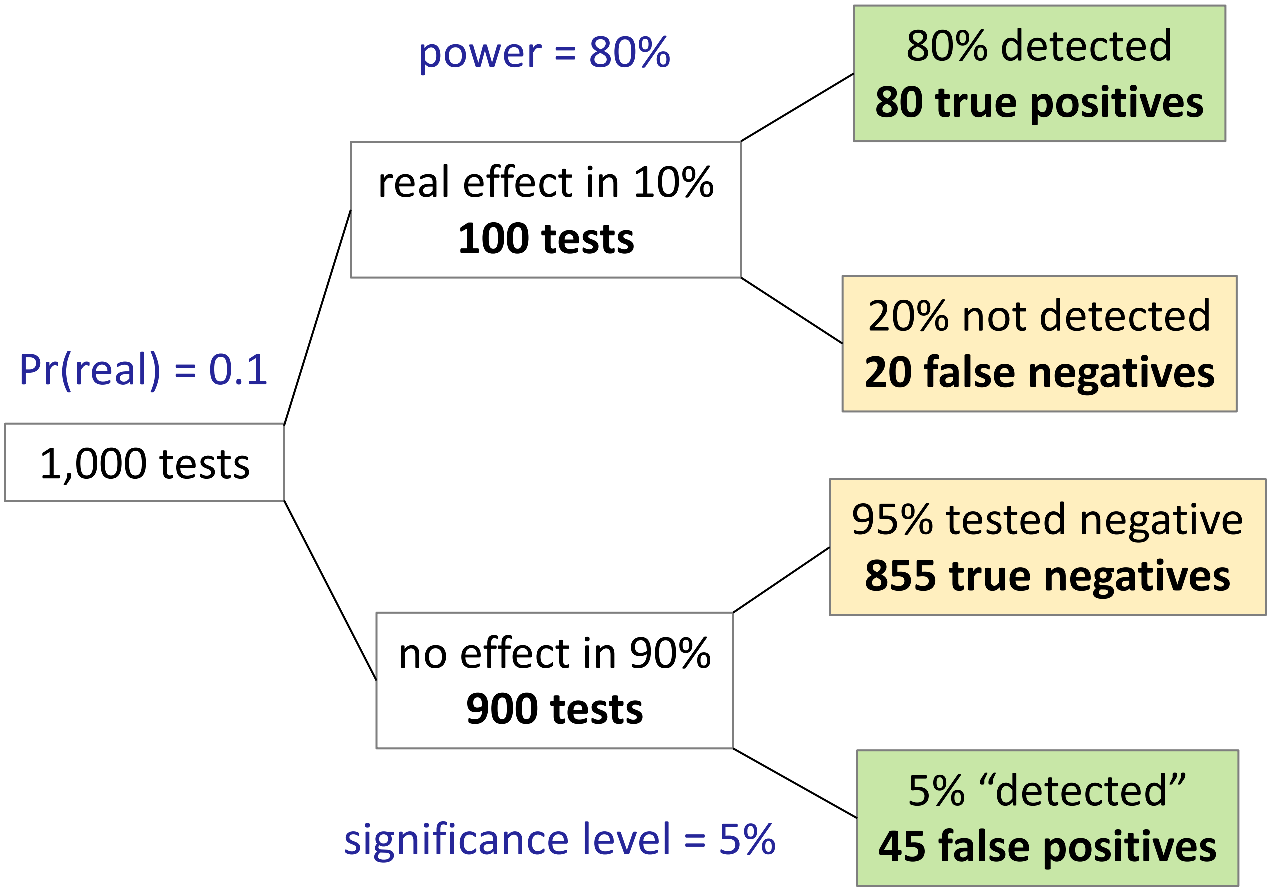


False positive rate

$$FPR = \frac{\text{false positives}}{\text{no effect}}$$

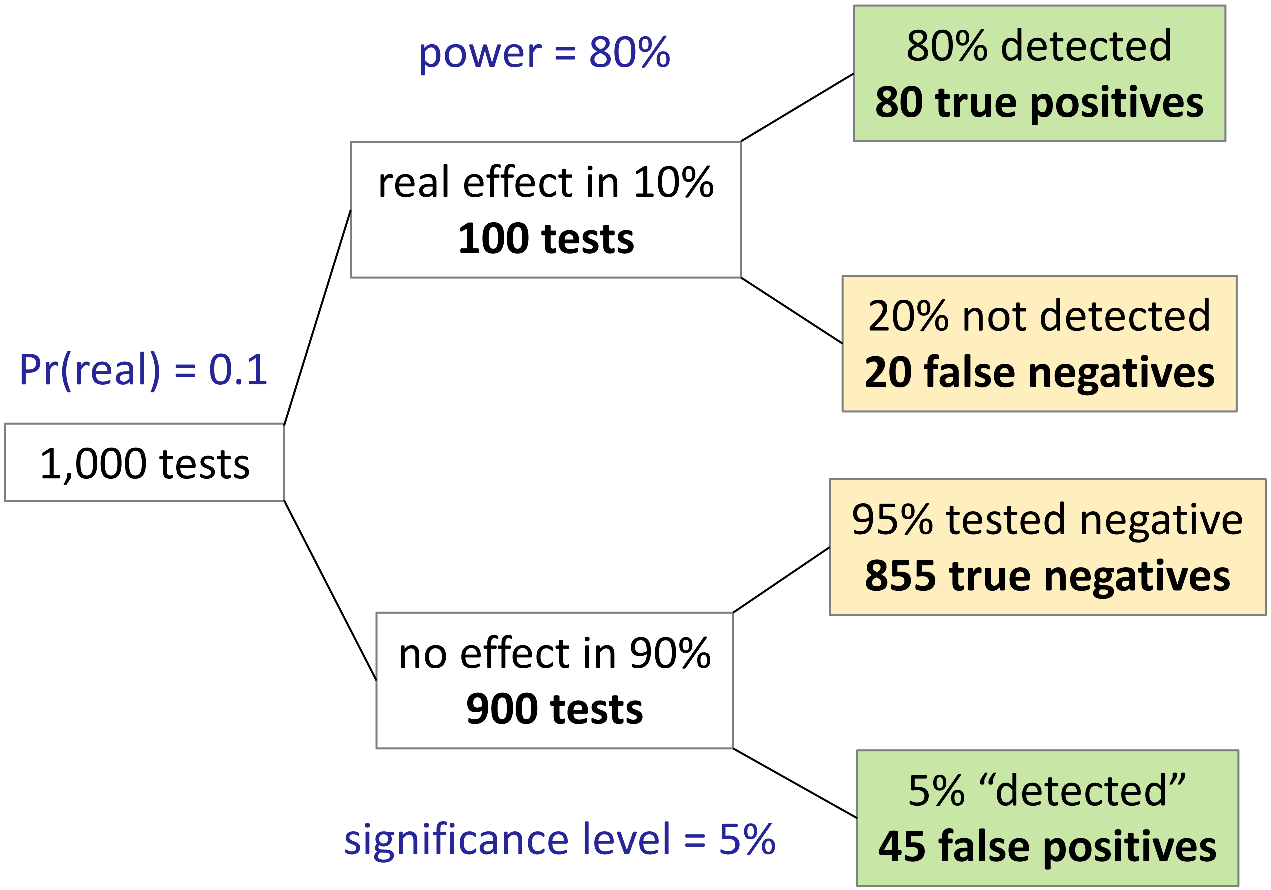
$$FPR = \frac{45}{900} = 0.05$$

False discovery rate

$$FDR = \frac{\text{false positives}}{\text{discoveries}}$$

$$FDR = \frac{45}{45 + 80} = 0.36$$

Colquhoun D., 2014, “An investigation of the false discovery rate and the misinterpretation of *p*-values”, *R. Soc. open sci.* **1**: 140216.



If you publish a $p < 0.05$ result, you have a 36% chance of making a fool of yourself

Colquhoun D., 2014, “An investigation of the false discovery rate and the misinterpretation of *p*-values”, *R. Soc. open sci.* **1**: 140216.

