MRC Centre for Global Infectious Disease Analysis
IMPERIAL

Malaria Molecular Surveillance Study Design Workshop

Module 3: Hypothesis testing and power

Null hypothesis testing

Sometimes we are simply trying to estimate something, e.g. prevalence. **We have seen how to perform sample size calculation based on precision arguments**.

In other cases, we have a specific question that we want to answer. This questions may be phrased as a **null hypothesis test**.

Null hypothesis testing

Sometimes we are simply trying to estimate something, e.g. prevalence. **We have seen how to perform sample size calculation based on precision arguments**.

In other cases, we have a specific question that we want to answer. This questions may be phrased as a **null hypothesis tests**.

A null hypothesis (H_0) is a statement of **no effect or difference** between groups. This is often a statement that nothing interesting is happening*

*Rather than trying to prove there is an effect, in null hypothesis testing we try to **disprove** that there is **no effect**.*

*Sometimes it can be very interesting if the null hypothesis is true

Null hypothesis testing

- Q: Has prevalence increased over the last 5 years?

- Q: Are certain genetic variants associated with gender, or occupation?

- Q: Does vaccine efficacy vary based on genetic markers?

Null hypothesis testing

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  H_0: Prevalence has remained the same over the last 5 years.

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- Q: Does vaccine efficacy vary based on genetic markers?

  H_0: Vaccine efficacy is the same irrespective of genetic markers.

Null hypothesis testing

Each test has a **test statistic**

One-sample z-test for proportions: tests prevalence against a known value

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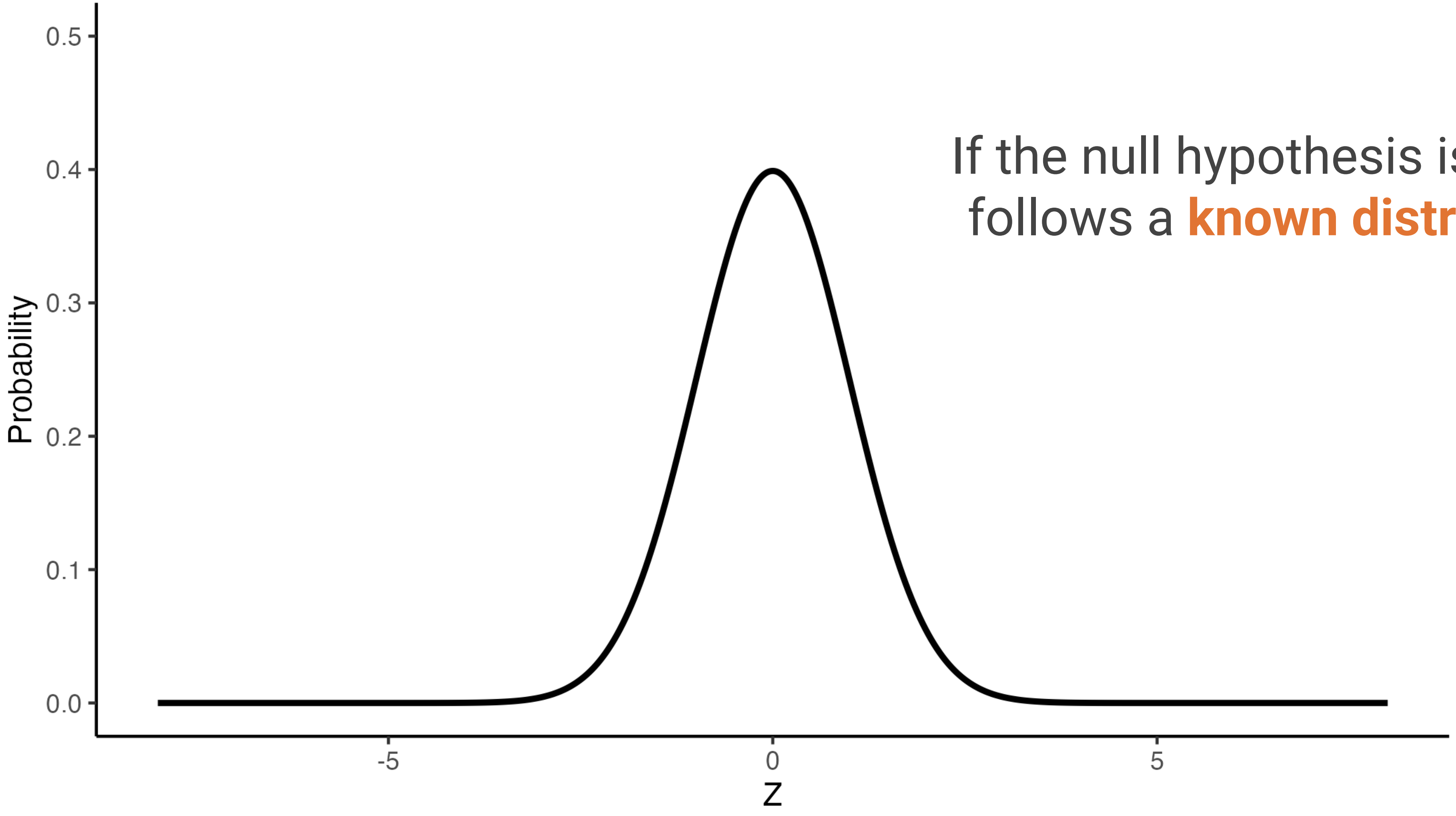
$$Z = \frac{\hat{p} - p_0}{\sqrt{\frac{\hat{p}(1-\hat{p})}{n}}}$$

Null hypothesis testing



If the null hypothesis is true, Z follows a **known distribution**

Null hypothesis testing

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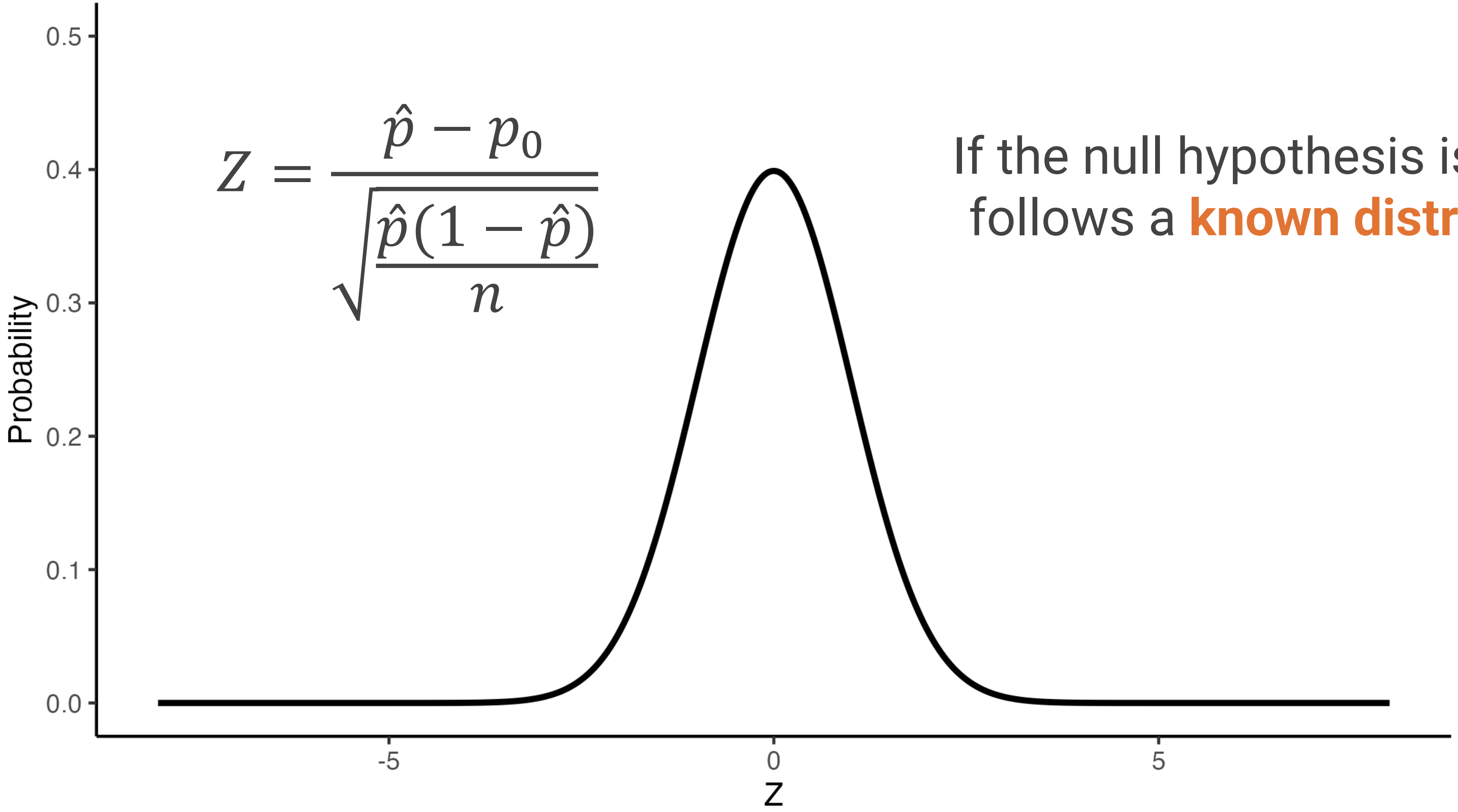

