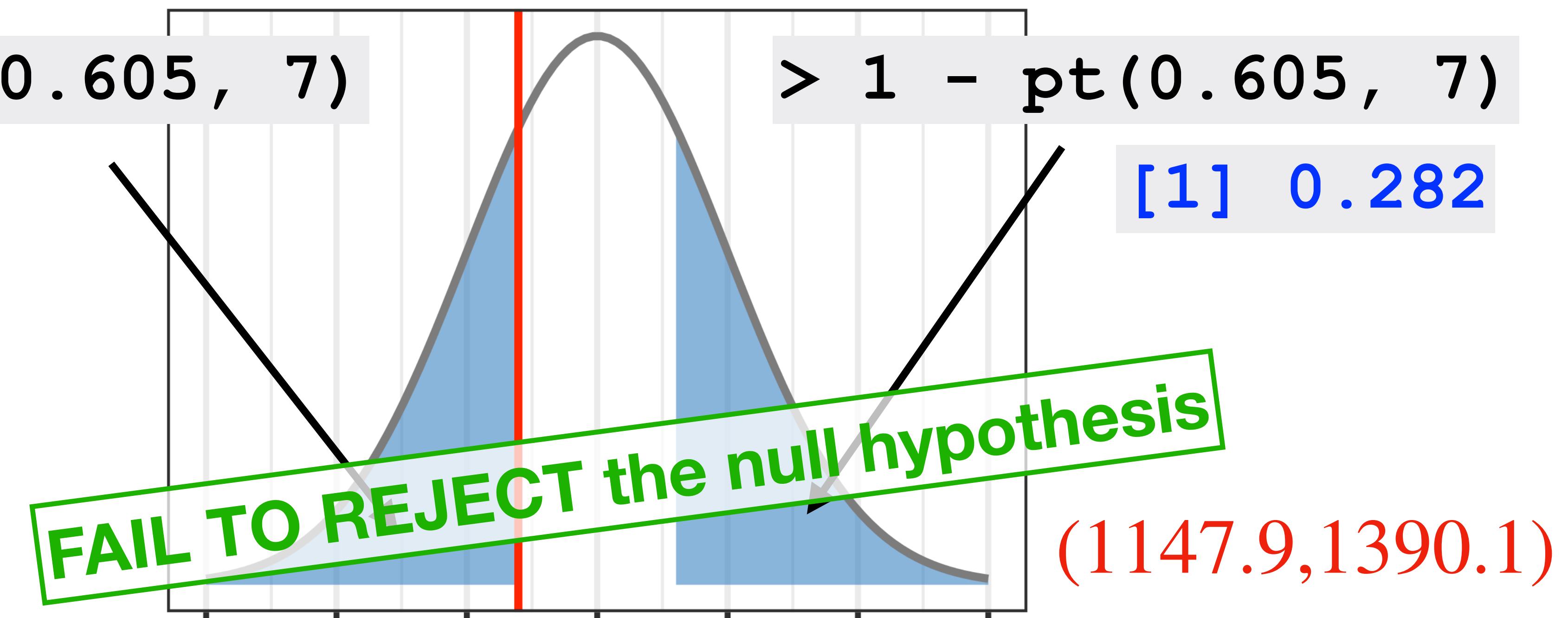
$$\alpha = 0.05$$

$$P > 0.1$$

$$P = 0.564$$

$$> 1 - pt(0.605, 7)$$

[1] 0.282



The data do not provide sufficient evidence at the 0.05 significance level that this sample is significantly different from the expected concentration 1,300 ng/gm ($P = 0.564$)

