Session 09: Hypothesis Testing

Stats 60/Psych 10
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Summer 2020

This time (and next week)

- Hypothesis testing
- What p-values mean - and don't mean
- Connection to z-scores

The three fundamental goals of statistics

- Describe
- Decide
- Predict

- Hypothesis testing provides us with a tool to make decisions in the face of uncertainty using data

Do checklists improve surgical outcomes?

A Surgical Safety Checklist to Reduce Morbidity and Mortality in a Global Population

N ENGL J MED 360;5 NEJM.ORG JANUARY 29, 2009

We hypothesized that a program to implement a 19-item surgical safety checklist designed to improve team communication and consistency of care would reduce complications and deaths associated with surgery.

Between October 2007 and September 2008, eight hospitals in eight cities… participated in the World Health Organization's Safe Surgery Saves Lives program.

The rate of death was 1.5% before the checklist was introduced and declined to 0.8% afterward (P = 0.003). Inpatient complications occurred in 11.0% of patients at baseline and in 7.0% after introduction of the checklist (P<0.001).

Huh?

Do body-worn cameras improve policing?

- 2,224 DC Metro PD officers randomly assigned to wear BWC or not
- Compared use of force and number of complaints between groups

THE LAB @ DC

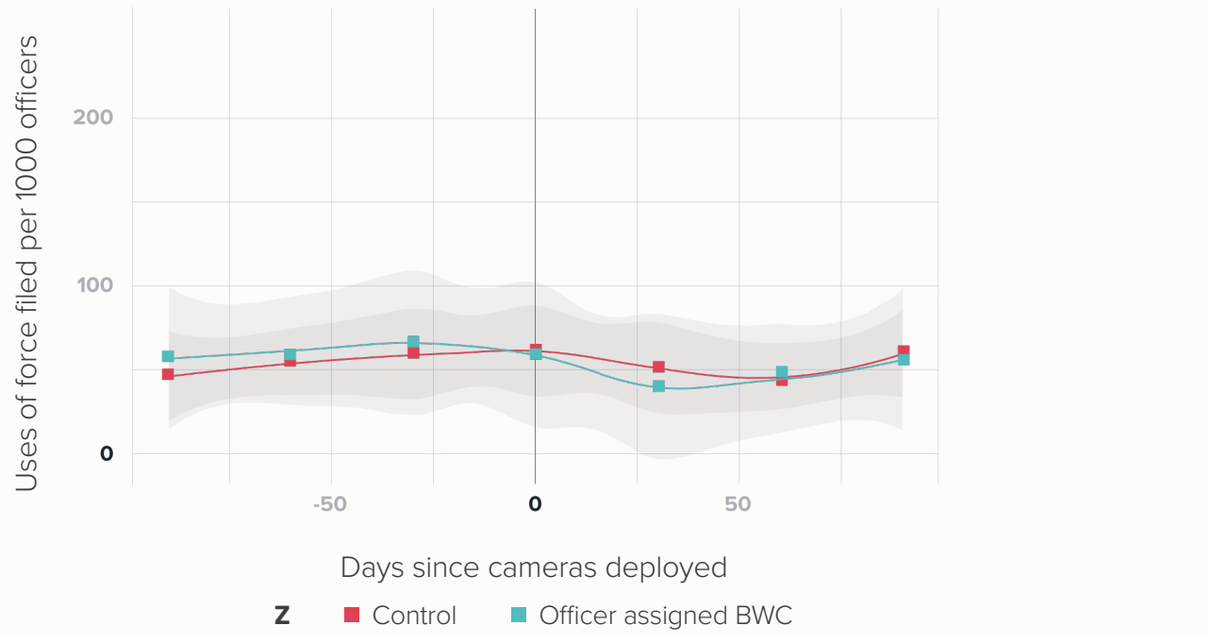
GOVERNMENT OF THE DISTRICT OF COLUMBIA
MURIEL BOWSER, MAYOR

Body worn cameras: no effect on policing outcomes

- "We are unable to reject the null hypotheses that BWCs have no effect on police use of force, citizen complaints, policing activity, or judicial outcomes."
- Did they just use a triple negative?
  - "unable to reject the null hypotheses"

FIG. 4. Uses of Force per 1,000 Officers, 90 days before and after BWC deployment.

This figure plots pre- and post-treatment uses of force for both control and treatment group officers. As the chart indicates, there is no statistically significant difference between the two groups in either the 90-day period before or after the deployment of BWCs (which occurs on day 0).



“Null hypothesis statistical testing” (NHST)

- The most commonly used approach to perform statistical tests
  - Gerrig & Zimbardo (2002): NHST is the “backbone of psychological research”
- Almost all researchers continue to use it
- Many people think that it’s a bad way to do science
  - Bakan (1966): “The test of statistical significance in psychological research may be taken as an instance of a kind of essential mindlessness in the conduct of research”
  - Luce (1988): Hypothesis testing is “a wrongheaded view about what constitutes scientific progress”

Prepare yourself for mental gymnastics

- Hypothesis testing is notoriously difficult to understand
- Because it's built in a way that violates our natural intuitions!

How you might think hypothesis testing should work

- We start with a hypothesis
  - Body-worn cameras will reduce police misconduct
- We collect some data
  - Randomized controlled trial comparing BWC to no BWC
- We determine whether the data provide convincing evidence in favor of the hypothesis
  - What is the likelihood that the hypothesis is true, given the data along with everything else we know?

How null hypothesis testing actually works

- We start with a hypothesis
  - Body-worn cameras will reduce police misconduct
- We flip it to generate a “null hypothesis”, which we assume is true
  - There is no effect of BWCs on police misconduct
- We collect some data
  - Randomized controlled trial comparing BWC to no BWC
- We determine how likely the data would have been, assuming that the hypothesis is wrong
  - If it is unlikely, then we we decide that we can “reject the null hypothesis “
  - If it is likely, then we “fail to reject the null hypothesis”
    - This doesn’t mean that we decide that there is no effect!

Why do you think we are spending two sessions talking about something that so many people think is a bad idea?

Top

The steps of null hypothesis testing

1. Make predictions based on your hypothesis (*before seeing the data*)
2. Collect some data
3. Identify null and alternative hypotheses
4. Fit a model to the data that represents the alternative hypothesis and compute a test statistic
5. Compute the probability of the observed value of that statistic assuming that the null hypothesis is true
6. Assess the “statistical significance” of the result

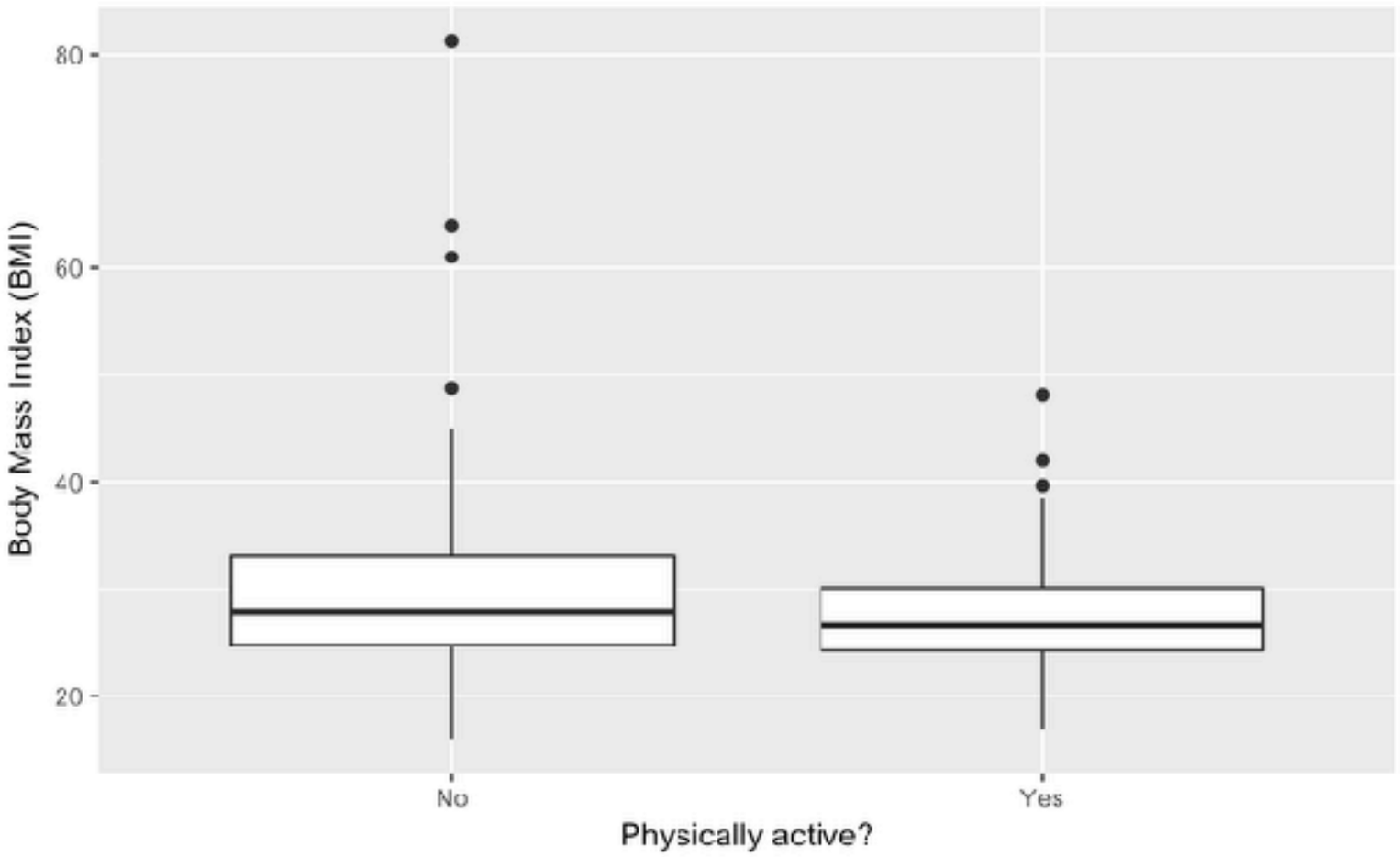
An example hypothesis: Is physical activity related to body mass index?