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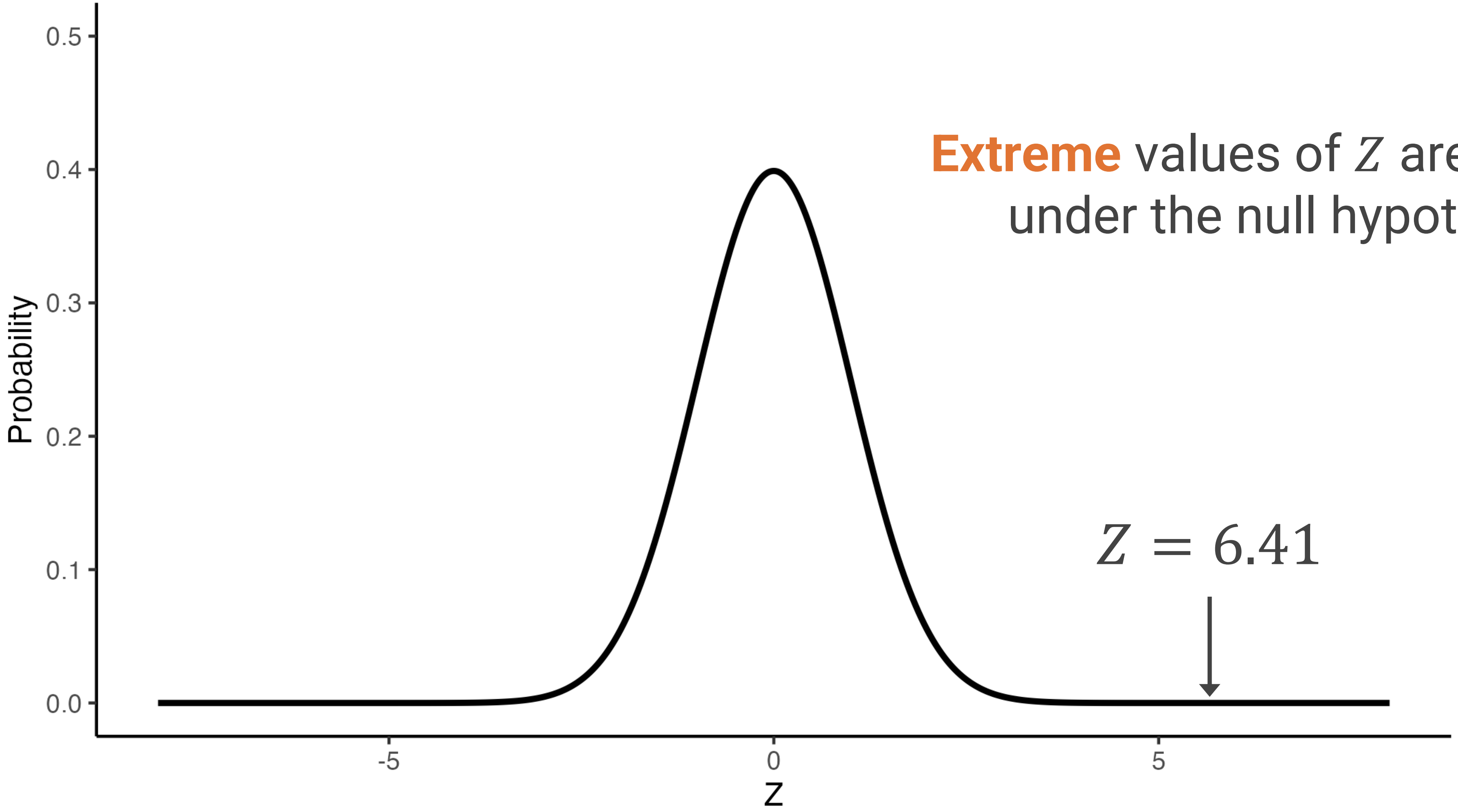
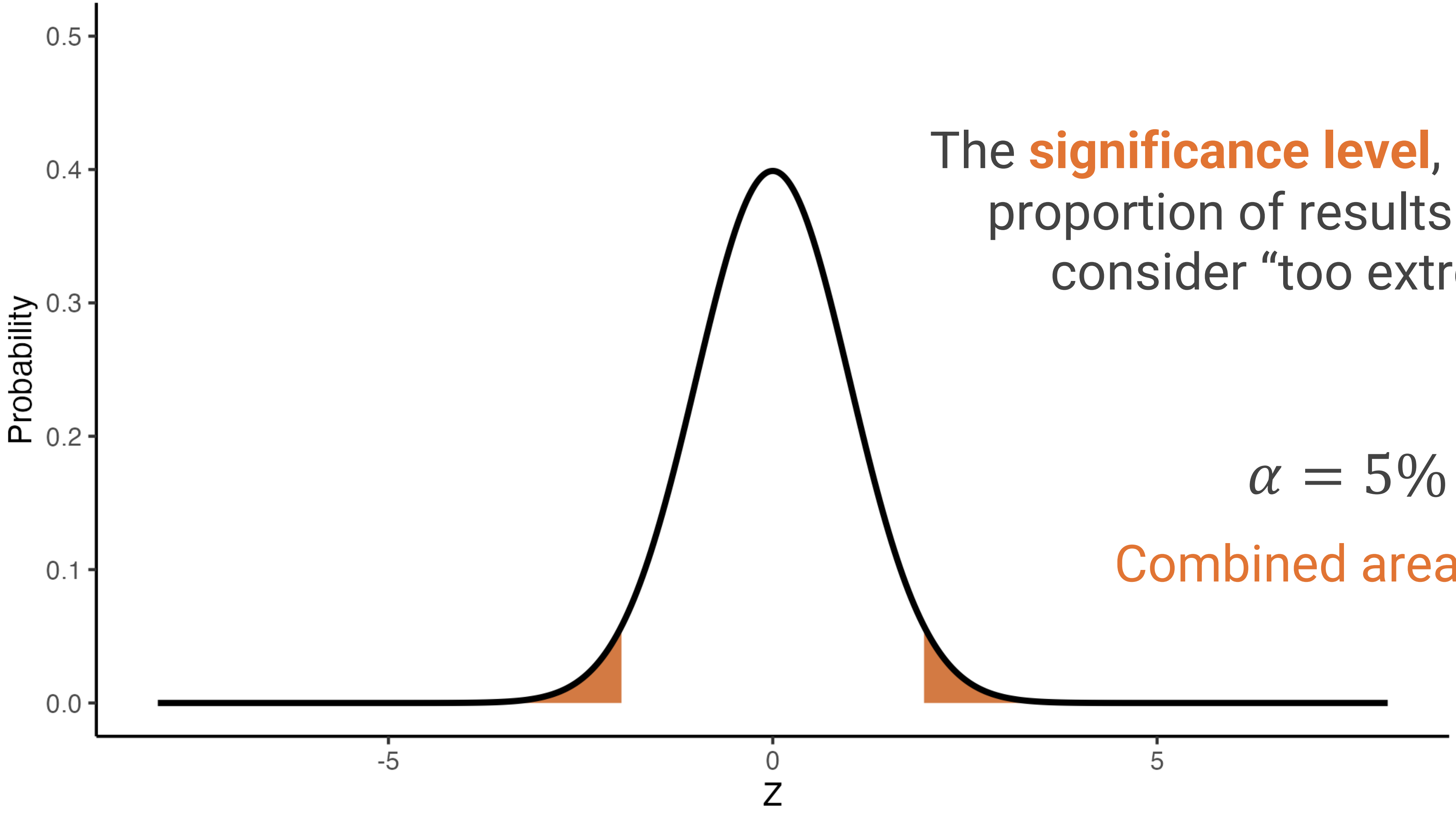


Extreme values of Z are unlikely under the null hypothesis

$$Z = 6.41$$

Null hypothesis testing

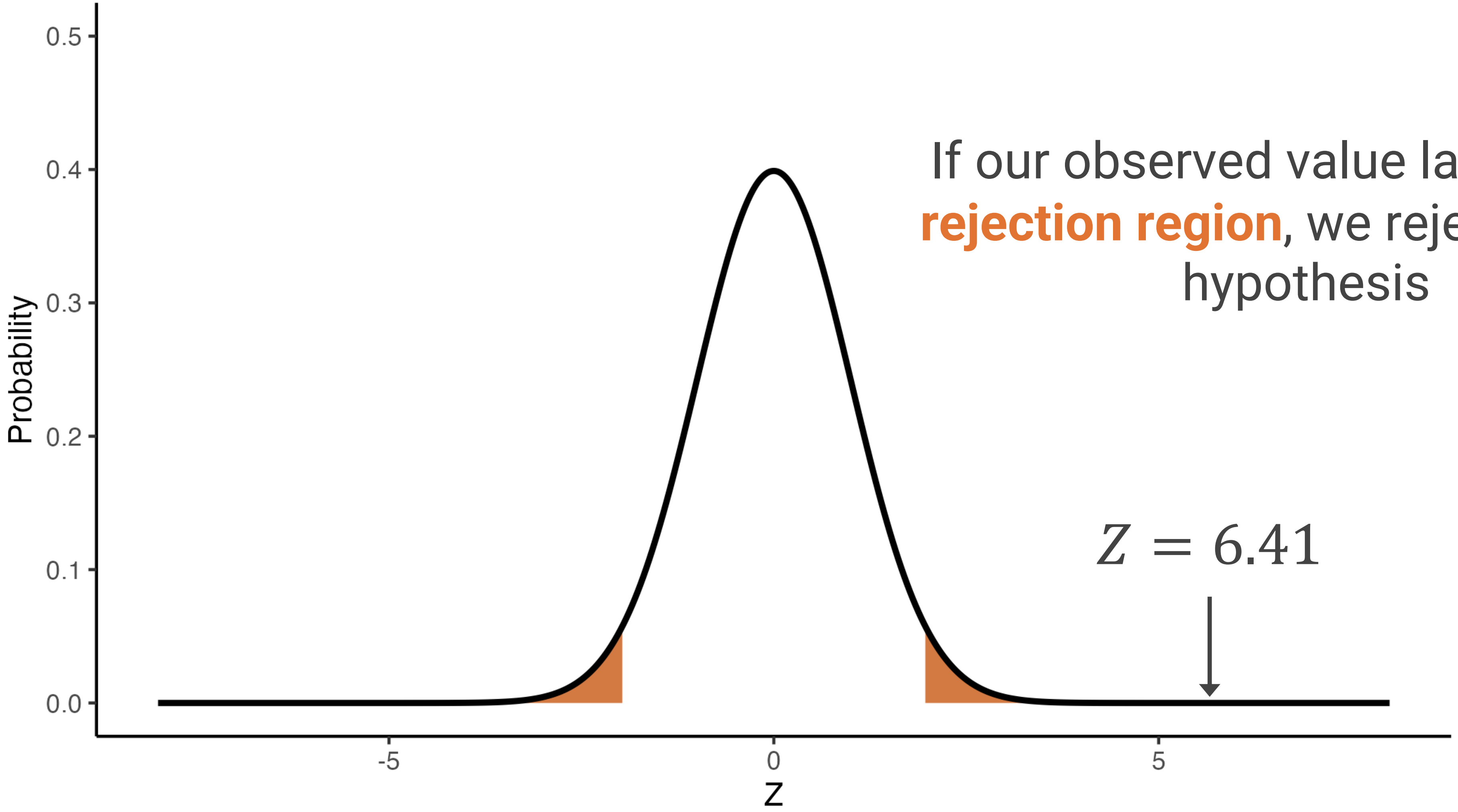


The **significance level**, α, sets the proportion of results that we consider "too extreme"