13. What’s wrong with p-values?

”Lies, damned lies, and statistics”

Benjamin Disraeli

A *p*-value of 5% implies that the probability of the null hypothesis being true is 5%

A p-value of 0.001 implies much more significant result than a p-value of 0.01

The p-value is the likelihood that the findings are due to chance p-value:

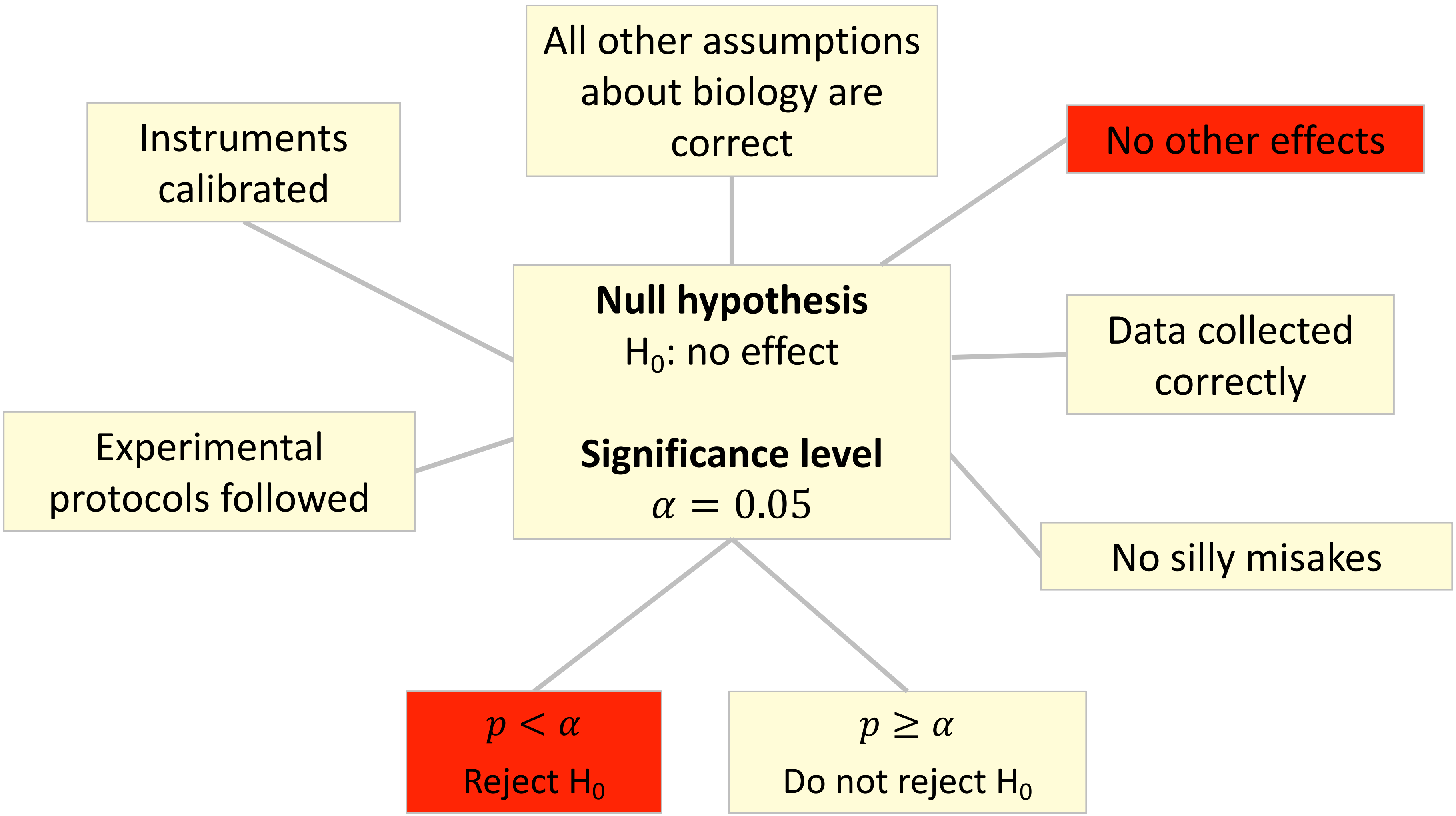
Given that H_0 is true, the probability of observed, or more extreme, data