- In the NHANES dataset, participants were asked whether they engage regularly in moderate or vigorous-intensity sports, fitness or recreational activities
- Also measured height and weight and computed Body Mass Index

$$BMI = \frac{Weight(kg)}{Height(m)^2}$$

- Hypothesis of interest: BMI is related to physical activity
- Prediction: BMI should be greater for inactive vs. active individuals

Step 2: Collect some data

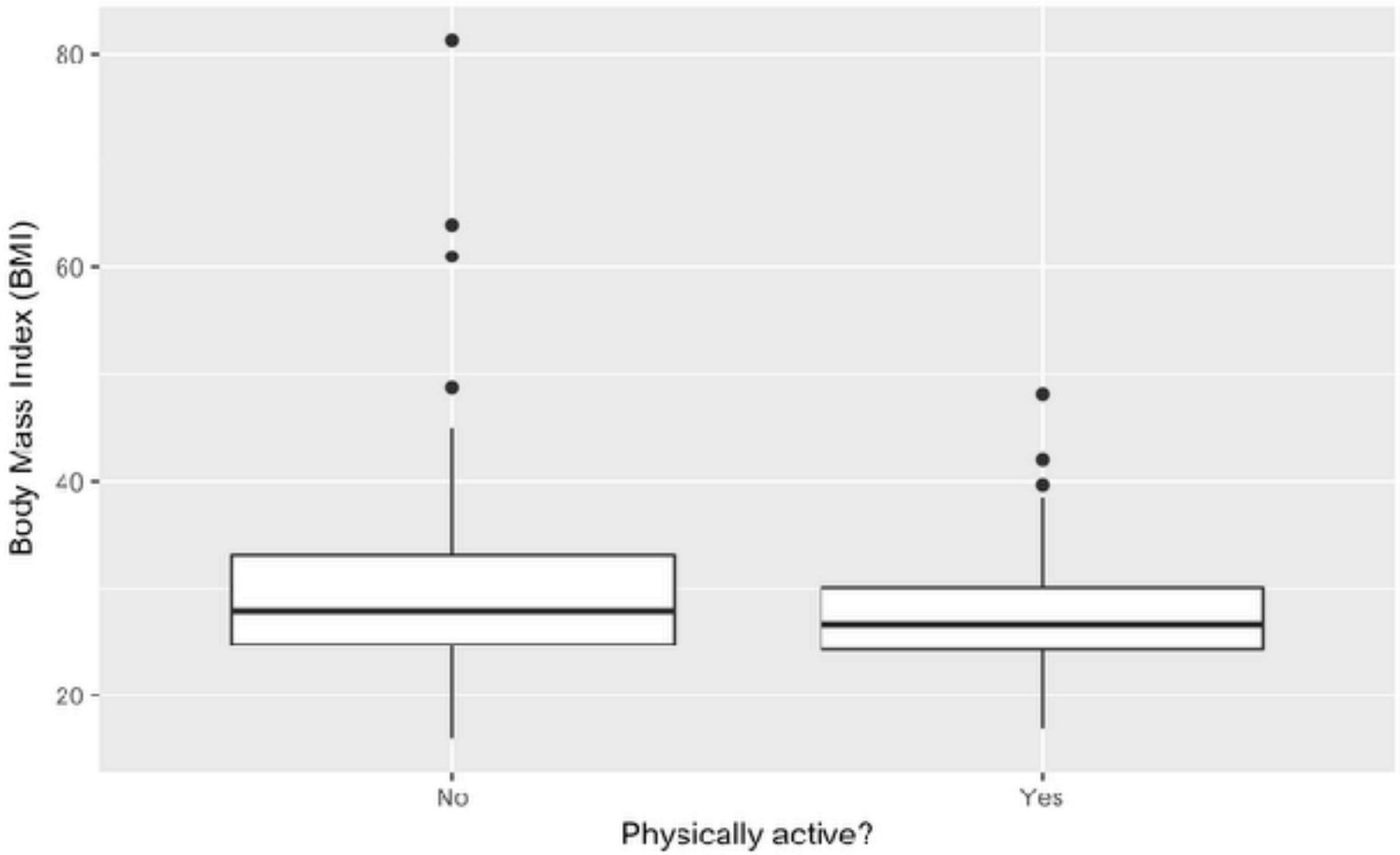


	N	mean BMI	SD
Active	125	27.41	5.07
Not Active	125	29.64	8.83

250 individuals sampled from NHANES

Exercise: compute confidence intervals

- What are the confidence intervals for the mean for each group?



	N	mean BMI	SD
Active	125	27.41	5.07
Not Active	125	29.64	8.83

Step 3: What are the "null hypothesis" (H_0) and "alternative hypothesis" (H_A)?

- H_0: The baseline against which we test our hypothesis of interest
  - What would the data look like if there was no effect?
  - Always involves some kind of equality (=, ≤, or ≥)
- This is compared to an "alternative hypothesis" (H_A)
  - What we expect if there actually is an effect
  - Always involves some kind of inequality (≠ ,>, or <)
- *Null hypothesis testing operates under the assumption that the null hypothesis is true*

BMI example: Null and alternative hypotheses

- H_A:
  - BMI for active people is less than BMI for inactive people in the population
    - $\mu_{active} < \mu_{inactive}$
    - This is a “directional” hypothesis
  - Could also have a “non-directional” hypothesis
    - $\mu_{active} \neq \mu_{inactive}$
- H_0:
  - BMI for active people is greater than or equal to BMI for inactive people in the population
    - $\mu_{active} \geq \mu_{inactive}$
    - $\mu_{active} = \mu_{inactive}$ (for non-directional H_A)

Step 4: Fit a model to the sample data and compute a test statistic

$$test\ statistic = \frac{signal}{noise} = \frac{effect}{error}$$

- The test statistic quantifies the amount of evidence against the null hypothesis, compared to the noise in the data
- It usually has a probability distribution associated with it
  - if not, then we can often compute one using simulation

BMI: What is our test statistic of interest?

- "Student's t" statistic
  - Measures the difference of means between two groups
  - Distributed according to a *t* distribution when the sample size is small and the population SD is unknown

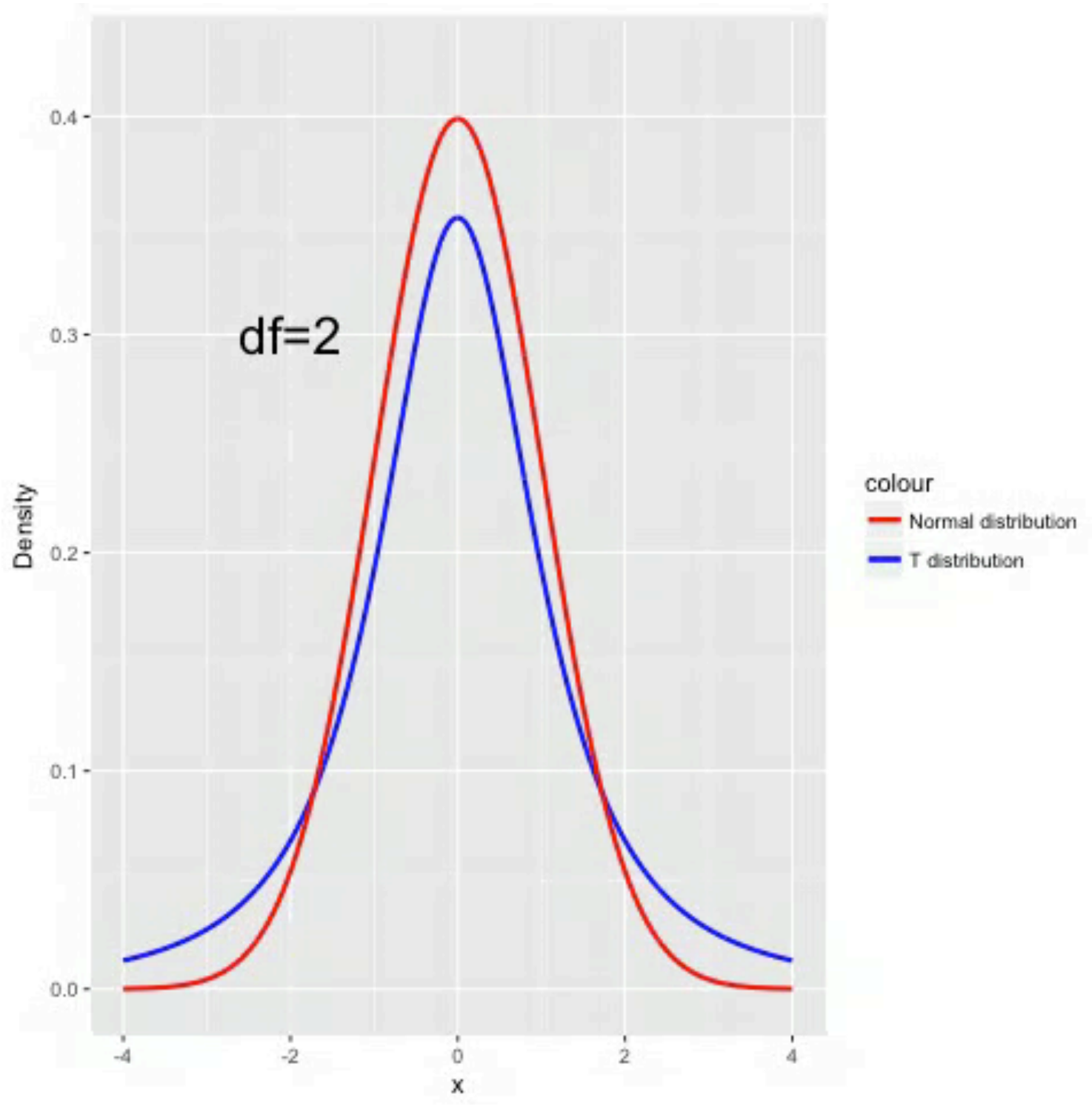
Statistician William Sealy Gosset, AKA "Student"

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{S_1^2}{N_1} + \frac{S_2^2}{N_2}}}$$

$\bar{X}_1$: sample mean S_1^2 : sample variance

N_1 : sample size

The t distribution vs. the normal (Z) distribution



Step 5: Determine the probability of the test statistic under the null hypothesis

- How likely is it that we would see an effect of this size if there really is no effect?
- To do this, we need to know the distribution of the statistic under the null hypothesis
- We can then ask how likely our observed value is within that distribution
- Two ways to determine this:
  - Theoretical distribution
  - Null distribution obtained using simulation

A simple example: Is this coin fair?