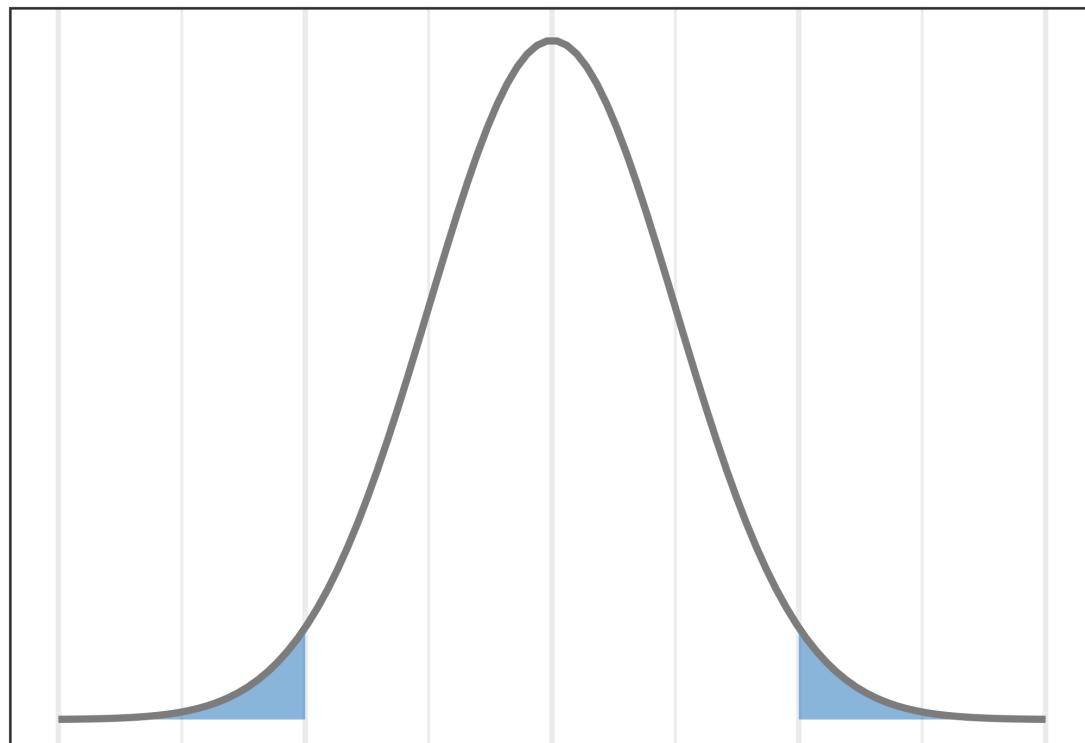
You performed qPCR to measure the expression of your gene of interest, *sqst-5*, after exposure to zinc in a sample of 7 *C. elegans*. You found the mean expression to be 2.9 units with a standard deviation of 1.6. Is the expression of *sqst-5* significantly different from 1 at the 0.05 level?