It is **not** the probability that H_0 is true

P-value is the degree to which the data are embarrassed by the null hypothesis

Nicholas Maxwell

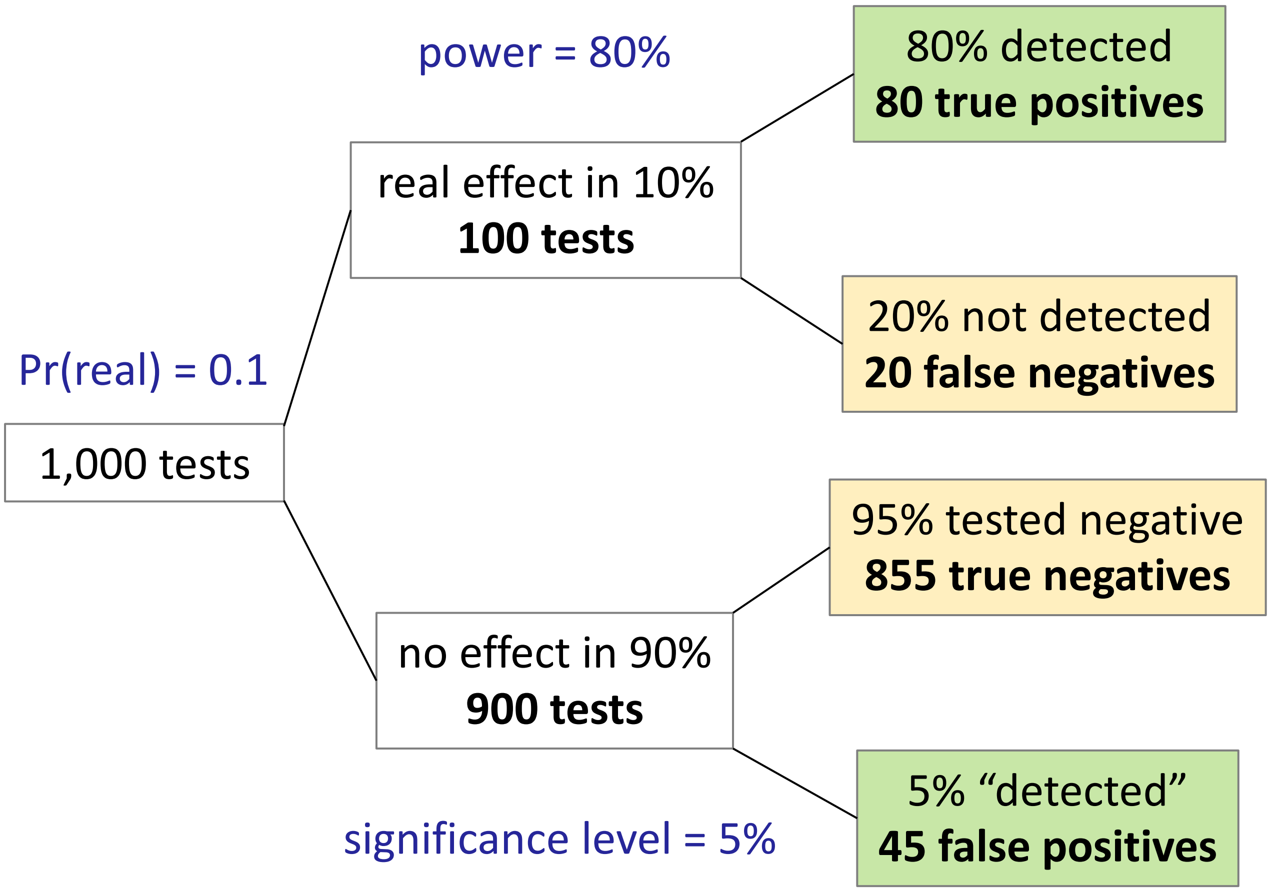
“All other assumptions”