- Do an experiment: 100 flips
- Statistic of interest: 70 heads
- H_0: p(heads)=0.5
- H_A: p(heads) ≠ 0.5
- How likely are we to observe 70 heads on 100 flips if H_0 is true?

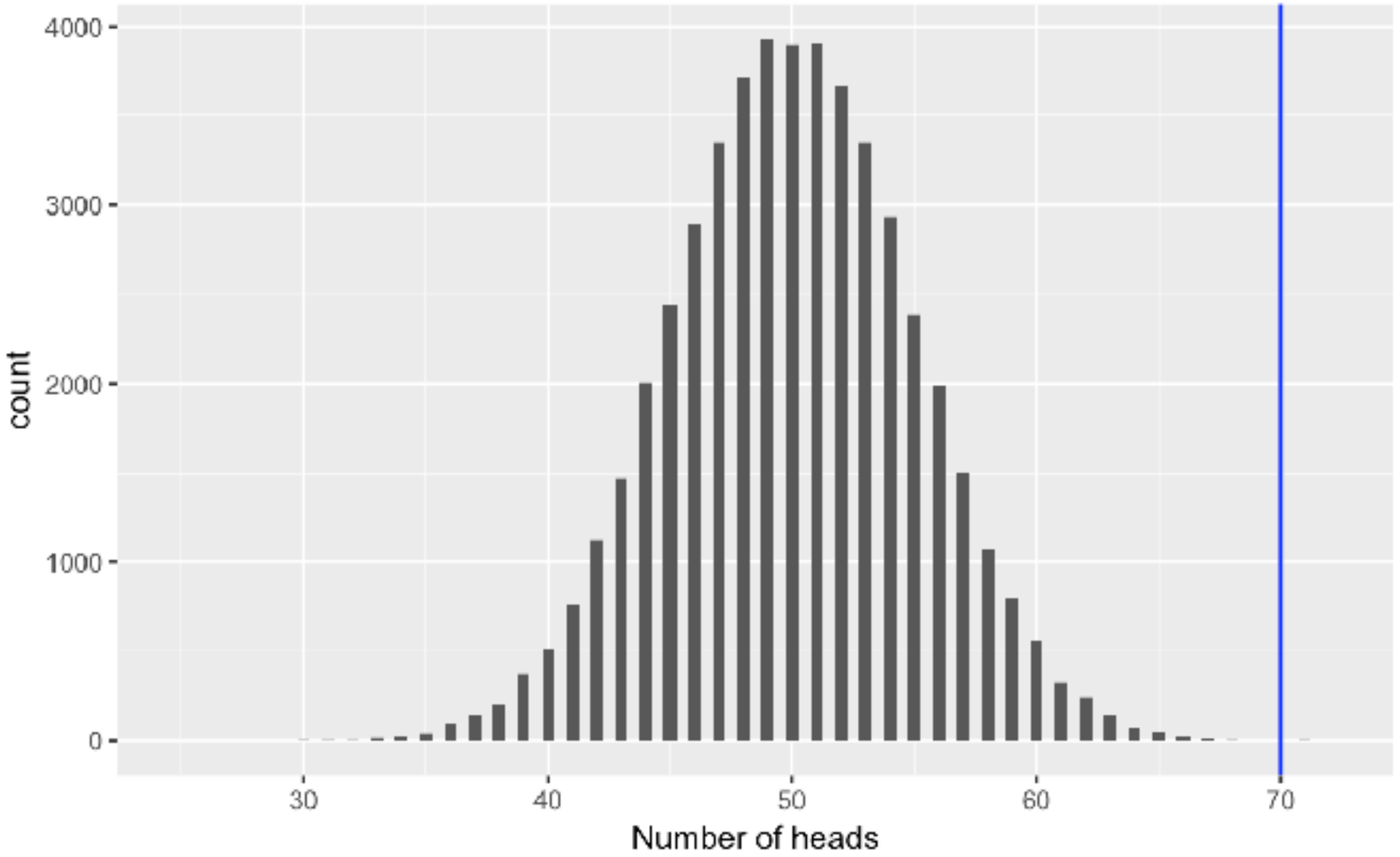
binomial distribution $$P(X \leq k) = \sum_{i=0}^{k} \binom{N}{k} p^i (1-p)^{n-i}$$

$P(X \leq 69 | p=0.5) = 0.99996$

$P(X \geq 70 | p=0.5) = 1 - 0.99996 = 0.00004$

Using random sampling to generate an empirical null distribution

- Draw random samples from a binomial distribution (using `rbinom()`)
- Compare them to the observed data



$$P(X \geq 70 | p=0.5) = 3/50000 = 0.00006$$

BMI example

- What would the t statistic look like if there was really no difference in BMI between active and inactive people?

Randomization

- We can make the null hypothesis true (on average) by randomly reordering group membership

Team	Squat
Football	325
Football	290
Football	290
Football	305
Football	370
XC	165
XC	180
XC	215
XC	175
XC	125

$t = 6.92$

$df = 8,$

$p(t_8 \geq 6.92) = 0.0001$

Randomization

- We can make the null hypothesis true (on average) by randomly reordering group membership

Team	Squat
Football	325
Football	290
XC	290
XC	305
Football	370
Football	165
Football	180
XC	215
XC	175
XC	125

$t = 0.83$

$df = 8$

$p(t_8 \geq 0.83) = 0.43$

Randomization

- We can make the null hypothesis true (on average) by randomly reordering group membership

Team	Squat
XC	325
XC	290
Football	290
Football	305
Football	370
XC	165
Football	180
Football	215
XC	175
XC	125