1. Generate a hypothesis and choose a significance level

$$H_0 : \bar{y} = 1$$

$$H_A : \bar{y} \neq 1$$

$$\alpha = 0.05$$



2. Calculate test statistic

$$t_s = \frac{\bar{y} - \mu}{s/\sqrt{n}} = \frac{2.9 - 1}{1.6/\sqrt{7}} = 3.35$$

3. Calculate the *P*-value

```
> pt(3.35, 6, lower.tail = F) * 2 = 0.0077 * 2 = 0.0154
```



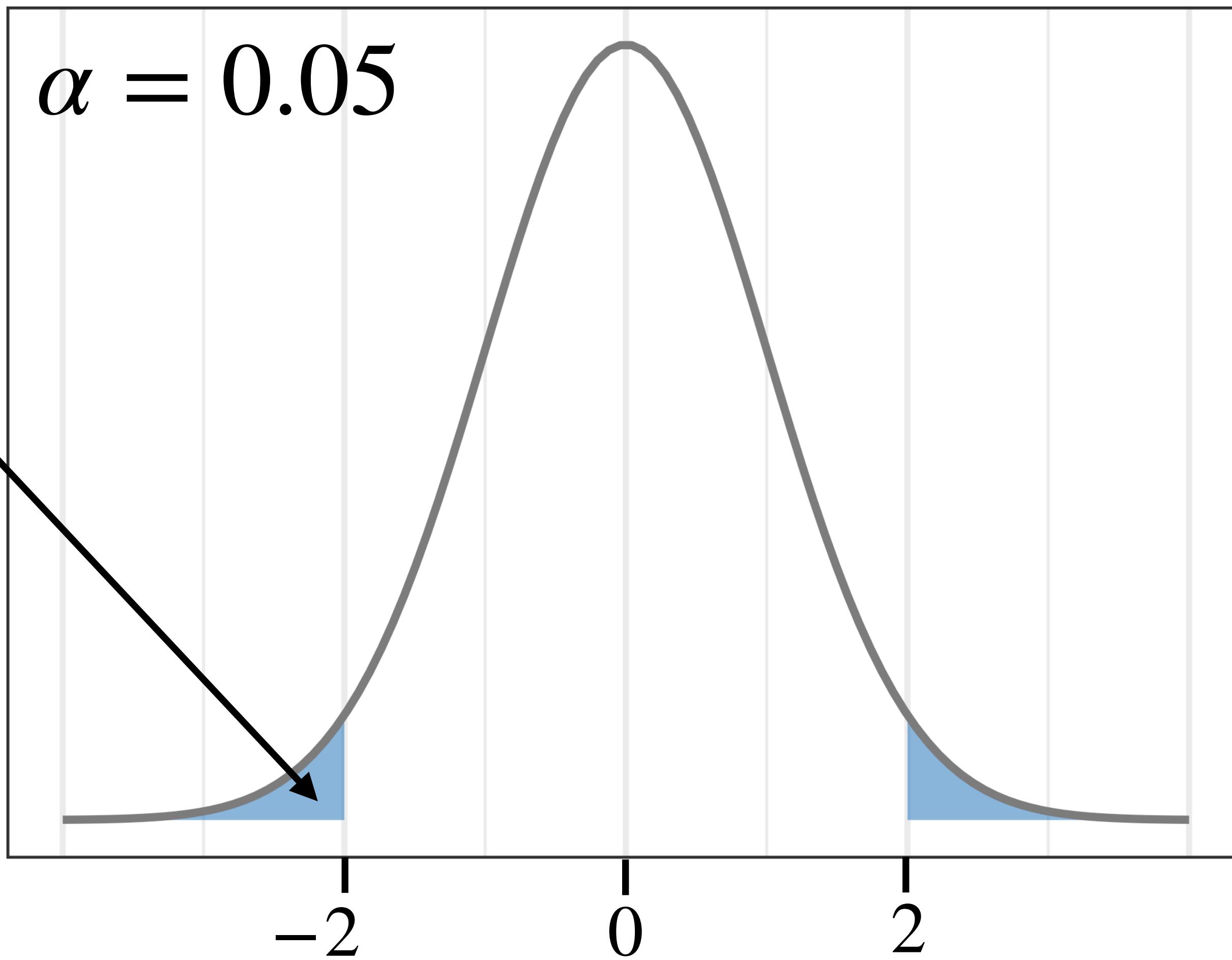
The probabilistic interpretation of α

If H_0 is true,

$$Pr[t_s > 2 | t_s < -2] = 0.05$$

If you performed
the experiment 100 times:

- **95** times it would not
reject the null
- **5** times it would reject
the null



Type I and type II errors

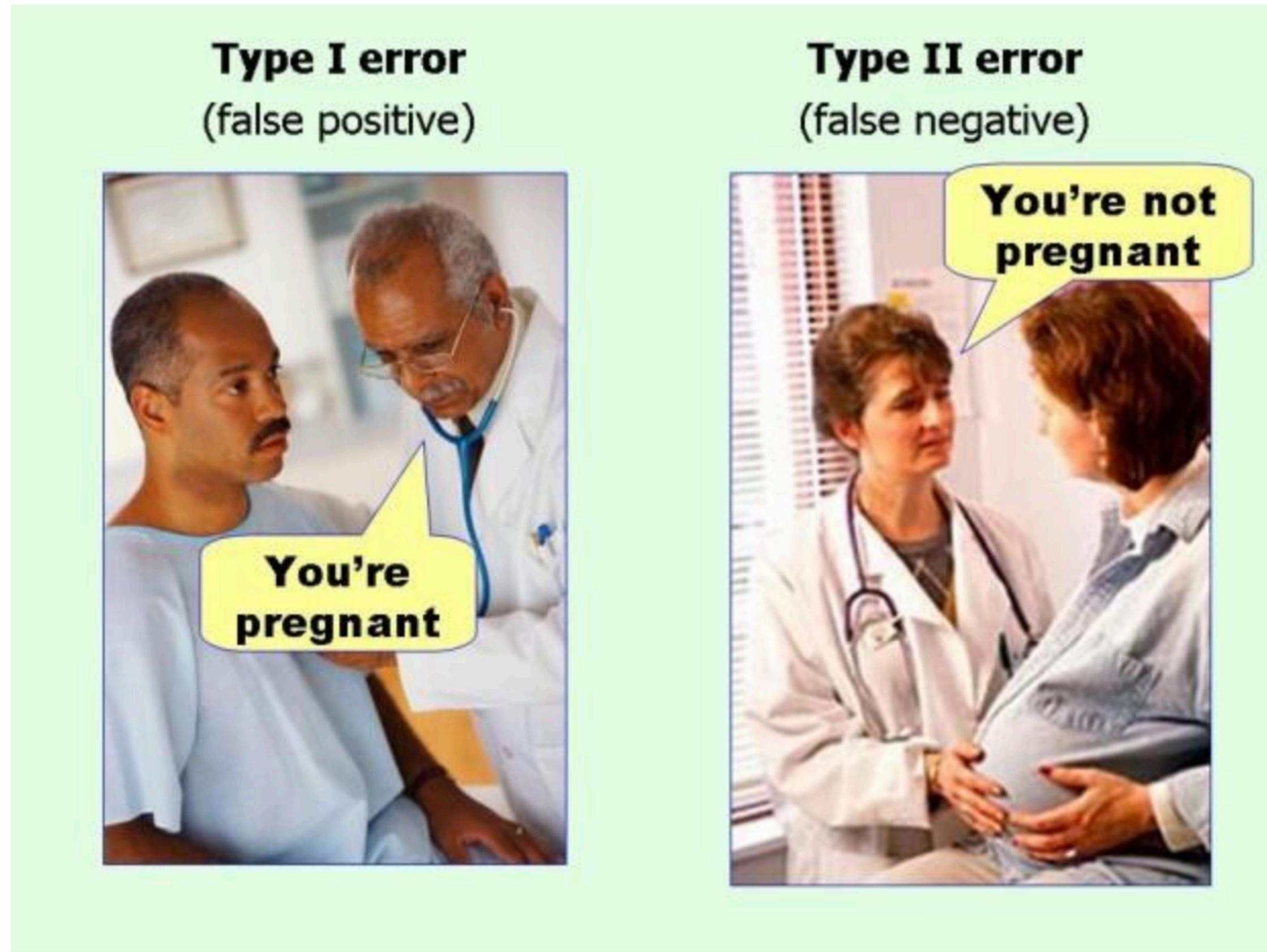
Null hypothesis is...	TRUE	FALSE
REJECTED		
NOT REJECTED		