$$\alpha = 5\%$$

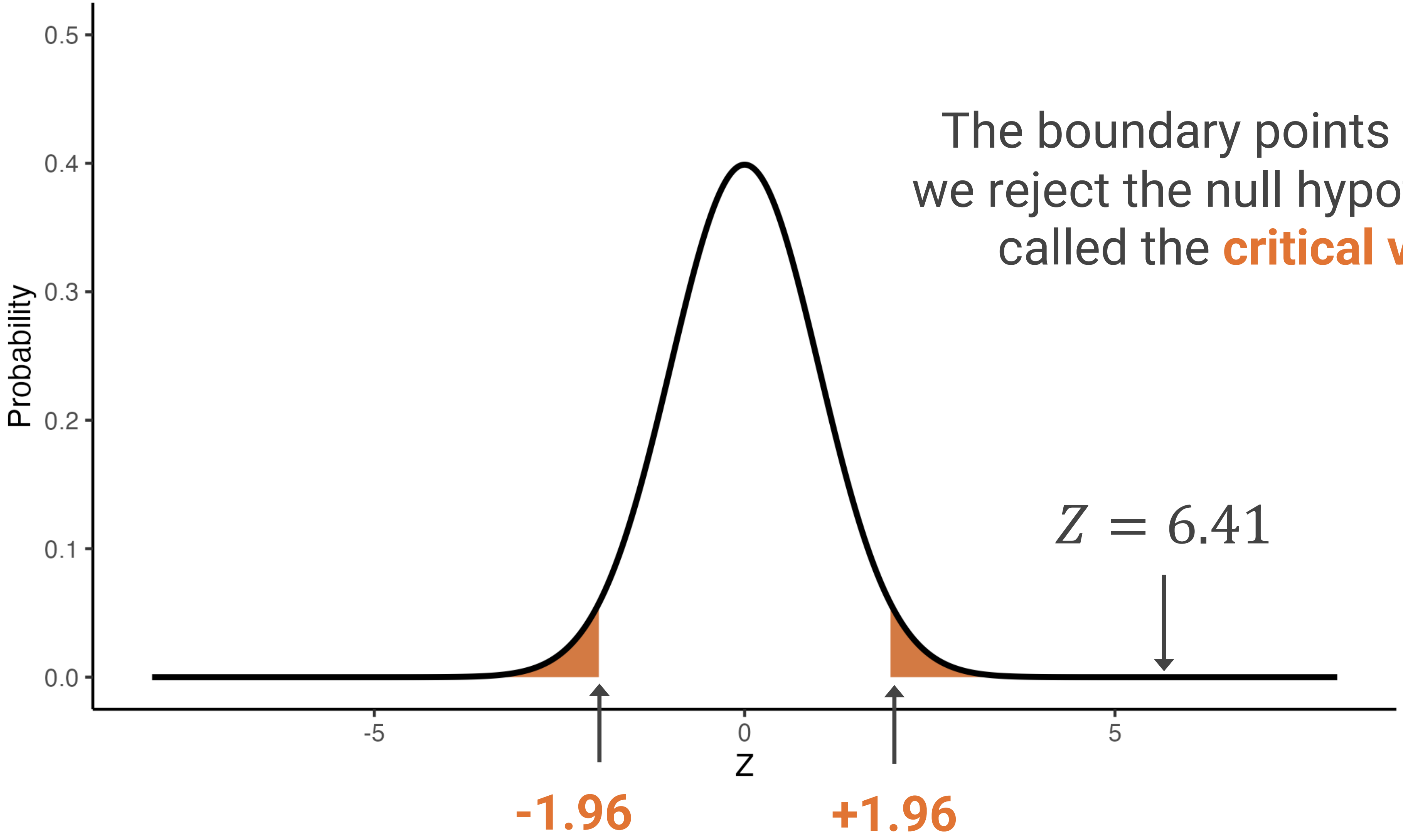
Combined area = 5%

Null hypothesis testing



If our observed value lands in the **rejection region**, we reject the null hypothesis

Null hypothesis testing



The boundary points at which we reject the null hypothesis are called the **critical values**

Null hypothesis testing

Calculate Z

↓

Is Z outside of the region -1.96 to 1.96?

No → Fail to reject the null hypothesis

Yes → Reject the null hypothesis

Null hypothesis testing

		Conclusion about H_0	
		Fail to reject	**Reject**
Truth about H_0	**True**	True negative	False positive
	False		

Null hypothesis testing

		Conclusion about H_0	
		Fail to reject	Reject
Truth about H_0	True	True negative $1 - \alpha$	False positive α
	False		

Null hypothesis testing

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α sets the **false positive rate** of a test. Using α we can control how often we incorrectly conclude that there is a real effect when there is none.

Null hypothesis testing

		Conclusion about H_0	
		Fail to reject	**Reject**
Truth about H_0	**True**	True negative $1-\alpha$	False positive α
	False	**What about this!?**	

α sets the **false positive rate** of a test. Using α we can control how often we incorrectly conclude that there is a real effect when there is none.

Power

In power analysis, we also specify an **alternative hypothesis**

H_0: The population prevalence equals p_0

H_1: The population prevalence equals p, which is different from p_0

Power

In power analysis, we also specify an **alternative hypothesis**

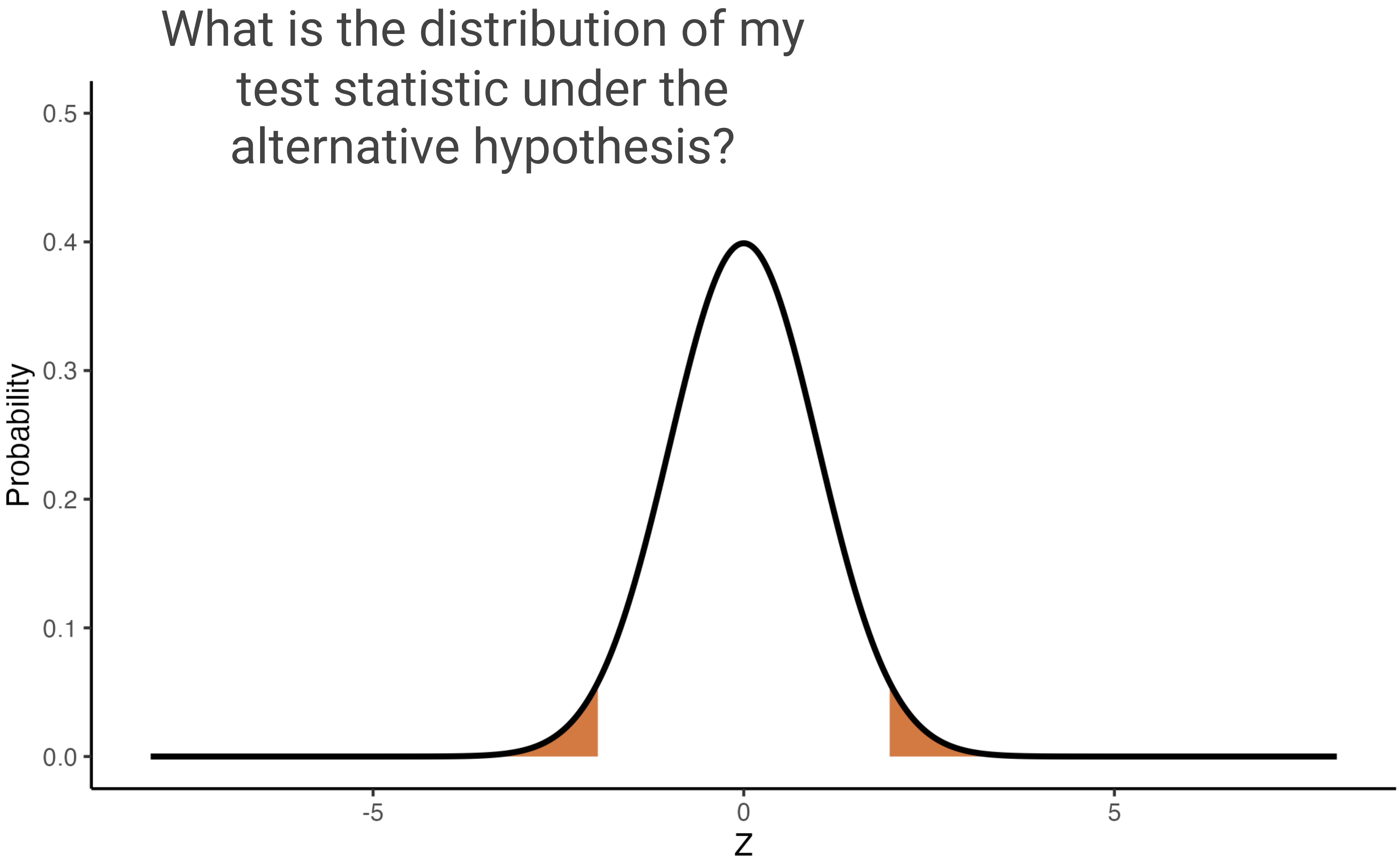
H_0: The population prevalence equals p_0

H_1: The population prevalence equals p, which is different from p_0

For example…

I want to test if the prevalence of *pfcrt* K76T mutations is significantly different from 10%. When powering this test, I assume the true prevalence of K76T mutations is 15%.