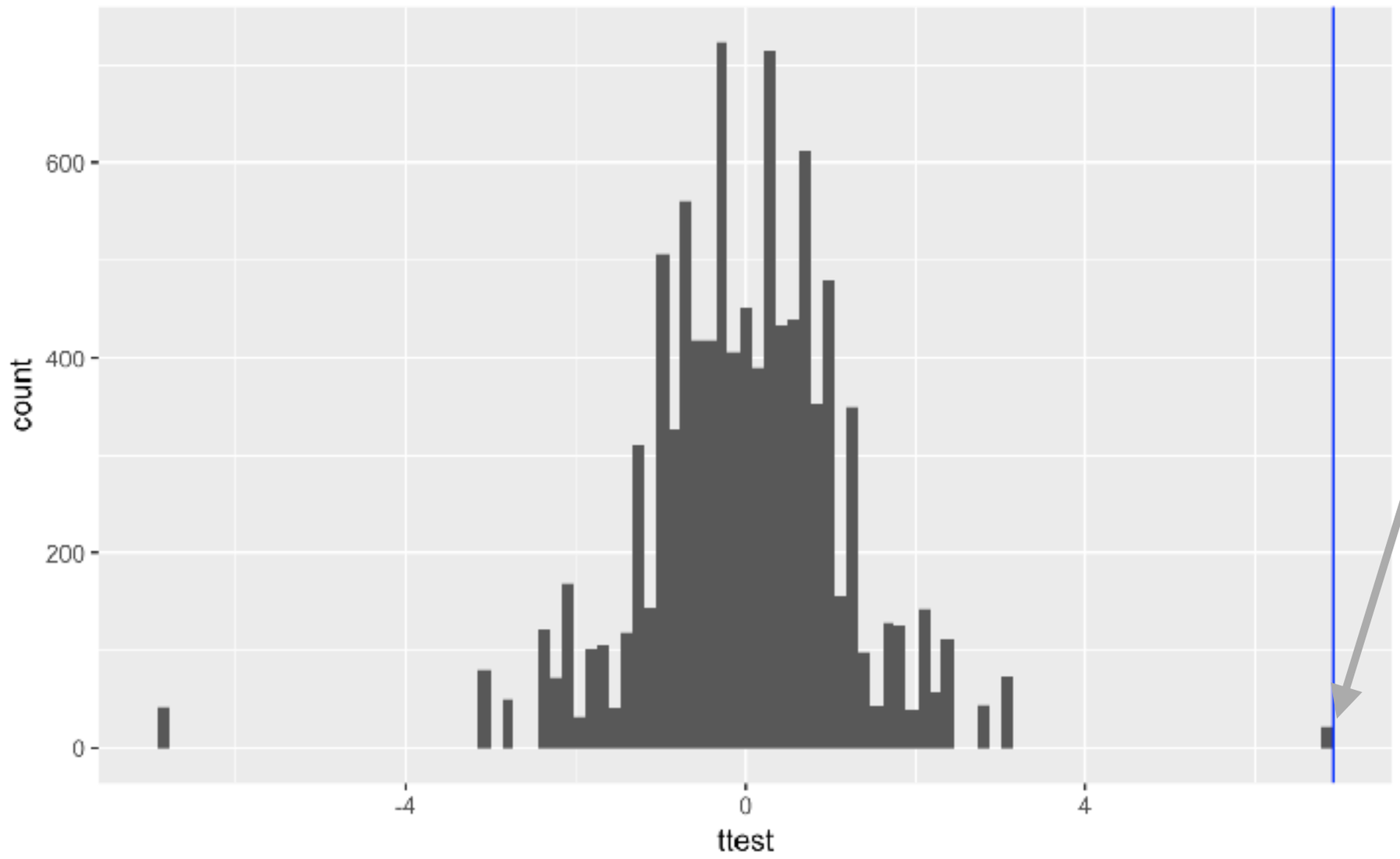
$t = 1.09$

$df = 8$

$p(t_8 \geq 1.09) = 0.30$

- Scramble 10,000 times to get distribution of t values under null hypothesis

$P(t_{random} \geq t_{observed}) = .0021$

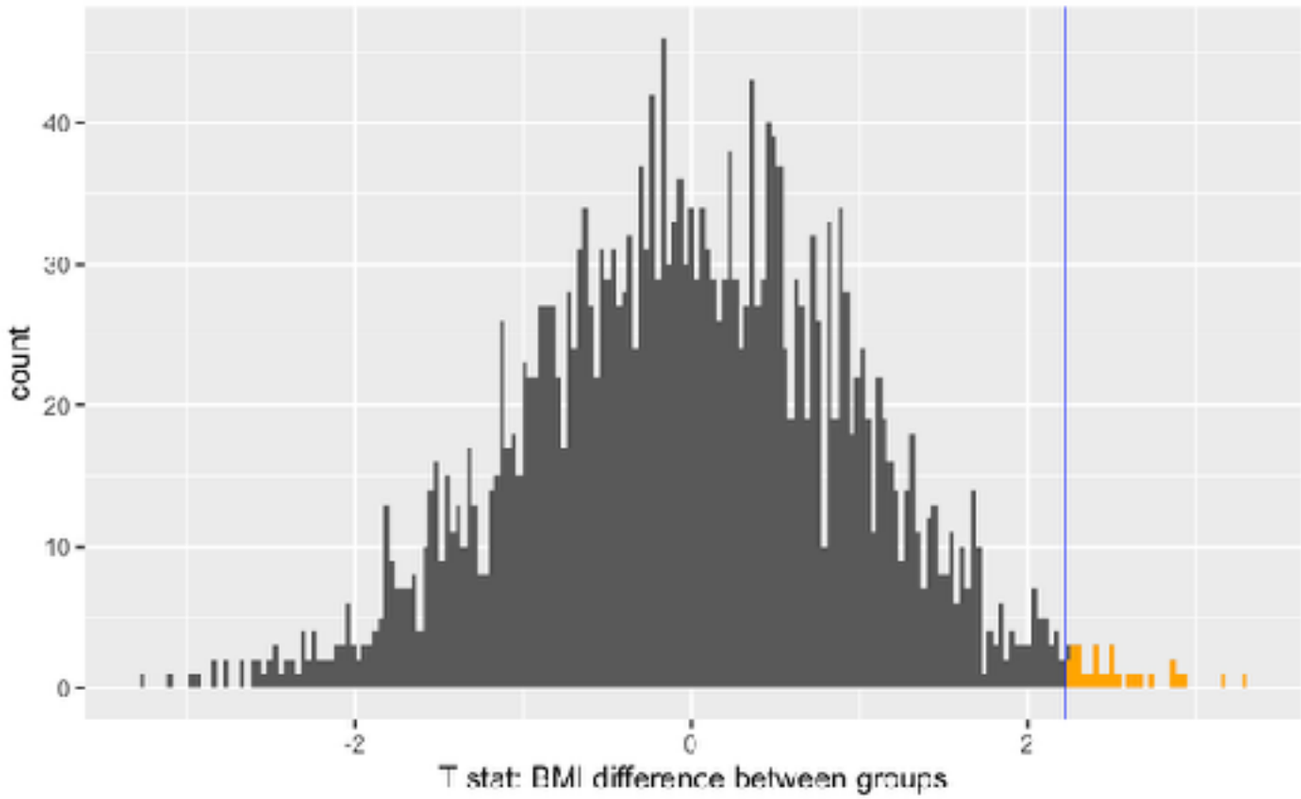


What happened here?

there are 3,628,800 possible permutations of 10 items

BMI example: randomization

- If there is no difference between groups, then the result should be no different from what we see if activity levels are randomly shuffled between people



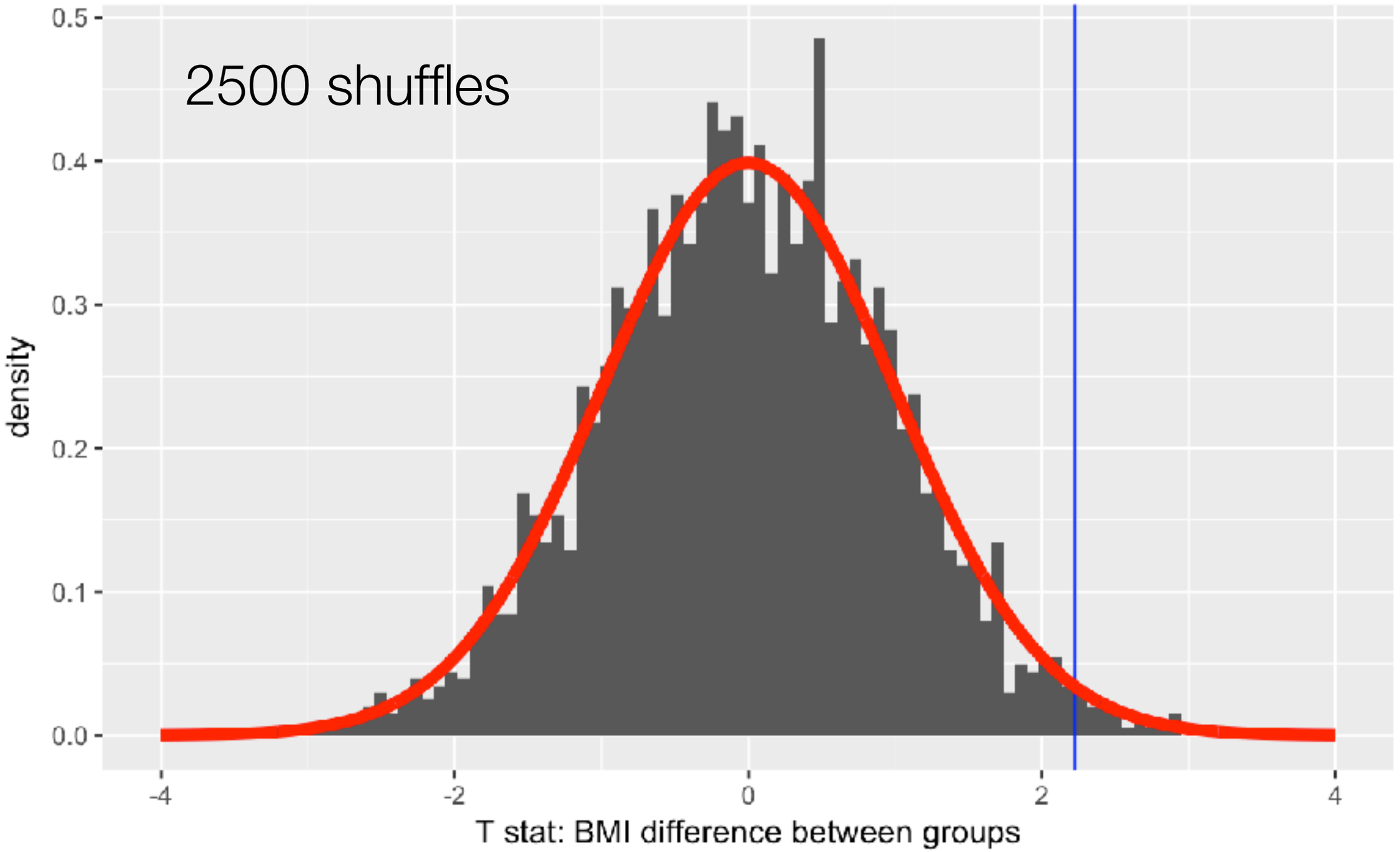
Largest difference in 2500 random shuffles: 3.21

Observed difference in actual data: 2.22

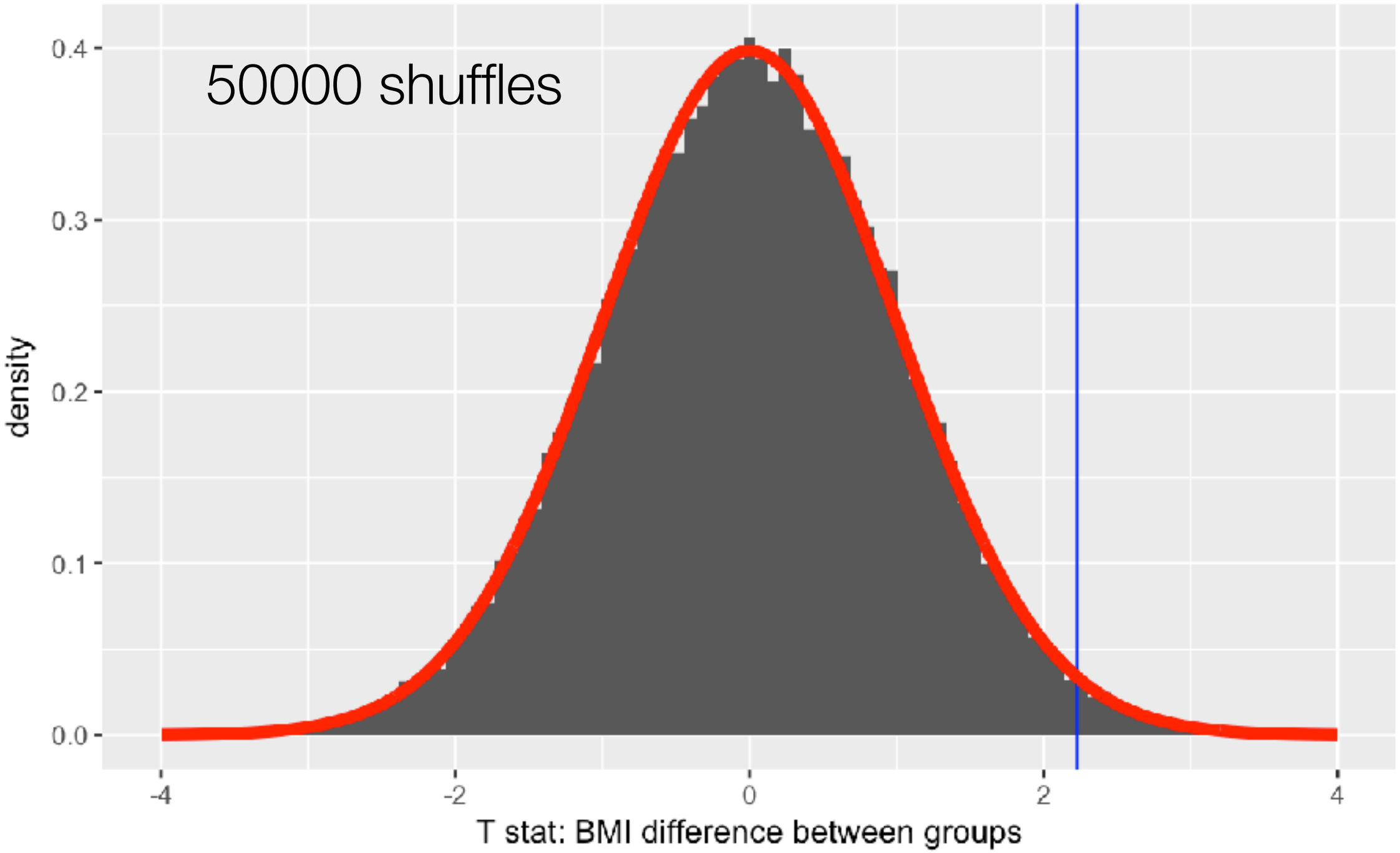
Number of shuffles with $t \geq 2.22$: 16