1

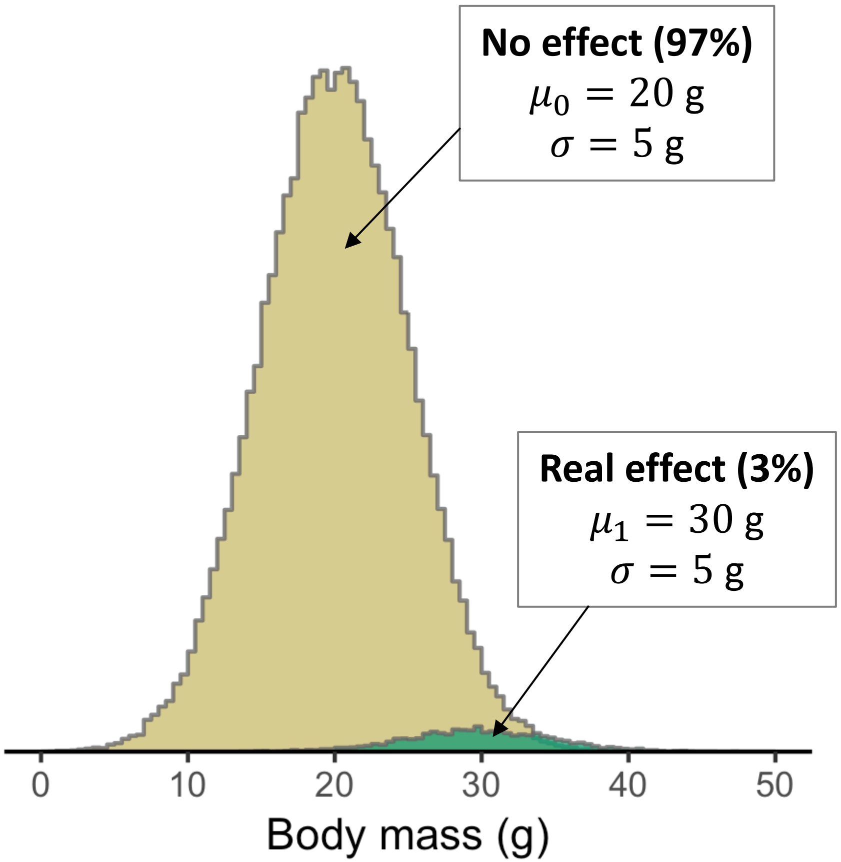
p-values test not only the null hypothesis, but everything else in the experiment

Why large false discovery rate?