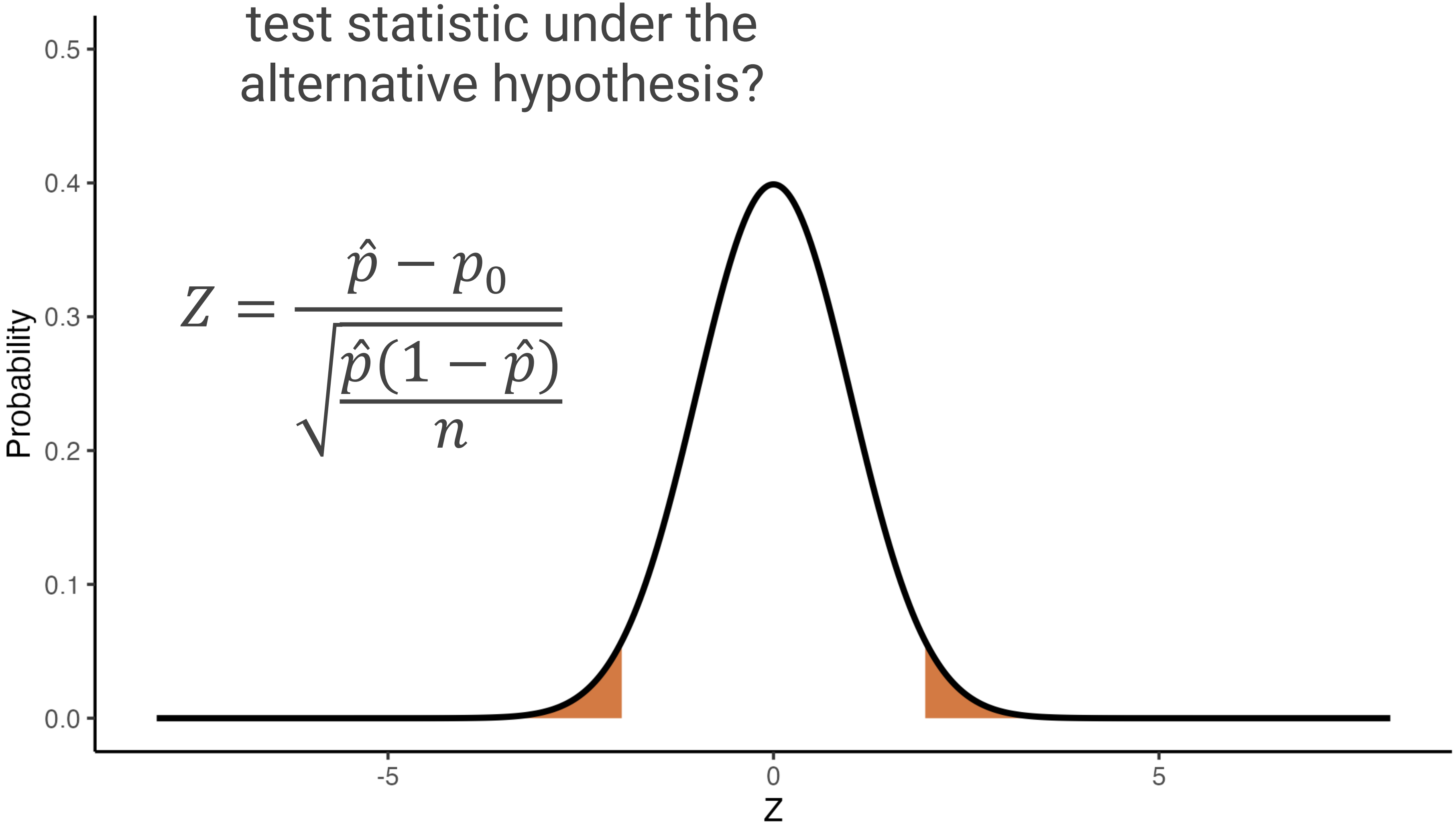
Power


What is the distribution of my test statistic under the alternative hypothesis?
Probability
0.5
0.4
0.3
0.2
0.1
0.0
-5
0
5
Z

Power

What is the distribution of my test statistic under the alternative hypothesis?

$$Z = \frac{\hat{p} - p_0}{\sqrt{\frac{\hat{p}(1-\hat{p})}{n}}}$$



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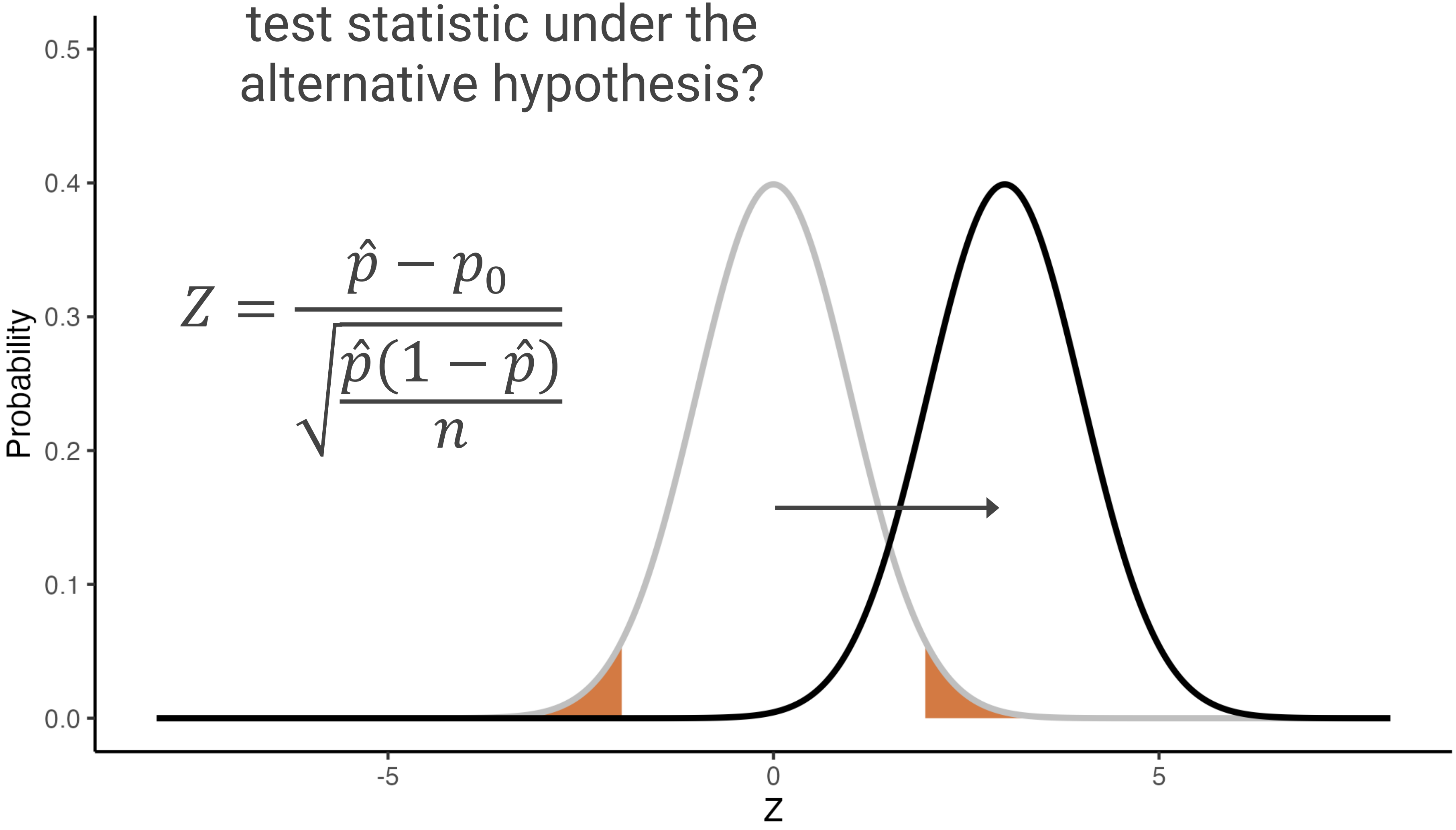
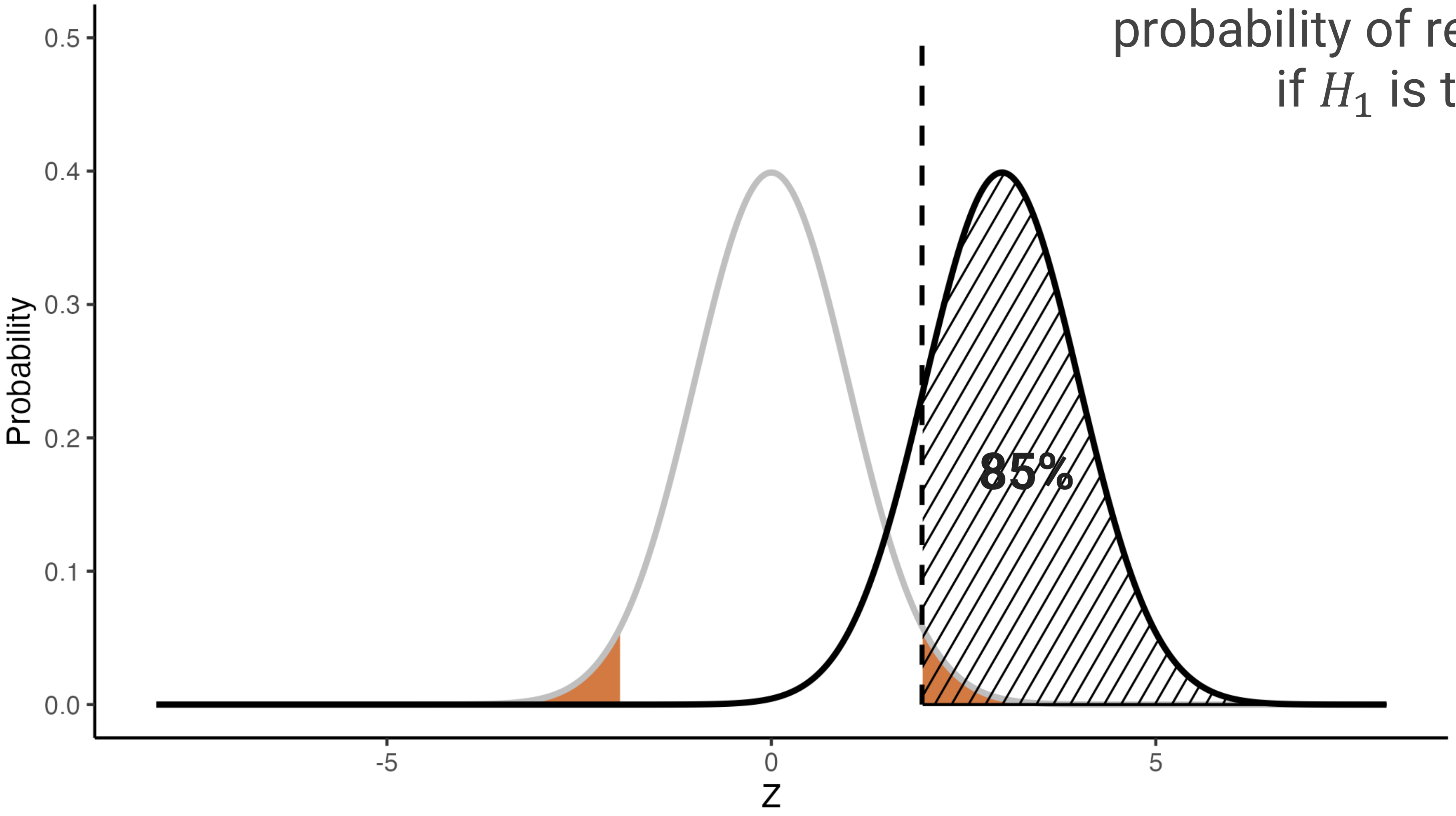
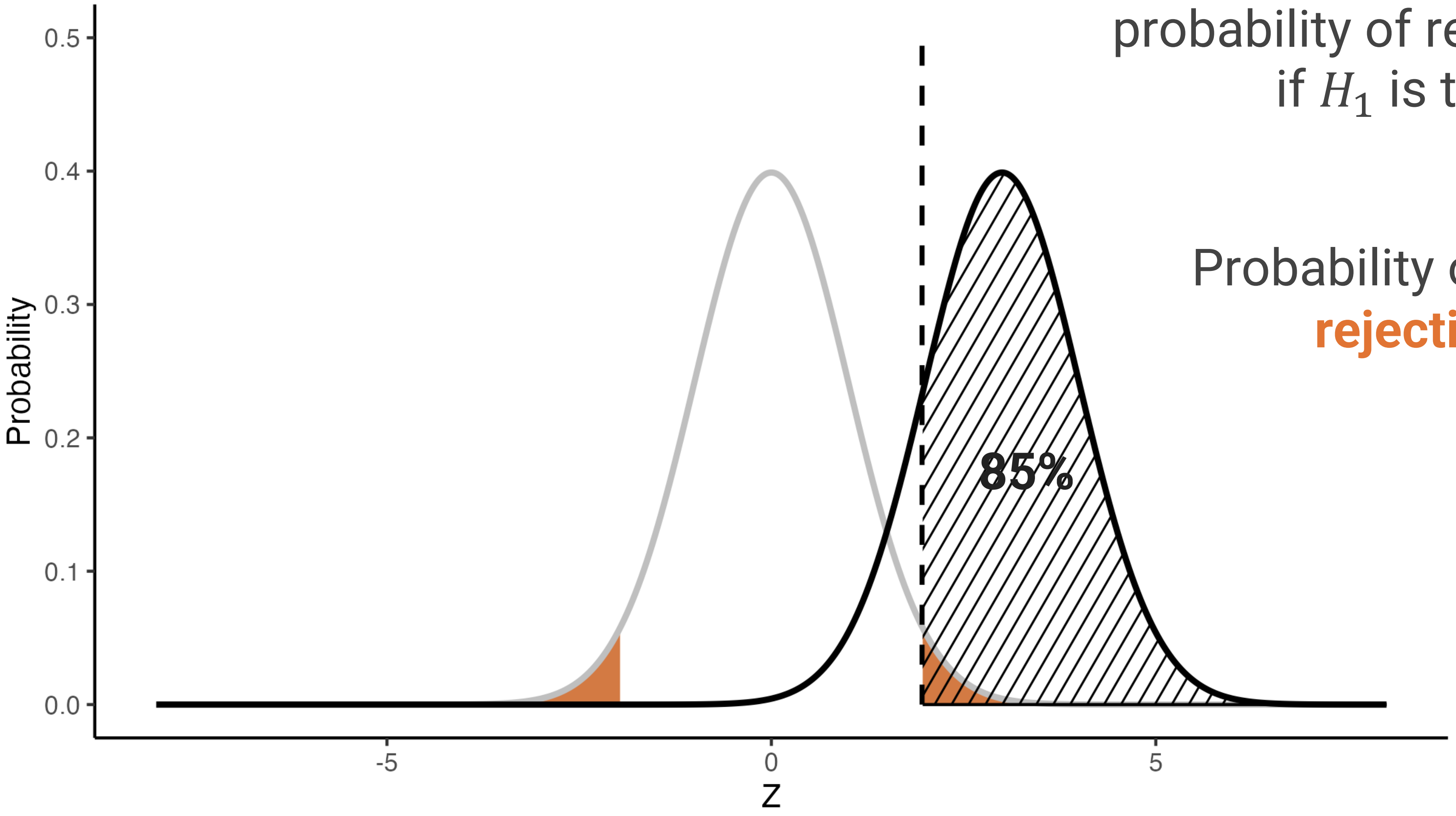