$p(t \geq 2.22 | H_0) = 16/2500 = 0.0064$

The *t* distribution vs permutation distribution



With enough random shuffles, the nonparametric and theoretical distributions can become very similar



Performing a *t* test in R

"formula notation: y ~ x"

```
ttestResult = t.test(BMI~PhysActive,
 data=NHANES_sample,var.equal=TRUE,
 alternative='greater')
```

BMI ~ PhysActive → "Does BMI differ as a function of the different values of PhysActive?

BMI example: dissecting the parametric test in R

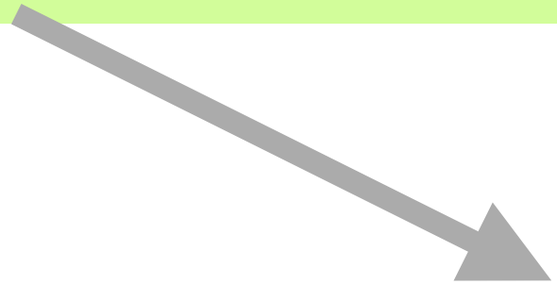
```
>ttestResult <- t.test(BMI~PhysActive,data=NHANES_sample,
    var.equal=TRUE,alternative='greater')
```

BMI example: parametric test in R

```
>ttestResult=t.test(BMI~PhysActive,data=NHANES_sample,
    var.equal=TRUE,alternative='greater')
```

```
  Two Sample t-test

data:  BMI by PhysActive
t = 2.4452, df = 248, p-value = 0.007587
alternative hypothesis: true difference in means is
greater than 0
95 percent confidence interval:
 0.7230215       Inf
sample estimates:
mean of x mean of y
 29.63752  27.41136
```



Directional alternative hypothesis

BMI example: parametric test in R

```
>ttestResult=t.test(BMI~PhysActive,data=NHANES_sample,
    var.equal=TRUE,alternative='greater')


  Two Sample t-test

data:  BMI by PhysActive
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```

t statistic computed on observed sample

BMI example: parametric test in R

```
>ttestResult=t.test(BMI~PhysActive,data=NHANES_sample,
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  Two Sample t-test

data:  BMI by PhysActive
t = 2.4452, df = 248, p-value = 0.007587
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```

N - 2 degrees of freedom (because we are estimating two parameters)

BMI example: parametric test in R

```
>ttestResult=t.test(BMI~PhysActive,data=NHANES_sample,
    var.equal=TRUE,alternative='greater')

  Two Sample t-test

data:  BMI by PhysActive
t = 2.4452, df = 248, p-value = 0.007587
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greater than 0
95 percent confidence interval:
 0.7230215       Inf
sample estimates:
mean of x mean of y
 29.63752  27.41136
```

probability of
$t \geq 2.44$ for
t(248)
in R:

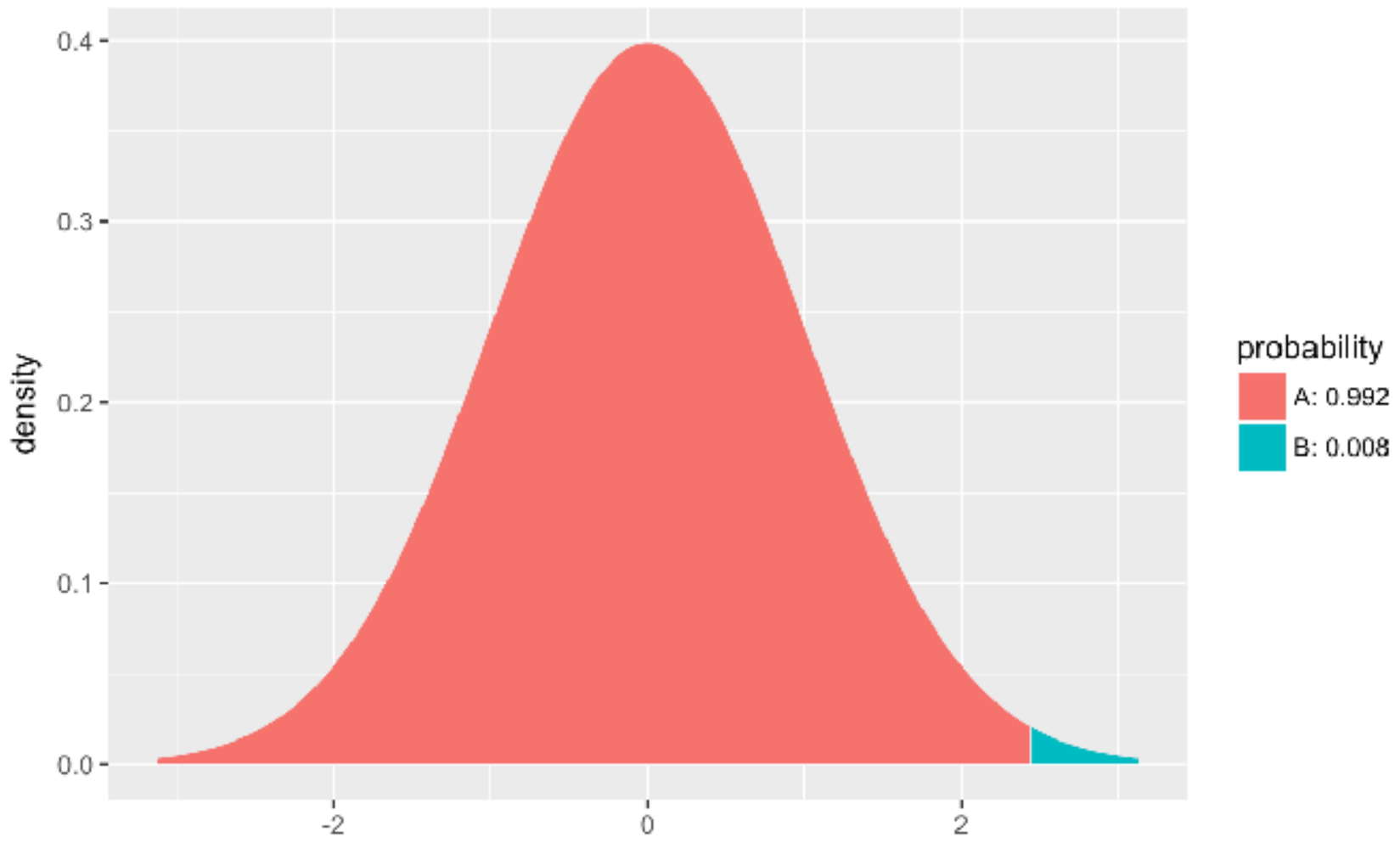
```
1 - pt(2.4452,248)
```

if we reran the test as a two-tailed (non-directional) test, the p-value would be:

- the same (0.0075)
- twice as large (0.015)
- half as large (0.00375)