$$\boxed{FDR = \frac{45}{45 + 80} = 0.36}$$

Simulated population of mice



Null hypothesis H_0: $\mu = 20$ g

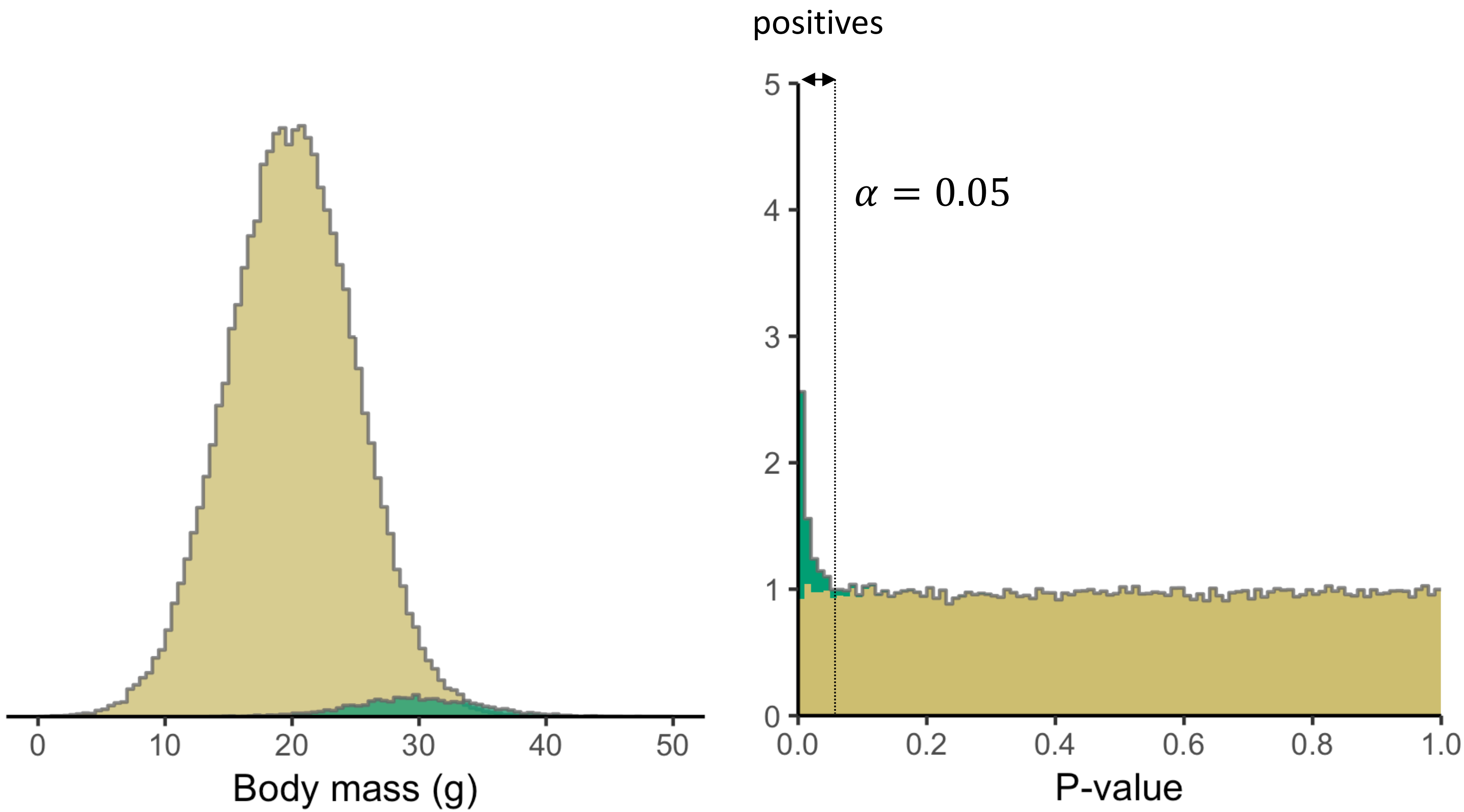
one-sample t-test

Power analysis

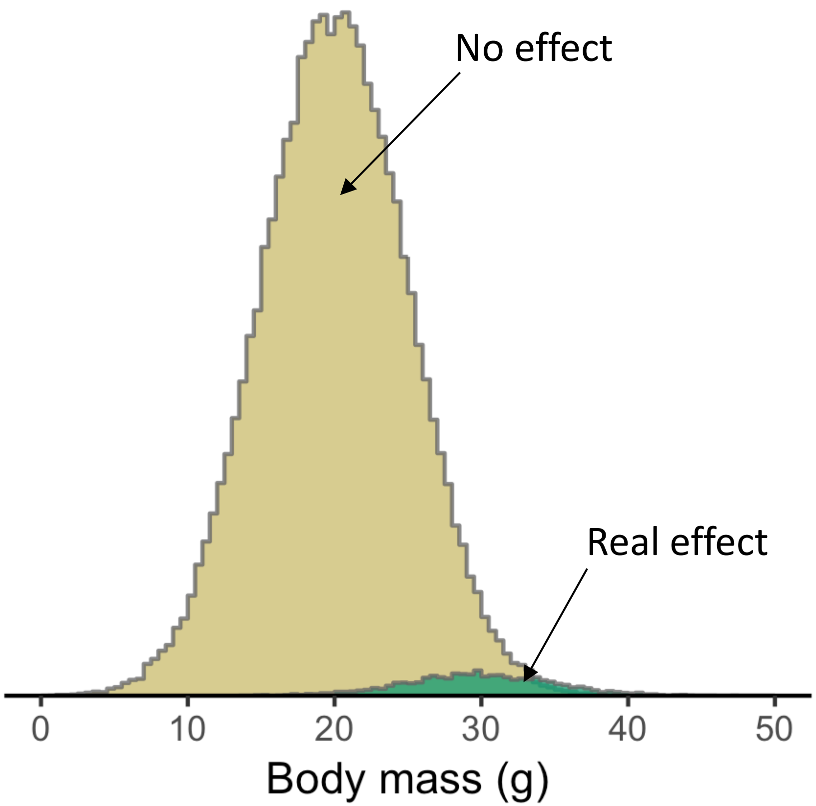
effect size	$d = 2$
power	$\mathcal{P} = 0.9$
significance level	$\alpha = 0.05$
sample size	$n = 5$

```
> pwr.t.test(d=2, sig.level=0.05,
power=0.9, type="one.sample")

     One-sample t test power calculation

              n = 4.912411
…
```