Power

Area under curve gives the probability of rejecting H_0 if H_1 is true



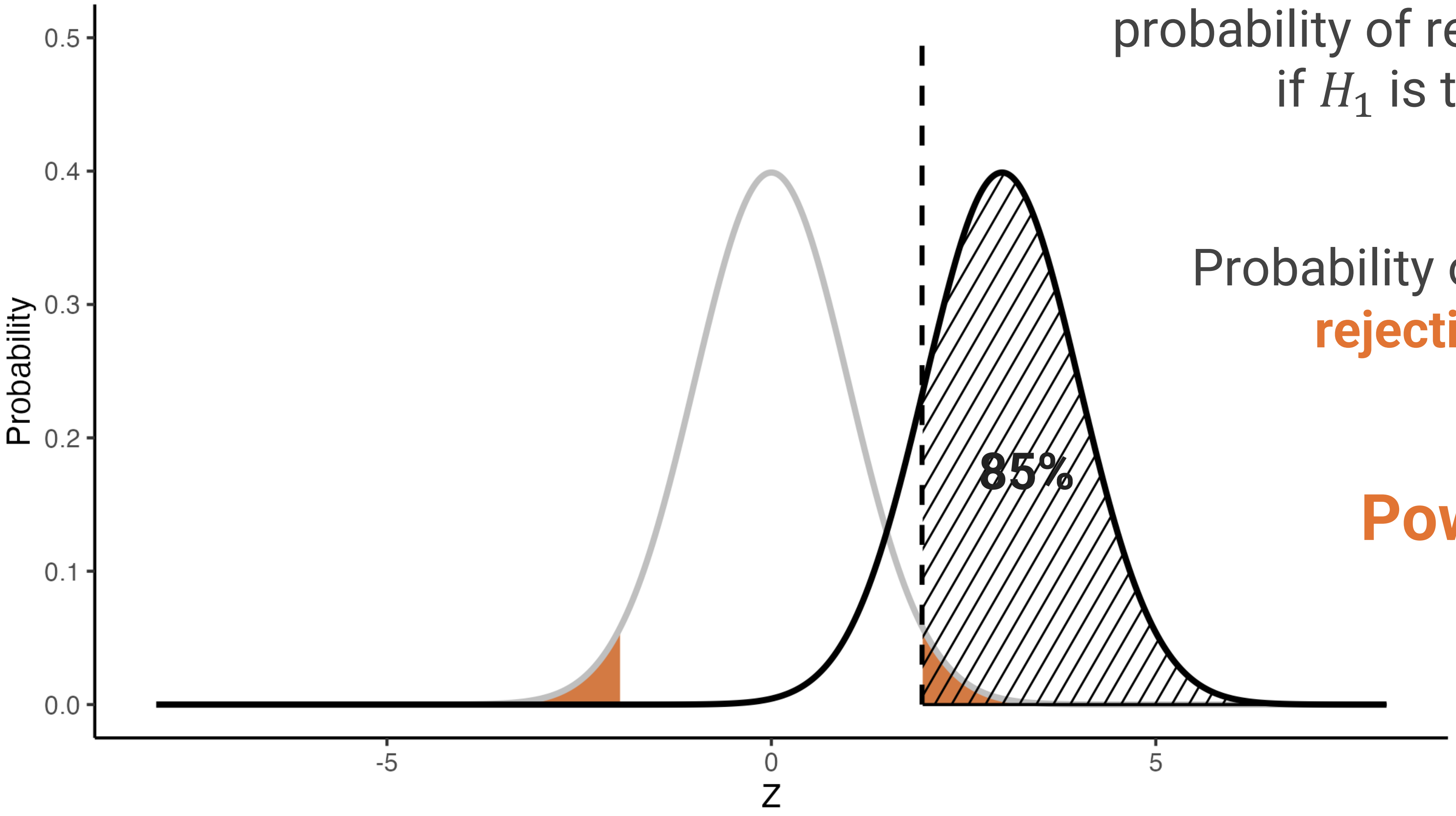
Power



Area under curve gives the probability of rejecting H_0 if H_1 is true

Probability of **correctly rejecting** H_0

Power



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Probability of **correctly rejecting** H_0

Power

Power

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	False	False negative	True positive

Power

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$1-\text{Power}$</td><td>True positive
Power</td></tr>
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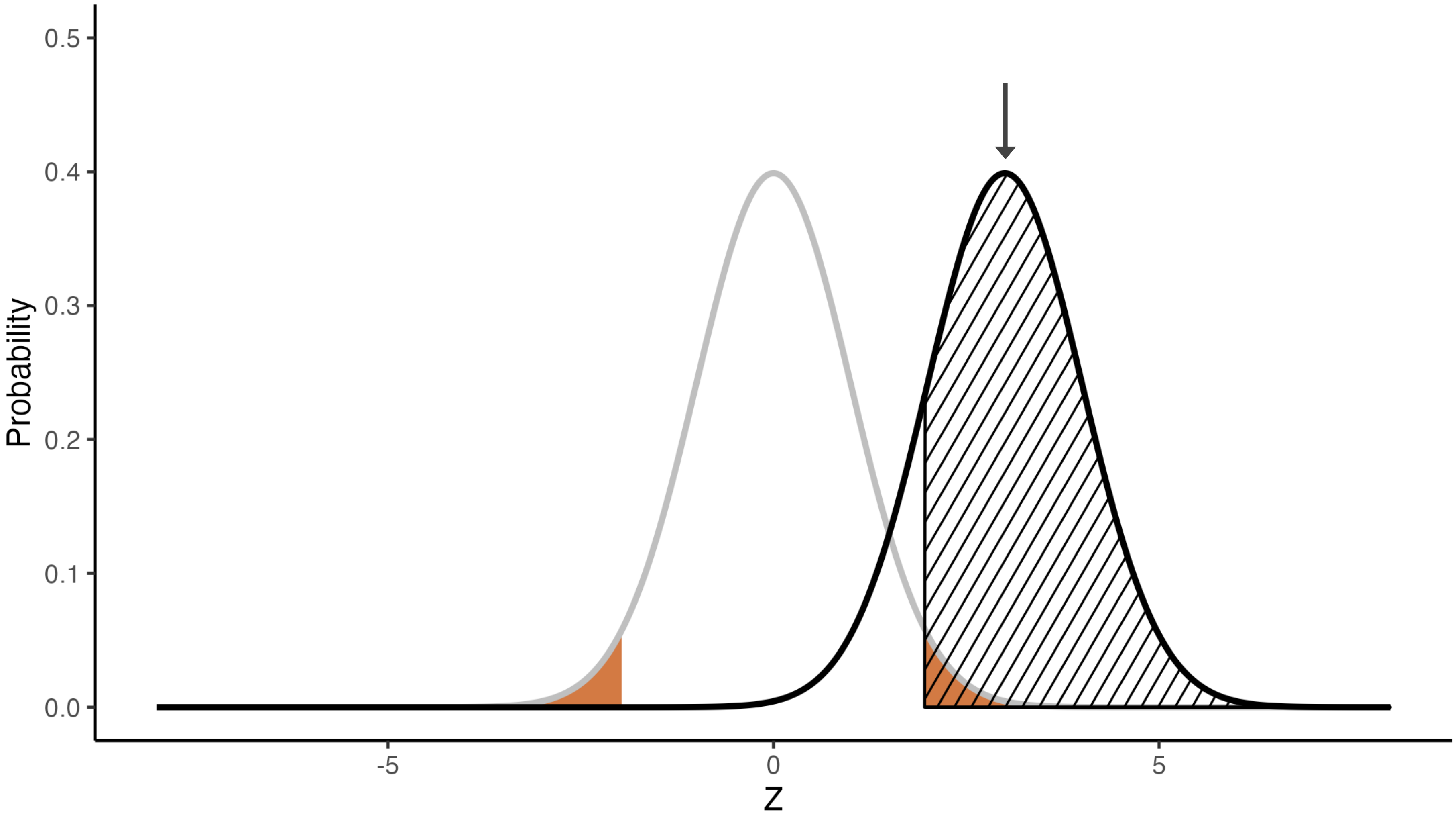
Power

		Conclusion about H_0	
		Fail to reject	Reject
Truth about H_0	True	True negative $1 - \alpha$	False positive α
	False	False negative $1 - \text{Power}$	True positive Power

Power is the probability of **correctly rejecting** the null hypothesis. It is the chance that we find something interesting, given that it is there.