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

1. In choosing α , we are choosing our level of protection against Type I errors
2. Experiment with small sample size has high risk of Type II error
3. We know more after rejecting the null than we do after a non-rejection

Tips to remembering type I and II errors



<http://www.effectsizefaq.com>



“When the boy cried wolf, the village committed Type I and then Type II errors, in that order”

“RAAR”

1. Reject when we should Accept
2. Accept when we should Reject



Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

You receive a positive test result even though you actually do not have COVID-19

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

You have COVID-19, but your test comes back negative.

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

The result of a clinical trial states that the new drug is ineffective but it can actually improve the symptoms of the disease.

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

The result of a clinical trial states that the new drug is effective but it actually does not improve the symptoms of the disease.

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

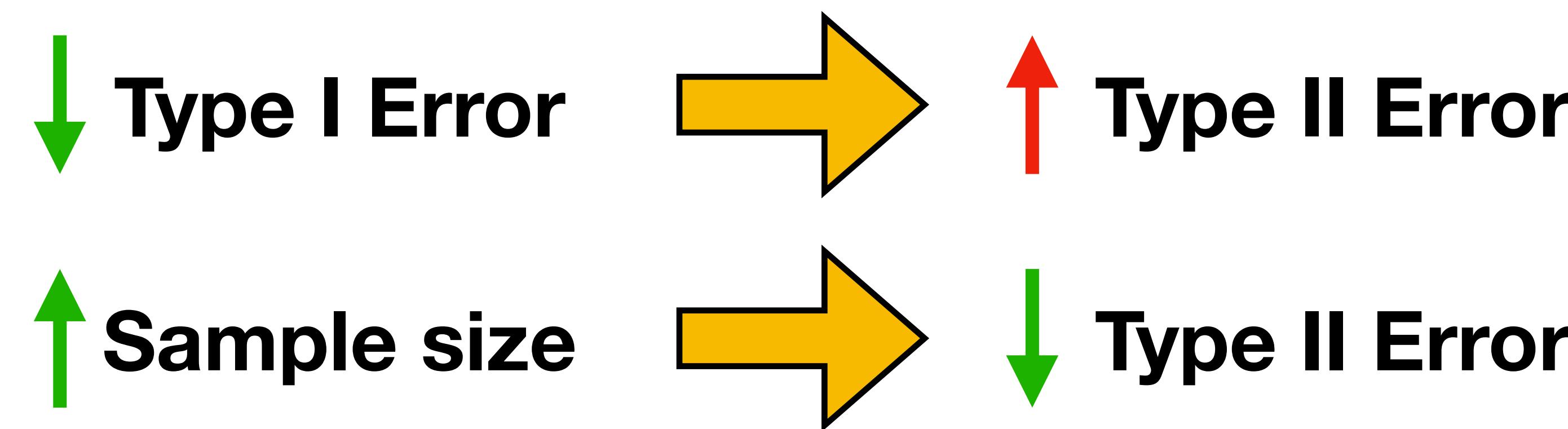
A man is on trial for killing his wife. He did not kill his wife, but yet was found guilty and punished for a crime he did not commit.