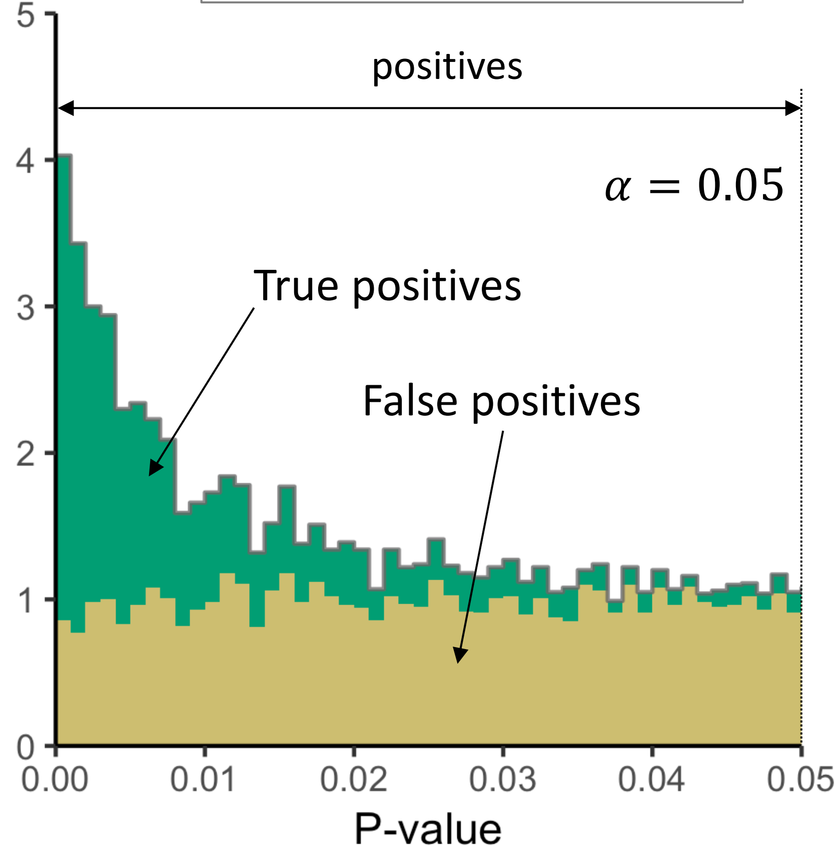
Gedankenexperiment: distribution of p-values