How do we calculate power?



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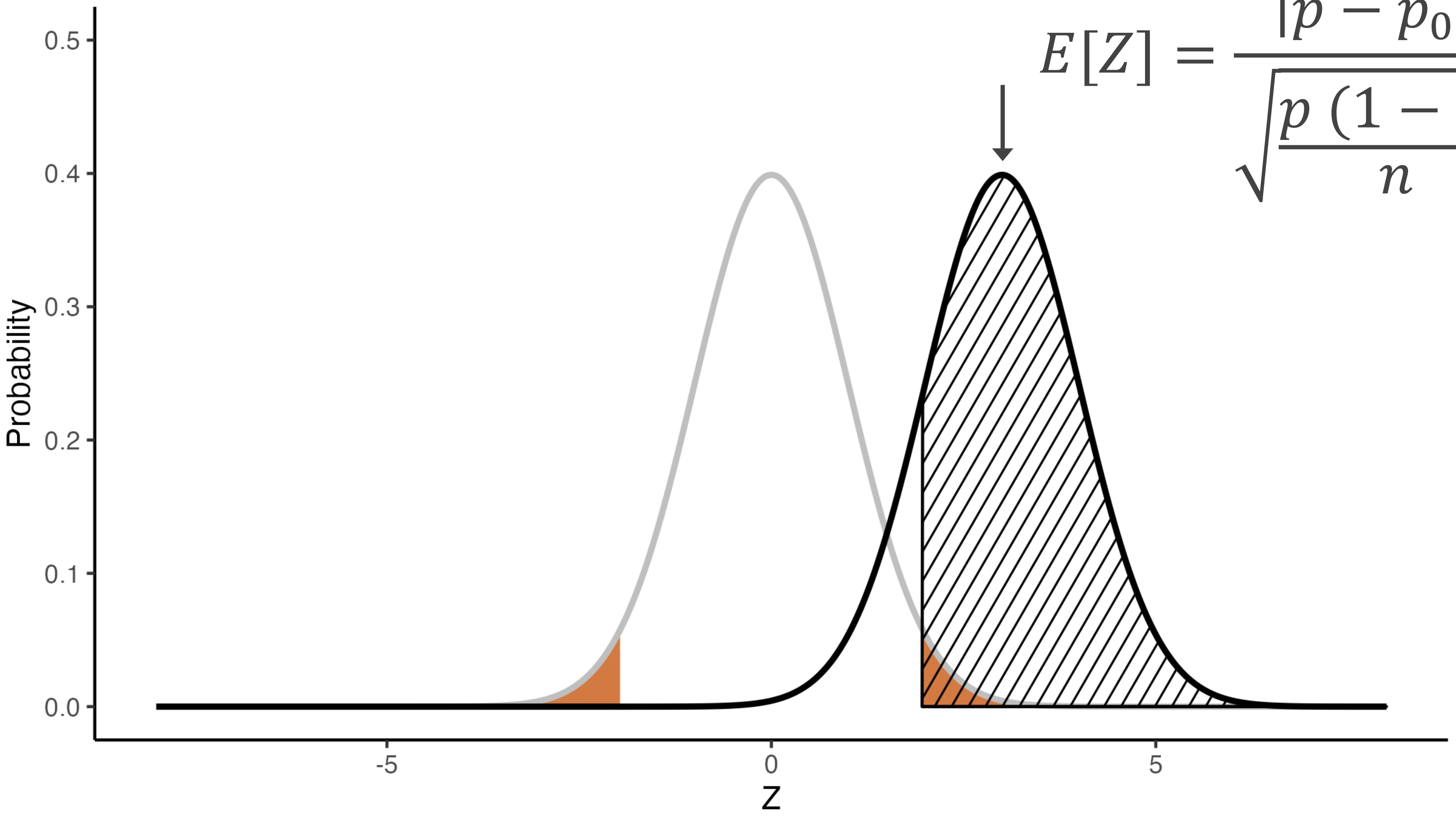
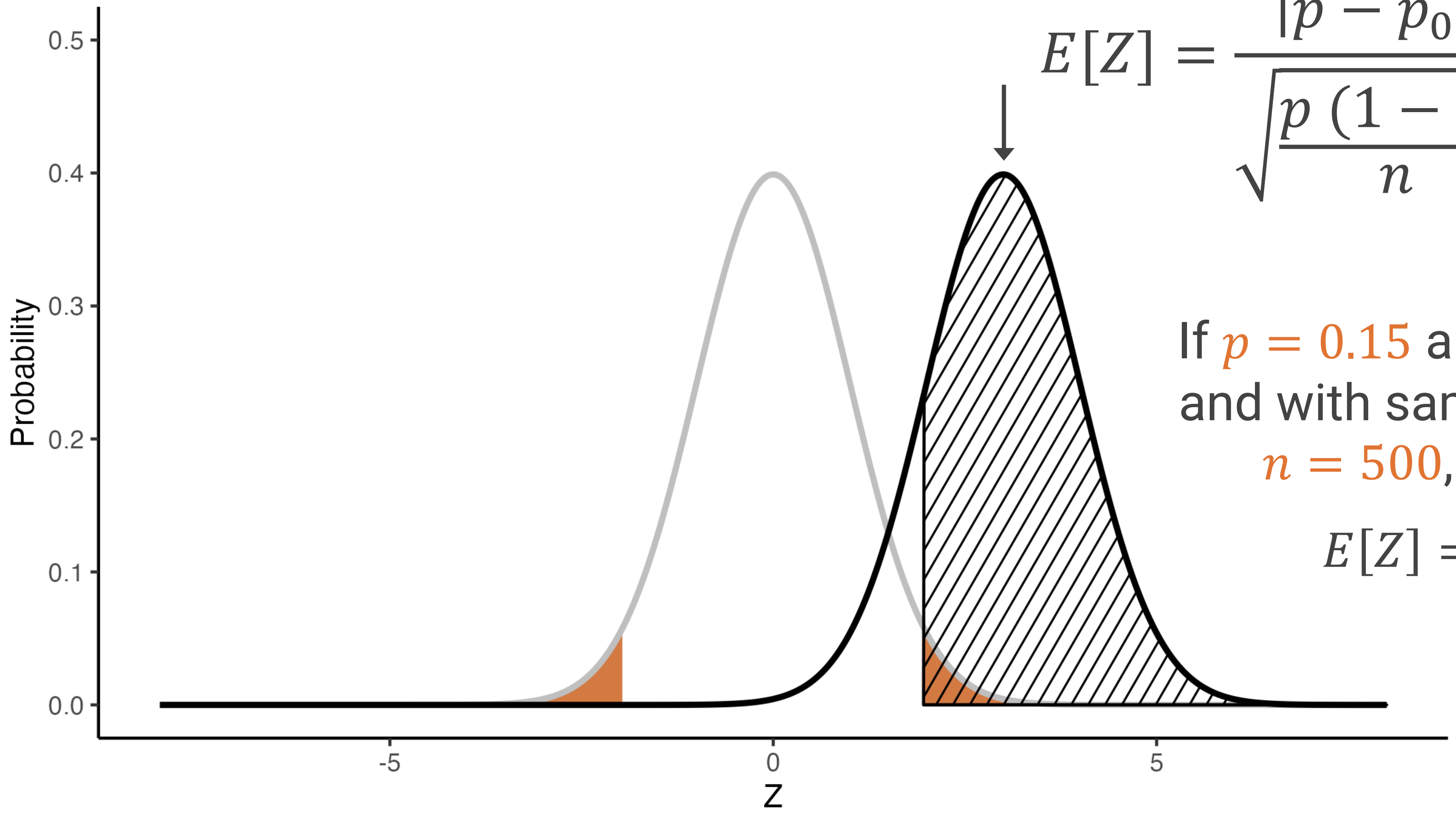


$$E[Z] = \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}$$

How do we calculate power?



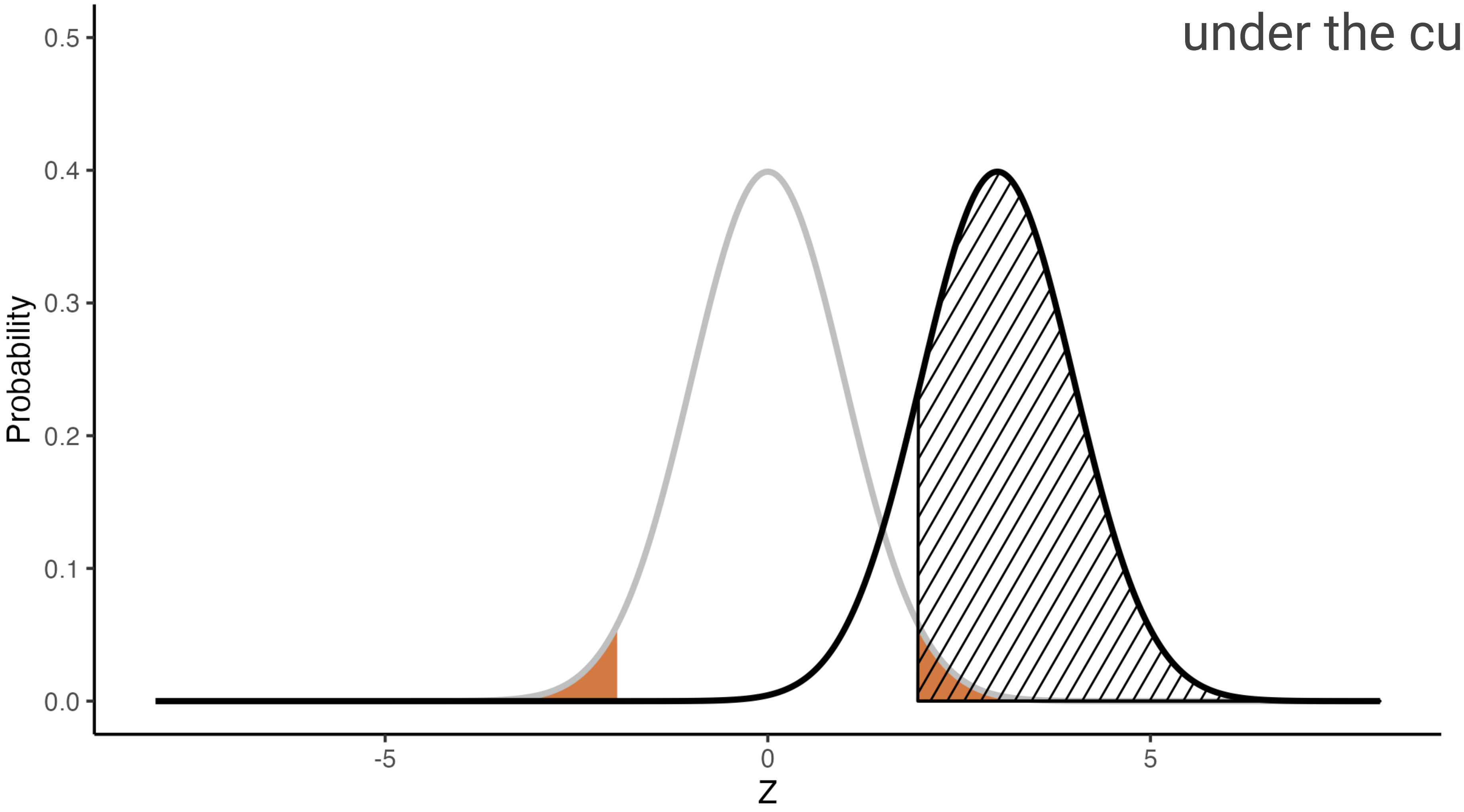
$$E[Z] = \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}$$

If $p = 0.15$ and $p_0 = 0.1$, and with sample size of $n = 500$, we find

$$E[Z] = 3.13$$

How do we calculate power?