Type I and type II errors

Null hypothesis is...	TRUE	FALSE
REJECTED	Type I error (<i>False positive</i>)	Correct!
NOT REJECTED	Correct!	Type II error (<i>False negative</i>)

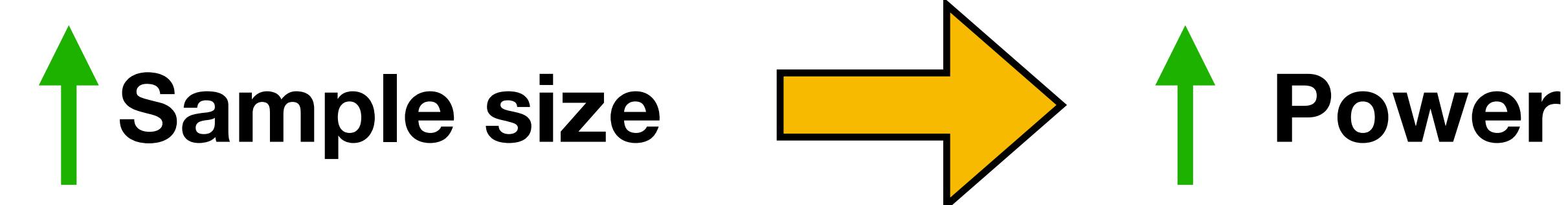
A man is on trial for killing his wife. He did in fact kill his wife, but yet was found innocent and released immediately.

A quick note on power



The **power** of a statistical test is the probability of the null hypothesis is **false** and you **reject** the null hypothesis

$$\text{Power} = 1 - \text{Type II Error}$$



Measure of **sensitivity** of a test: ability to detect a difference between means when the difference truly exists

You performed qPCR to measure the expression of your gene of interest, *sqst-5*, after exposure to zinc in a sample of 7 *C. elegans*. You found the mean expression to be 2.9 units with a standard deviation of 1.6. Is the expression of *sqst-5* significantly **greater than 1** at the 0.05 level?

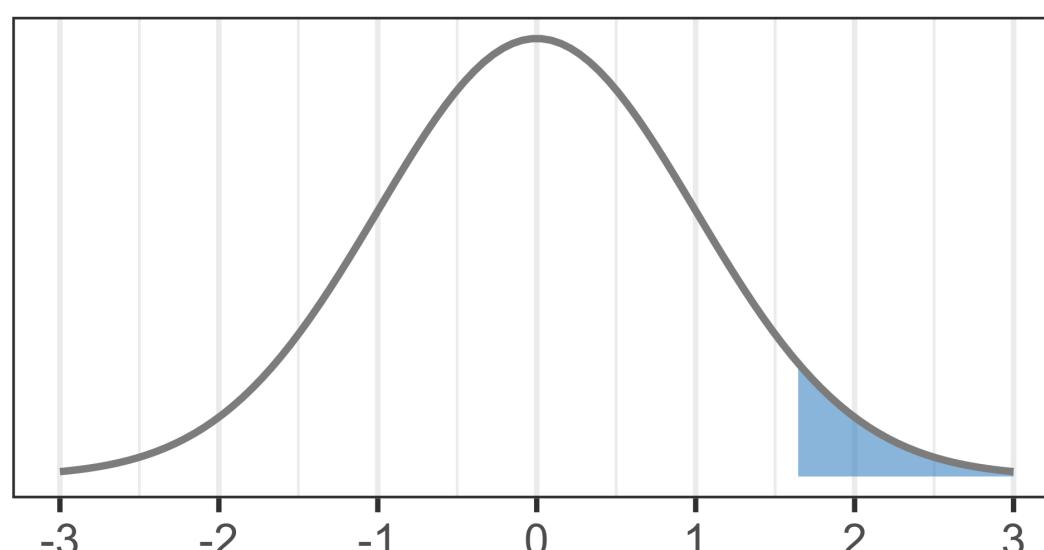
1. Generate a hypothesis and choose a significance level

$$H_0 : \bar{y} = 1$$

$$H_A : \bar{y} > 1$$

$$\alpha = 0.05$$

“Directional alternative”



$$t_s = \frac{\bar{y} - \mu}{s/\sqrt{n}} = \frac{2.9 - 1}{1.6/\sqrt{7}} = 3.35$$

Same t statistic

3. Calculate the P-value

```
> pt(3.35, 6, lower.tail = F)
```

= 0.0077



When should you use a one-sided t test?