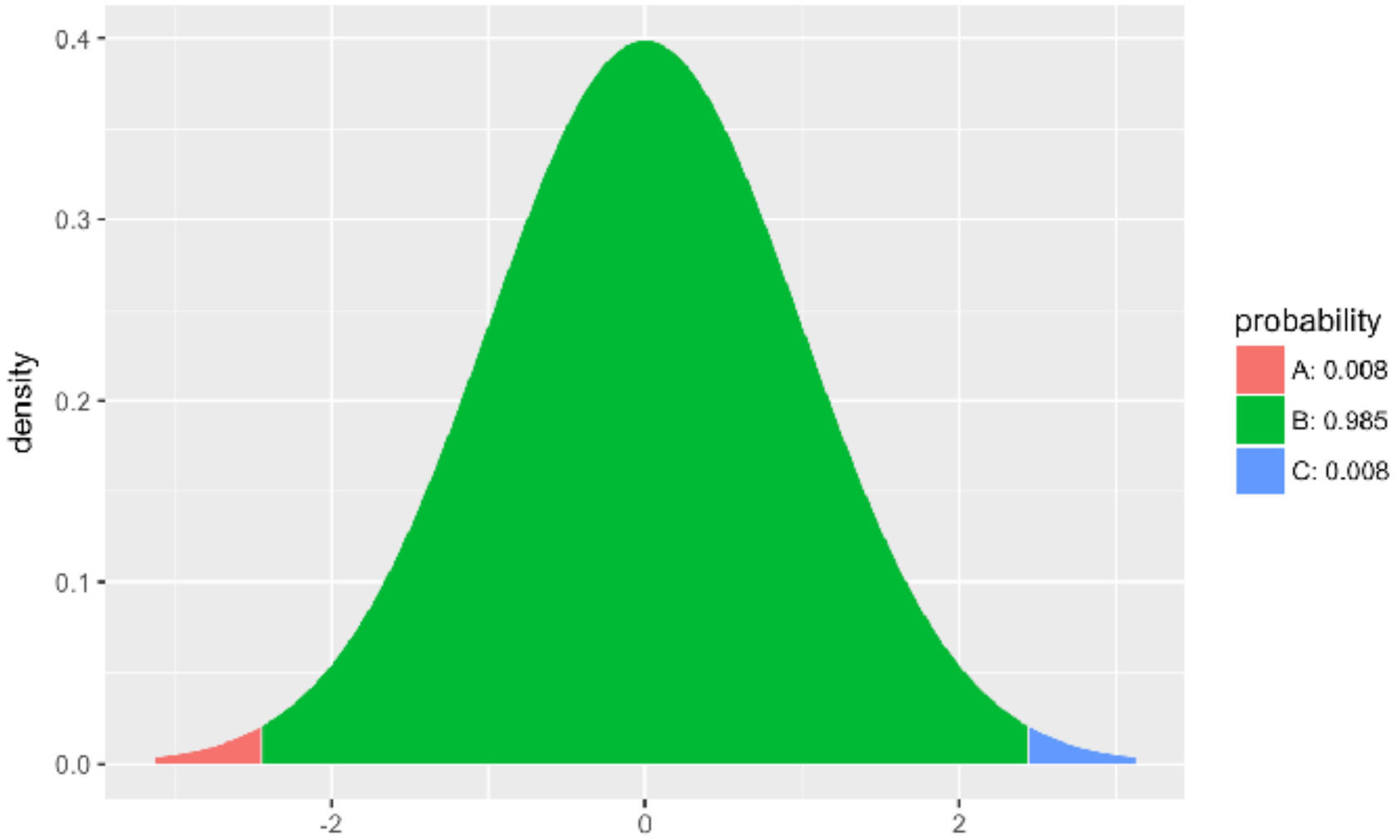
One-tailed vs two-tailed tests

- Directional test:
  - p-value = 1 - $p(t_{observed} \geq t_{248})$



One-tailed vs two-tailed tests

- Two-tailed (non-directional test)
  - p-value = 1 - $p(t_{observed} \geq t_{248}) + p(t_{observed} \leq t_{248})$



Two-tailed results

```
ttestResult = t.test(BMI~PhysActive,data=NHANES_sample,var.equal=TRUE,
    alternative='two.sided')

   Two Sample t-test

data:  BMI by PhysActive
t = 2.4452, df = 248, p-value = 0.01517
alternative hypothesis: true difference in means is not equal
to 0
95 percent confidence interval:
 0.4329999 4.0193201
sample estimates:
mean of x mean of y
 29.63752  27.41136
```

p-value is twice as large for two-tailed test versus one-tailed test: data are less surprising!

Step 6: Assess the “statistical significance” of the result

- What does “statistical significance” mean?
- How much evidence against the null hypothesis do we require before rejecting it?

The (in)famous p<0.05

- "If P is between .1 and .9 there is certainly no reason to suspect the hypothesis tested. If it is below .02 it is strongly indicated that the hypothesis fails to account for the whole of the facts. We shall not often be astray if we draw a conventional line at .05"
- "it is convenient to draw the line at about the level at which we can say: Either there is something in the treatment, or a coincidence has occurred such as does not occur more than once in twenty trials"

Sir Ronald Fisher

"the single most important figure in 20th century statistics" - Efron

# p<0.05 was never meant to be a fixed rule

- Fisher:
  - "no scientific worker has a fixed level of significance at which from year to year, and in all circumstances, he rejects hypotheses; he rather gives his mind to each particular case in the light of his evidence and his ideas"
- It probably became a ritual because of the difficulty in computing exact p-values in early days
  - All of the charts had entry for .05

TABLE IV.—TABLE OF t

n.	P=·9	·8	·7	·6	·5	·4	·3	·2	·1	·05	·02	·01
1	·158	·325	·510	·727	1·000	1·376	1·963	3·078	6·314	12·706	31·821	63·657
2	·142	·289	·445	·617	·816	1·061	1·386	1·886	2·920	4·303	6·965	9·925
3	·137	·277	·424	·584	·765	·978	1·250	1·638	2·353	3·182	4·541	5·841
4	·134	·271	·414	·569	·741	·941	1·190	1·533	2·132	2·776	3·747	4·604
5	·132	·267	·408	·559	·727	·920	1·156	1·476	2·015	2·571	3·365	4·032
6	·131	·265	·404	·553	·718	·906	1·134	1·440	1·943	2·447	3·143	3·707
7	·130	·263	·402	·549	·711	·896	1·119	1·415	1·895	2·365	2·998	3·499
8	·130	·262	·399	·546	·706	·889	1·108	1·397	1·860	2·306	2·896	3·355
9	·129	·261	·398	·543	·703	·883	1·100	1·383	1·833	2·262	2·821	3·250
10	·129	·260	·397	·542	·700	·879	1·093	1·372	1·812	2·228	2·764	3·169
11	·129	·260	·396	·540	·697	·876	1·088	1·363	1·796	2·201	2·718	3·106
12	·128	·259	·395	·539	·695	·873	1·083	1·356	1·782	2·179	2·681	3·055
13	·128	·259	·394	·538	·694	·870	1·079	1·350	1·771	2·160	2·650	3·012
14	·128	·258	·393	·537	·692	·868	1·076	1·345	1·761	2·145	2·624	2·977
15	·128	·258	·393	·536	·691	·866	1·074	1·341	1·753	2·131	2·602	2·947
16	·128	·258	·392	·535	·690	·865	1·071	1·337	1·746	2·120	2·583	2·921
17	·128	·257	·392	·534	·689	·863	1·069	1·333	1·740	2·110	2·567	2·898
18	·127	·257	·392	·534	·688	·862	1·067	1·330	1·734	2·101	2·552	2·878
19	·127	·257	·391	·533	·688	·861	1·066	1·328	1·729	2·093	2·539	2·861
20	·127	·257	·391	·533	·687	·860	1·064	1·325	1·725	2·086	2·528	2·845
21	·127	·257	·391	·532	·686	·859	1·063	1·323	1·721	2·080	2·518	2·831
22	·127	·256	·390	·532	·686	·858	1·061	1·321	1·717	2·074	2·508	2·819
23	·127	·256	·390	·532	·685	·858	1·060	1·319	1·714	2·069	2·500	2·807
24	·127	·256	·390	·531	·685	·857	1·059	1·318	1·711	2·064	2·492	2·797
25	·127	·256	·390	·531	·684	·856	1·058	1·316	1·708	2·060	2·485	2·787
26	·127	·256	·390	·531	·684	·856	1·058	1·315	1·706	2·056	2·479	2·779
27	·127	·256	·389	·531	·684	·855	1·057	1·314	1·703	2·052	2·473	2·771
28	·127	·256	·389	·530	·683	·855	1·056	1·313	1·701	2·048	2·467	2·763
29	·127	·256	·389	·530	·683	·854	1·055	1·311	1·699	2·045	2·462	2·756
30	·127	·256	·389	·530	·683	·854	1·055	1·310	1·697	2·042	2·457	2·750
∞	·12566	·25335	·38532	·52440	·67449	·84162	1·03643	1·28155	1·64485	1·95996	2·32634	2·57582

Fisher (1925)

Arguments against p<0.05

comment

Redefine statistical significance

We propose to change the default *P*-value threshold for statistical significance from 0.05 to 0.005 for claims of new discoveries.

Daniel J. Benjamin, James O. Berger, Magnus Johannesson, Brian A. Nosek, E.-J. Wagenmakers, Richard Berk, Kenneth A. Bollen, Björn Brembs, Lawrence Brown, Colin Camerer, David Cesarini, Christopher D. Chambers, Merlise Clyde, Thomas D. Cook, Paul De Boeck, Zoltan Dienes, Anna Dreber, Kenny Easwaran, Charles Efferson, Ernst Fehr, Fiona Fidler, Andy P. Field, Malcolm Forster, Edward I. George, Richard Gonzalez, Steven Goodman, Edwin Green, Donald P. Green, Anthony Greenwald, Jarrod D. Hadfield, Larry V. Hedges, Leonhard Held, Teck Hua Ho, Herbert Hoijtink, Daniel J. Hruschka, Kosuke Imai, Guido Imbens, John P. A. Ioannidis, Minjeong Jeon, James Holland Jones, Michael Kirchler, David Laibson, John List, Roderick Little, Arthur Lupia, Edouard Machery, Scott E. Maxwell, Michael McCarthy, Don Moore, Stephen L. Morgan, Marcus Munafó, Shinichi Nakagawa, Brendan Nyhan, Timothy H. Parker, Luis Pericchi, Marco Perugini, Jeff Rouder, Judith Rousseau, Victoria Savalei, Felix D. Schönbrodt, Thomas Sellke, Betsy Sinclair, Dustin Tingley, Trisha Van Zandt, Simine Vazire, Duncan J. Watts, Christopher Winship, Robert L. Wolpert, Yu Xie, Cristobal Young, Jonathan Zinman and Valen E. Johnson

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Why is 0.05 problematic?