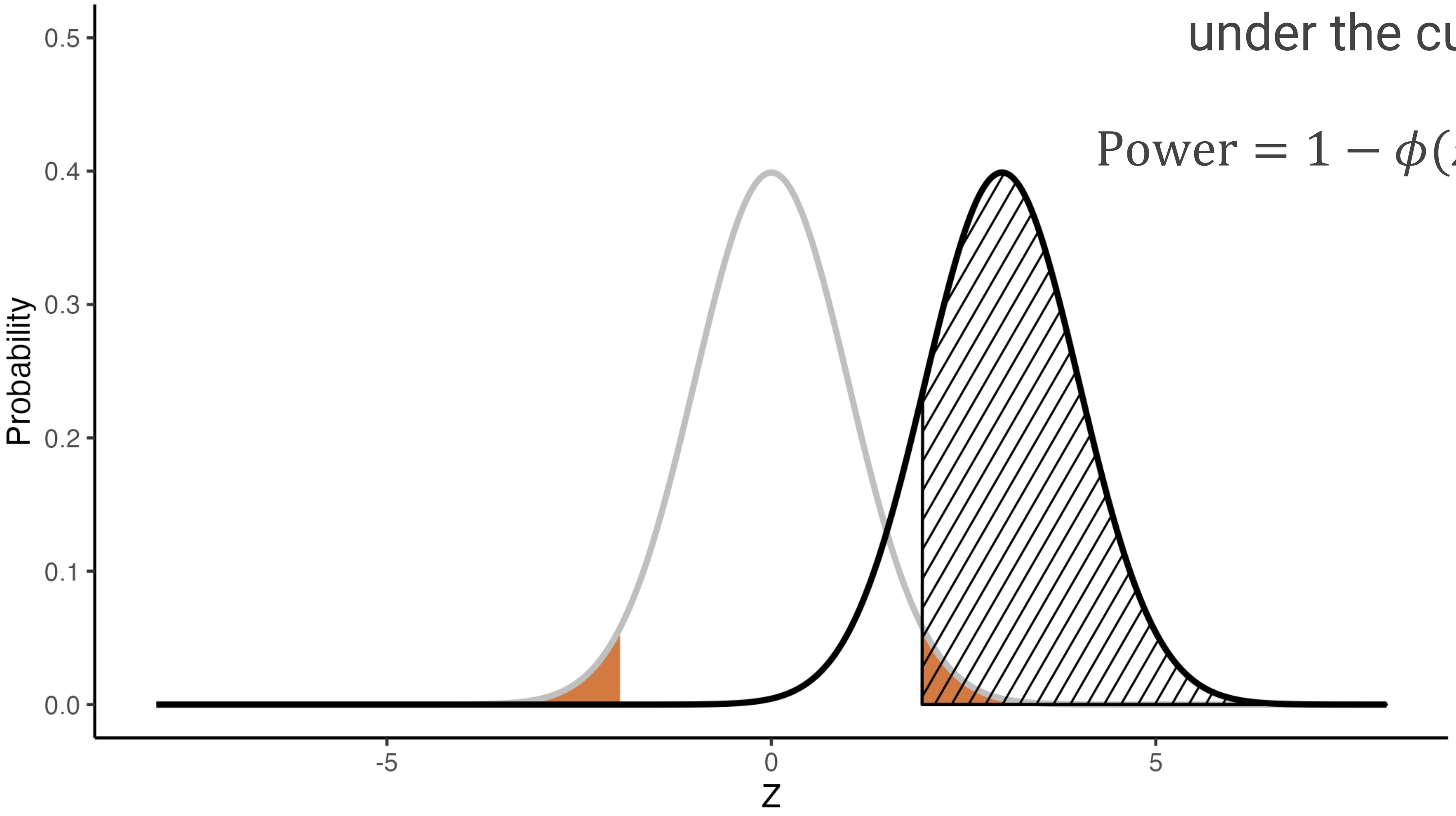
The function $\phi()$ gives us the area under the curve



How do we calculate power?

The function $\phi()$ gives us the area under the curve

$$\text{Power} = 1 - \phi(z_{1-\alpha/2} - E[Z])$$



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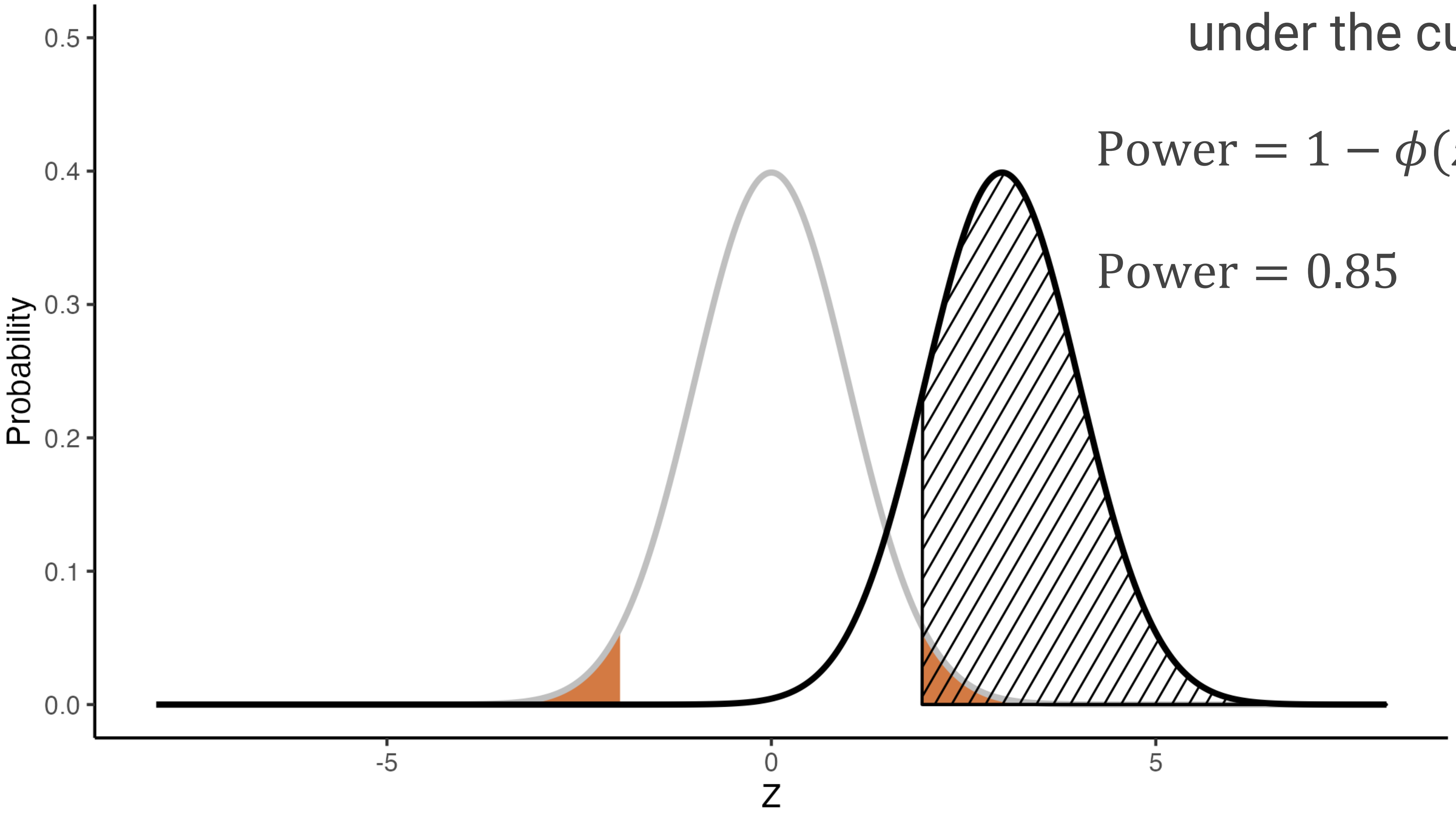
$$\text{Power} = 1 - \phi(z_{1-\alpha/2} - E[Z])$$

$$\text{Power} = 0.85$$



Power as a function of sample size

$$\text{Power} = 1 - \phi(z_{1-\alpha/2} - E[Z])$$

Power as a function of sample size

$$\text{Power} = 1 - \phi\left(z_{1-\alpha/2} - \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}\right)$$

Power as a function of sample size

$$\text{Power} = 1 - \phi\left(z_{1-\alpha/2} - \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}\right)$$

Power varies as a function of sample size

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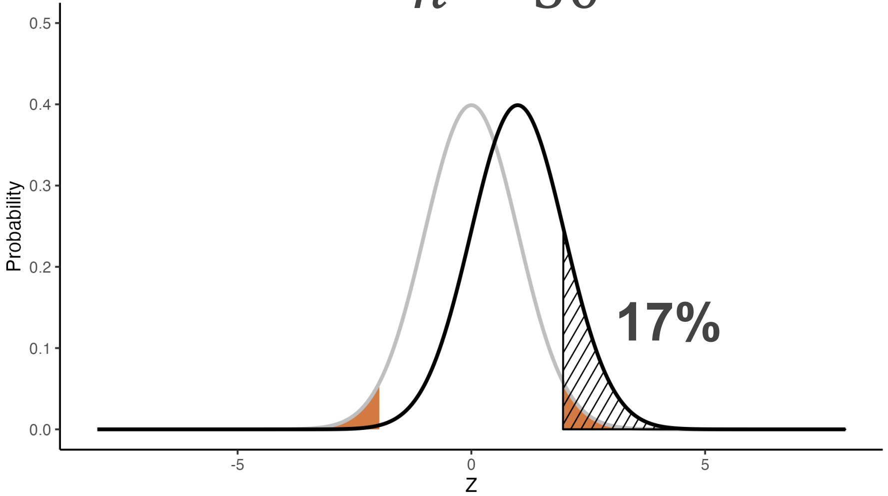
Power varies as a function of sample size