- If the **alternative hypothesis** is generated before seeing the data **and there is no scientific interest** in results in the opposite direction
 - i.e. drug in clinical trial decreases disease symptoms (we aren't expecting the drug to *increase* disease symptoms...)
- If you use a **directional alternative hypothesis** when it is not justified, you pay the price of a doubled risk of Type I error
 - Always best to default to a **non-directional alternative hypothesis**

More interpretation on **statistical significance**

- Some might say there is a “significant difference” because $P < 0.05$
 - **Significant** means “substantial” or “important” but really what we mean to say is that we **reject the null hypothesis**
 - If a difference is **important** (as opposed to statistically significant) cannot be decided with a P -value
 - Can use the magnitude of the differences in means
 - Also requires specific expertise/knowledge in the research area

More interpretation on statistical significance

Lactate dehydrogenase (LD) is an enzyme that may show elevated activity following damage to the heart muscle or other tissues. A study of 270 individuals showed a mean value of 60 and standard deviation of 11. If a value of 58 or lower is considered “normal”, should we be concerned about the elevated levels of LD in our study?

$$t_s = \frac{\bar{y} - \mu}{s/\sqrt{n}} = \frac{60 - 58}{11/\sqrt{270}} = 2.98$$

```
> pt(2.98, 269, lower.tail = F) = 0.0015  
= 0.0031 (if two-tailed)
```

With large sample sizes, small differences in means can be statistically significant, but does that mean the difference is important?

A final note on statistical significance

If a value of 58 or lower is considered “normal”, should we be concerned about the elevated levels of LD in our study?

95% confidence interval	Is the difference significant?	Is the difference important?
(59, 61)	YES	NO

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(59, 61)	YES	NO
(63, 68)	YES	YES

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(59, 61)	YES	NO
(63, 68)	YES	YES
(60, 65)	YES	UNSURE

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(59, 61)	YES	NO
(63, 68)	YES	YES
(60, 65)	YES	UNSURE
(56, 59)	NO	NO

A final note on statistical significance

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(59, 61)	YES	NO
(63, 68)	YES	YES
(60, 65)	YES	UNSURE
(56, 59)	NO	NO
(57, 67)	NO	UNSURE

Calculating the **effect size**

The **effect size** is the difference between the sample mean and the population mean relative to the **standard deviation** of the sample

$$\text{Effect size} = \frac{|\bar{y} - \mu|}{s}$$

Effect size = signal to noise ratio

With large sample sizes, small differences in means can be statistically significant, but does that mean the difference is important?

Calculating the effect size

The **effect size** is the difference between the sample mean and the population mean relative to the **standard deviation** of the sample

$$\text{Effect size} = \frac{|\bar{y} - \mu|}{s}$$

Effect size = signal to noise ratio
i.e. populations differ by 0.27 SD



Small effect sizes lead to overlapping populations

Calculating the effect size

The **effect size** is the difference between the sample mean and the population mean relative to the **standard deviation** of the sample

$$\text{Effect size} = \frac{|\bar{y} - \mu|}{s}$$

Effect size = signal to noise ratio

i.e. populations differ by 1.5 SD



Large effect sizes create more distinction between populations

Calculating the effect size

The **effect size** is the difference between the sample mean and the population mean relative to the **standard deviation** of the sample

X

$$\text{Effect size} = \frac{|\bar{y} - \mu|}{\mu}$$

Effect size = signal to noise ratio

i.e. Sample is 22% longer than pop.



Large effect sizes create more distinction between populations

Lactate dehydrogenase (LD) is an enzyme that may show elevated activity following damage to the heart muscle or other tissues. A study of 270 individuals showed a mean value of 60 and standard deviation of 11. If a value of 58 or lower is considered “normal”, should we be concerned about the elevated levels of LD in our study?

$$\text{Effect size} = \frac{|\bar{y} - \mu|}{s}$$

$$\text{Effect size} = \frac{|60 - 58|}{11} = 0.181$$