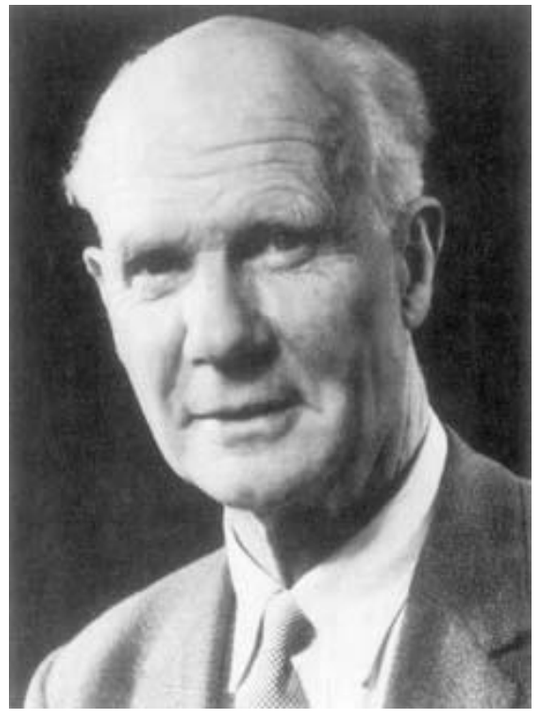
- $p<0.05$ indicates relatively weak evidence against the null
  - We will return to this later…

Statistical inference as decision making: Neyman/Pearson

- "no test based upon a theory of probability can by itself provide any valuable evidence of the truth or falsehood of a hypothesis. But we may look at the purpose of tests from another viewpoint. Without hoping to know whether each separate hypothesis is true or false, we may search for rules to govern our behaviour with regard to them, in following which we insure that, in the long run of experience, we shall not often be wrong"
- We don't know which specific decisions are right or wrong, but if we follow the rules, we know how often wrong decisions will occur

Jerzy Neyman

Egon Pearson



Example: statistical quality control

Peanut Butter	Insect filth (AOAC 968.35)	Average of 30 or more insect fragments per 100 grams
	Rodent filth (AOAC 968.35)	Average of 1 or more rodent hairs per 100 grams
	Grit (AOAC 968.35)	Gritty taste and water insoluble inorganic residue is more than 25 mg per 100 grams
	DEFECT SOURCE: *Insect fragments - preharvest and/or post harvest and/or processing insect infestation, Rodent hair - post harvest and/or processing contamination with animal hair or excreta, Grit - harvest contamination* Significance: *Aesthetic*	

https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/SanitationTransportation/ucm056174.htm

Statistical decision

Reality	Reject H_0	Fail to Reject H_0
H_A is true	Correct (*hit*)	Type II error (*miss* or *false negative*)
H_0 is true	Type I error (*false alarm* or *false positive*)	Correct (*correct rejection*)

P(Type I error) = $\boldsymbol{\alpha}$

The long-run probability of rejecting H_0 when it is true

Statistical decision

Reality	Reject H_0	Fail to Reject H_0
H_A is true	Correct (*hit*)	Type II error (*miss* or *false negative*)
H_0 is true	Type I error (*false alarm* or *false positive*)	Correct (*correct rejection*)

P(Type I error) = $\boldsymbol{\alpha}$ — The long-run probability of rejecting H_0 when it is true

P(Type II error) = $\boldsymbol{\beta}$ — The long-run probability of failing to rejecting H_0 when H_A is true

Statistical decision

Reality	Reject H_0	Fail to Reject H_0
H_A is true	1-β (statistical power)	β
H_0 is true	α (false positive rate)	1-α

alpha: How likely are we to reject H_0 when H_0 is true?

Statistical decision

Reality

	Reject H_0	Fail to Reject H_0
H_A is true	1-β (statistical power)	β
H_0 is true	α (false positive rate)	1-α

alpha: How likely are we to reject H_0 when H_0 is true?

power: How likely are we to reject H_0 when H_A is true?

Breakout!

- Researchers generally set their false positive rate to 0.05, but their false negative rate (1-power) to 0.2
- Why might protecting from false positives be more important than protecting from false negatives?

Hypothesis testing demo

- In RStudio:
  - `library(shiny)`
  - `runGitHub("psych10/psych10", subdir="inst/hypothesis/")`

You run an experiment comparing means between two groups, and you find a significant difference (p=.01). Which of the following does this imply?

You have absolutely disproved the null hypothesis

You have found the probability of the null hypothesis being true

You know, if you decide to reject the null hypothesis, the probability that you are making the wrong decision

You have a reliable experimental finding in the sense that if the experiment were repeated a great number of times, you would obtain a significant result on 99% of occasions.

None of the above

What does a significant result mean?

- You run an experiment comparing means between two groups, and you find a significant difference (p=.01)
  - Does it mean that you have absolutely disproved the null hypothesis?
  -

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  - Does it mean that you have absolutely proved your experimental hypothesis?

What does a significant result mean?

- You run an experiment comparing means between two groups, and you find a significant difference (p=.01)
  - Does it mean that you have absolutely disproved the null hypothesis?
  - Does it mean that you have absolutely proved your experimental hypothesis?
    - No - statistics cannot prove or disprove hypotheses!
    - It provides relative evidence against the null

What does a significant result mean?

- Does it mean that you have found the probability of the null hypothesis being true?
- Does it mean that you can deduce the probability of the altnernative hypothesis being true?

- No: The p-value is the probability of the data, not the probability of any hypothesis
  - p-value = $P(D|H_0)$
  - If we want to know $P(H_0|D)$, what do we need to use?
  - And what do we need to know in order to use it?

What does a significant result mean?

- Does it mean that you know, if you decide to reject the null hypothesis, the probability that you are making the wrong decision?
  - Restate this: P(H_0 is true|p<alpha)?

What does a significant result mean?

- Does it mean that you know, if you decide to reject the null hypothesis, the probability that you are making the wrong decision?
  - Restate this: P(H_0 is true|p<alpha)?
  - p-values are probabilities of data, not hypotheses!

NHST in a modern context

- Null hypothesis statistical testing can become very challenging in the context of modern science and big data
- Traditionally, researchers measured very few variables on each individual
- In modern science, we can often measure millions of variables per individual
  - Genomics
  - Brain imaging

A real-life example of hypothesis testing in action

- We know that schizophrenia has a strong genetic basis
  - About 80% of variation in schizophrenia is due to genetic differences
- Research has begun to look at which specific genes are involved
- Look at many places in the genome where people differ in their genetic code ("polymorphisms")
  - Usually about 1 million different locations
- Test whether people with schizophrenia are more likely to have a different version of the genetic code at that location

The problem with multiple hypothesis tests

- Let's say we did 1 million hypothesis tests at $p < 0.05$
  - # of expected errors if the null hypothesis is true
    - N * alpha = 1,000,000 * 0.05 = 50,000
  - $p < 0.05$ is appropriate to control the error rate for a single test
- What we really want to control is the "familywise error rate" - the likelihood of at least one false positive across our entire "family" of tests
- With 1 million tests at $p < 0.05$, the familywise error rate will be ~1
  - Every study will have false positives

Controlling for multiple comparisons

- If all of the tests are independent, we can control this by dividing our alpha level by the number of tests
  - "Bonferroni correction"
  - For 1 million tests, this would be:
    - $p < 0.05/1{,}000{,}000$ (5e-08)
- This ensures that we expect a false positive finding in only 1 out of every 20 studies

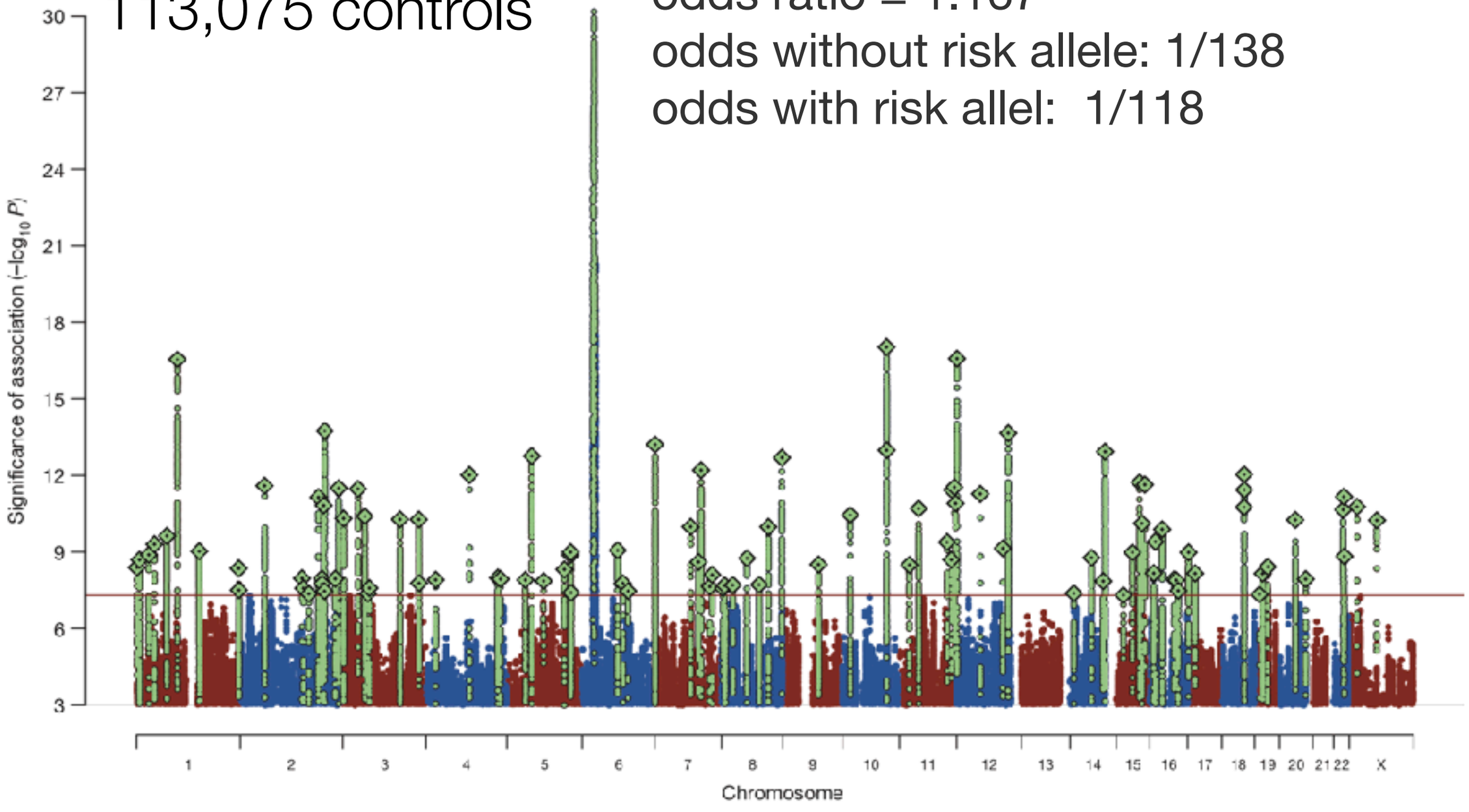
Simulating the effects of multiple testing

```
nTests=10000

uncAlpha=0.05
uncOutcome=replicate(nTests,
            sum(rnorm(nTests)<qnorm(uncAlpha)))

print(paste('uncorrected:',mean(uncOutcome>0)))
[1] "uncorrected: 1"

corAlpha=0.05/nTests
corOutcome=replicate(nTests,
              sum(rnorm(nTests)<qnorm(corAlpha)))

print(paste('corrected:',mean(corOutcome>0)))
[1] "corrected: 0.047"
```