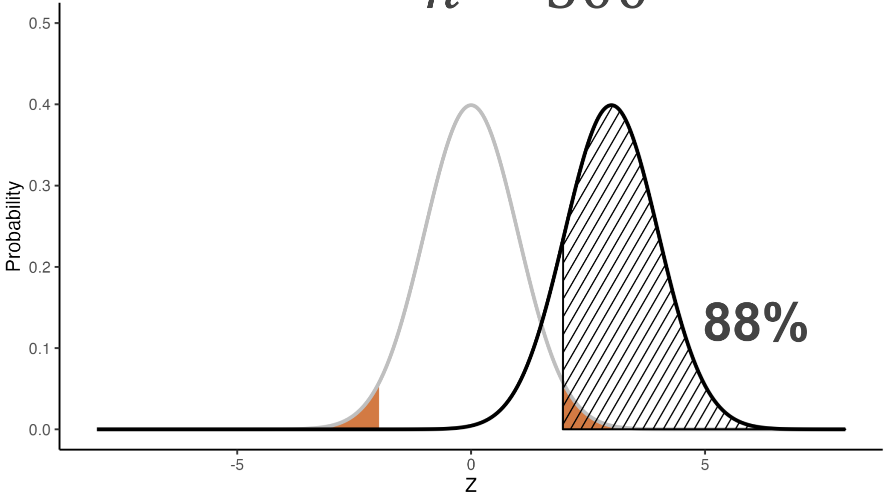
Small sample

$n = 50$

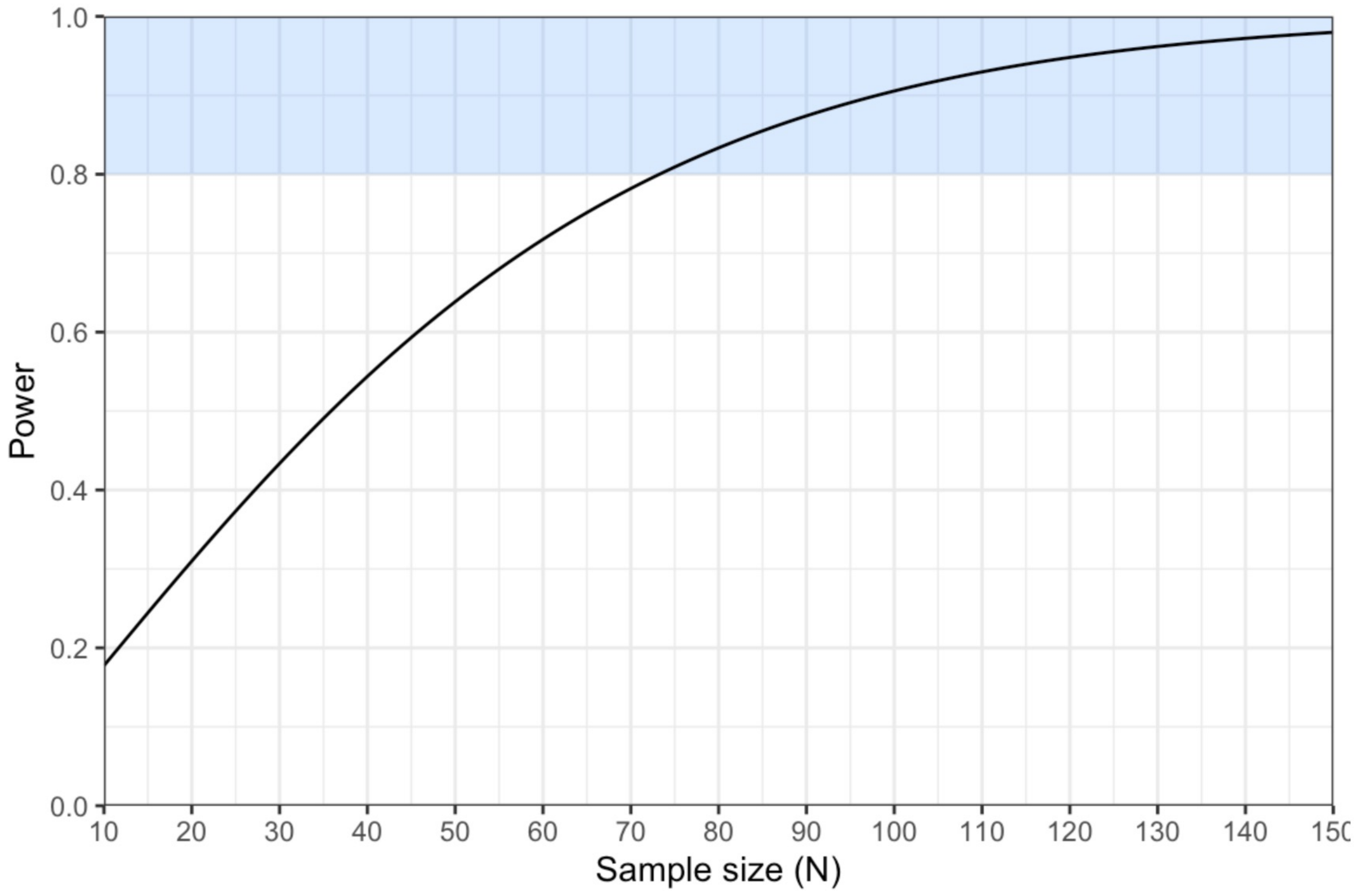


Large sample

$n = 500$

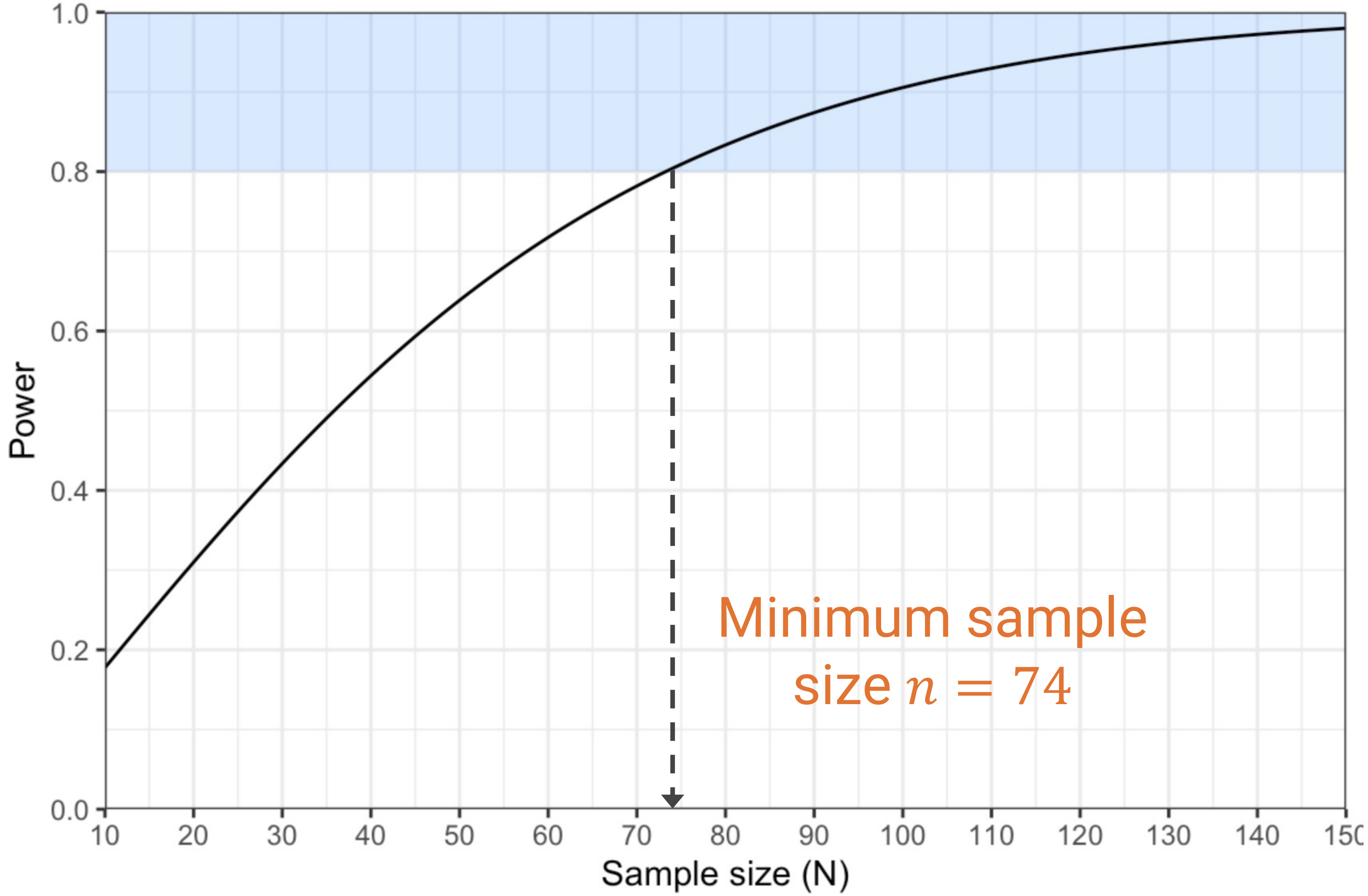


Power curves



80% power

Power curves



80% power

Minimum sample size $n = 74$

Sample size formulae

$$\text{Power} = 1 - \phi\left(z_{1-\alpha/2} - \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}\right)$$

Can we reverse-engineer this to find the value of n that achieves a target power?

Sample size formulae

$$\text{Power} = 1 - \phi\left(z_{1-\alpha/2} - \frac{|p - p_0|}{\sqrt{\frac{p(1-p)}{n}}}\right)$$

Can we reverse-engineer this to find the value of n that achieves a target power?

$$n = \left(z_{1-\beta} + z_{1-\frac{\alpha}{2}}\right)^2 \frac{p(1-p)}{(p - p_0)^2}$$

Where $\beta = 1 - \text{Power}$. For 80% power, we find $z_{1-\beta} = 0.84$

Summary

- We can ask questions using **null hypothesis tests**
- A null hypothesis is a statement of **no effect/difference** between groups
- The significance level α controls the **false-positive rate**
- **Power** is the true positive rate. It is the chance of **correctly rejecting the null hypothesis**.
- Power increases with sample size. We can use power curves or sample size formulae to choose a value of n

Activity

Format: Interactive R code, accessed through the web

- Short quiz on hypothesis testing
- **Test for change in prevalence**
  - Calculate power
  - Calculate minimum sample size
- **Test for detection of rare *pfk13* variant**
  - Calculate power
  - Calculate minimum sample size

Please follow your own link!

https://tinyurl.com/bd4um5mj