“Manhattan plot” of genetic associations with schizophrenia

36,989 cases
113,075 controls

odds ratio = 1.167
odds without risk allele: 1/138
odds with risk allel: 1/118

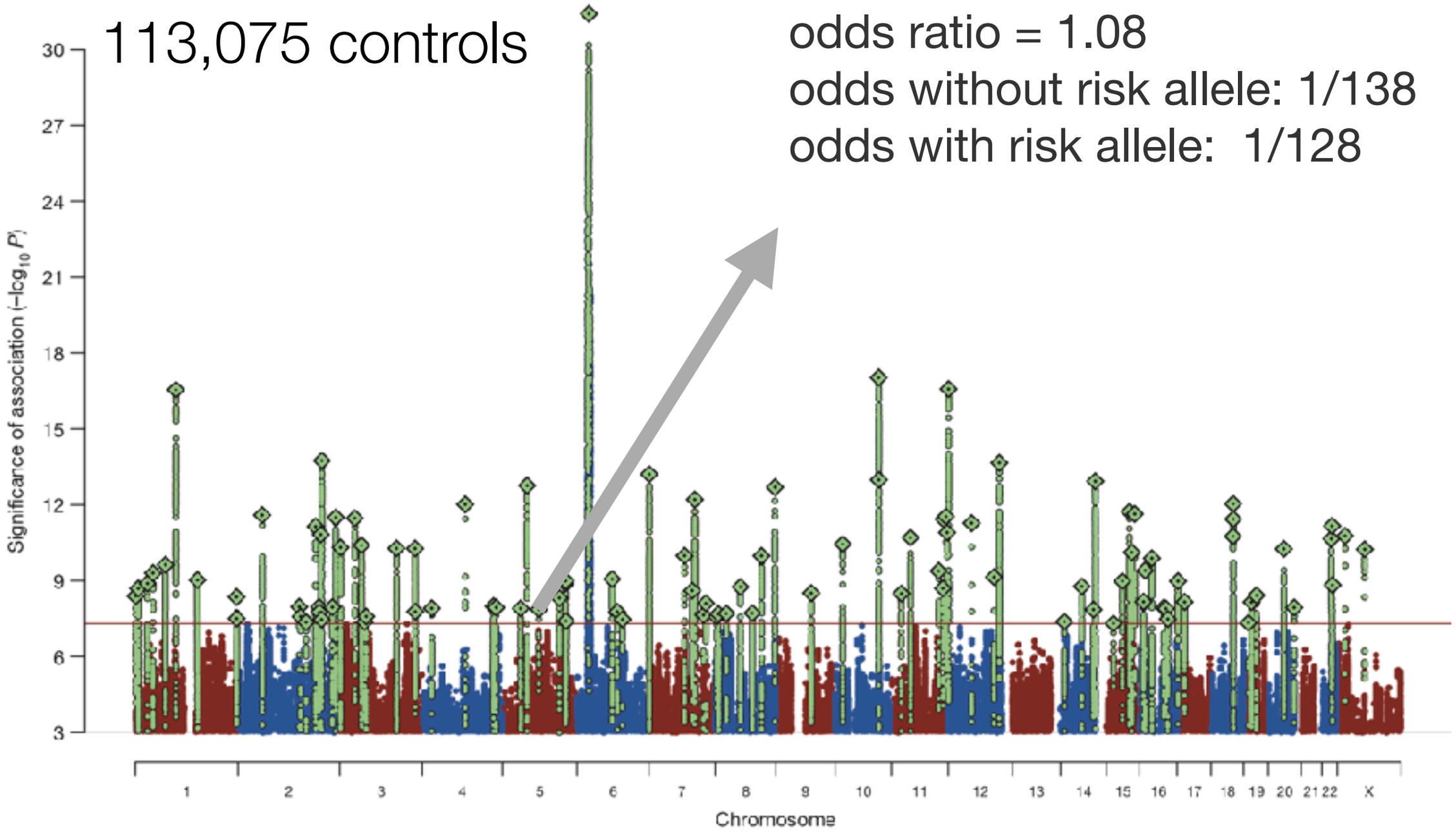


PGC, 2014

“Manhattan plot” of genetic associations with schizophrenia

36,989 cases
113,075 controls

odds ratio = 1.08
odds without risk allele: 1/138
odds with risk allele: 1/128

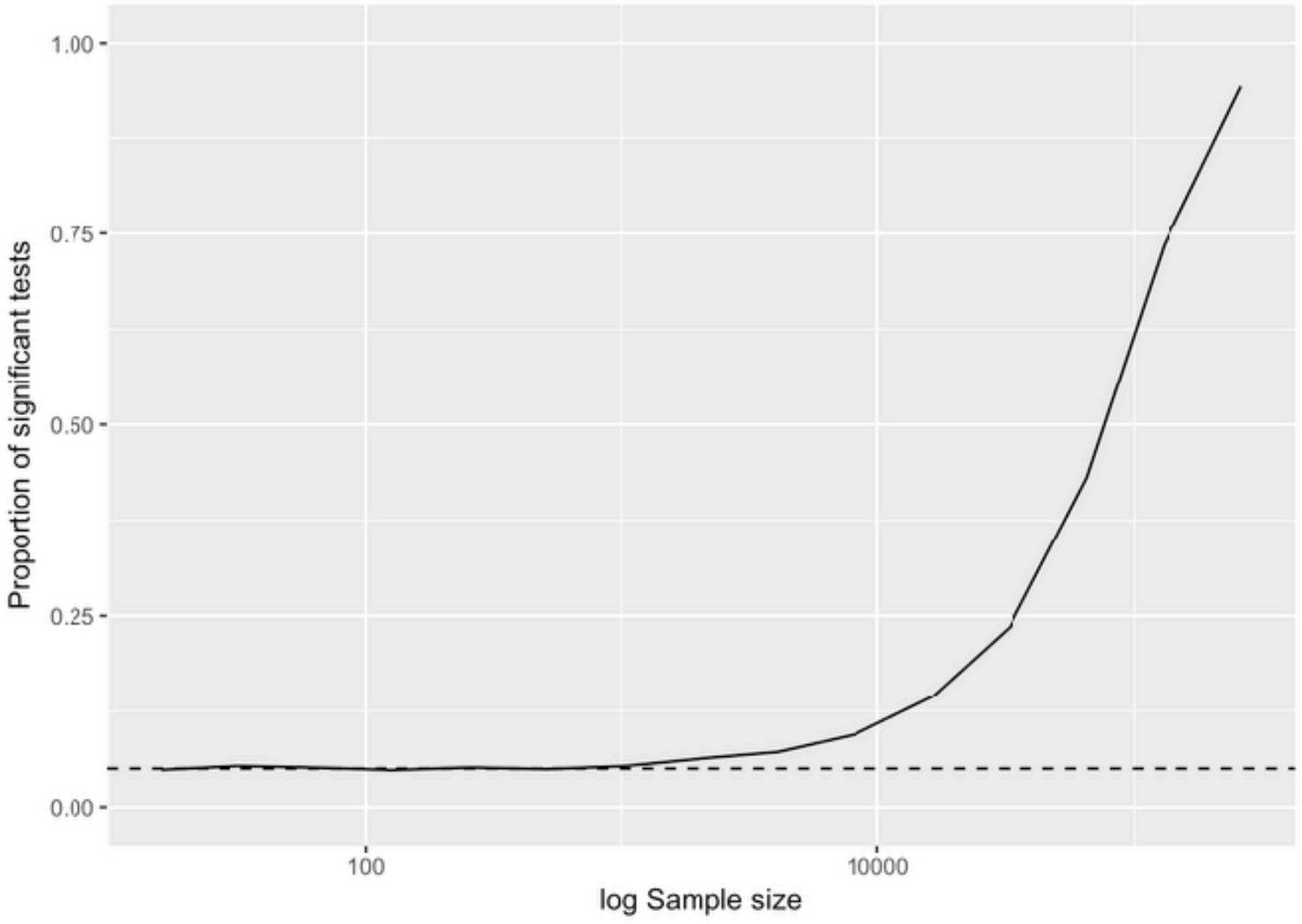


PGC, 2014

Statistical significance and sample size

- Meehl's paradox
  - In many areas of science (such as physics), higher N provides more precise models
  - Using NHST, as N becomes large, everything becomes significant

True effect size = 0.01 SD



Recap

- We can use statistics to test hypotheses
- P-values provide us a measure of how surprising the data would be if there was truly no effect
  - They do not necessarily tell us how strong the effect is
- We can use either theoretical distributions or randomization to determine the distribution of our statistic under the null hypothesis
- When we perform multiple tests, we have to adjust our threshold to prevent inflation of false positive rates