Gedankenexperiment: “significant” p-values



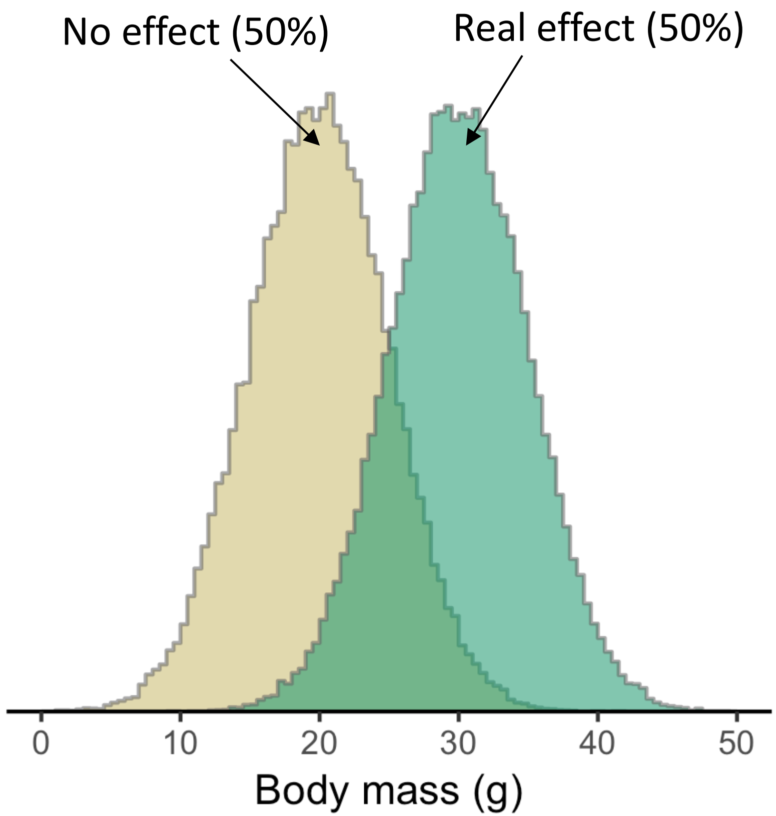
$$FDR = \frac{FP}{FP + TP} \approx 0.63$$



2

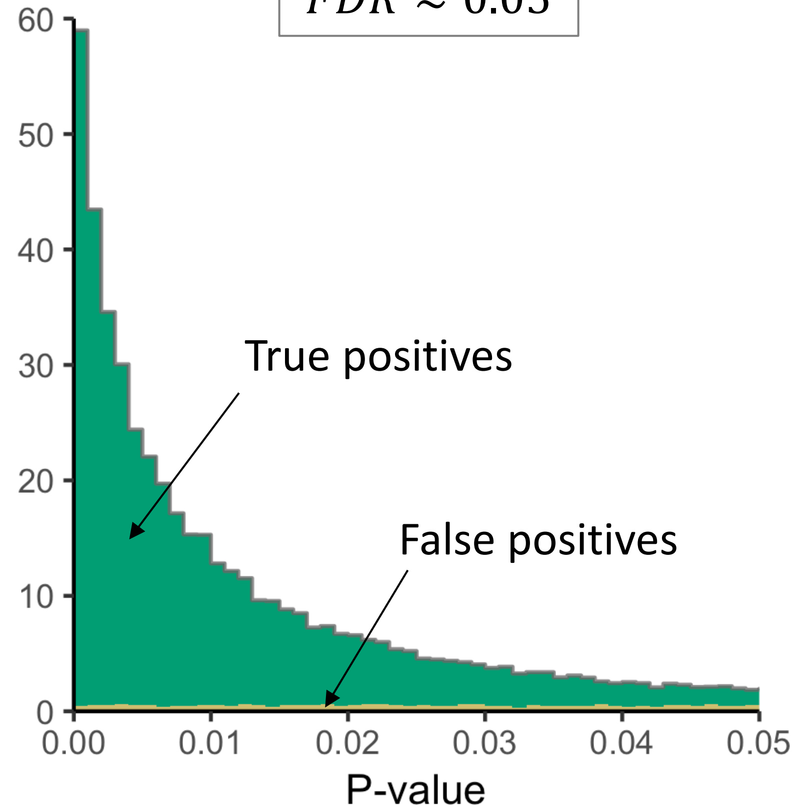
The chance of making a fool of yourself can be much larger than $\alpha = 0.05$

FDR depends on the probability of real effect



$$\alpha = 0.05$$

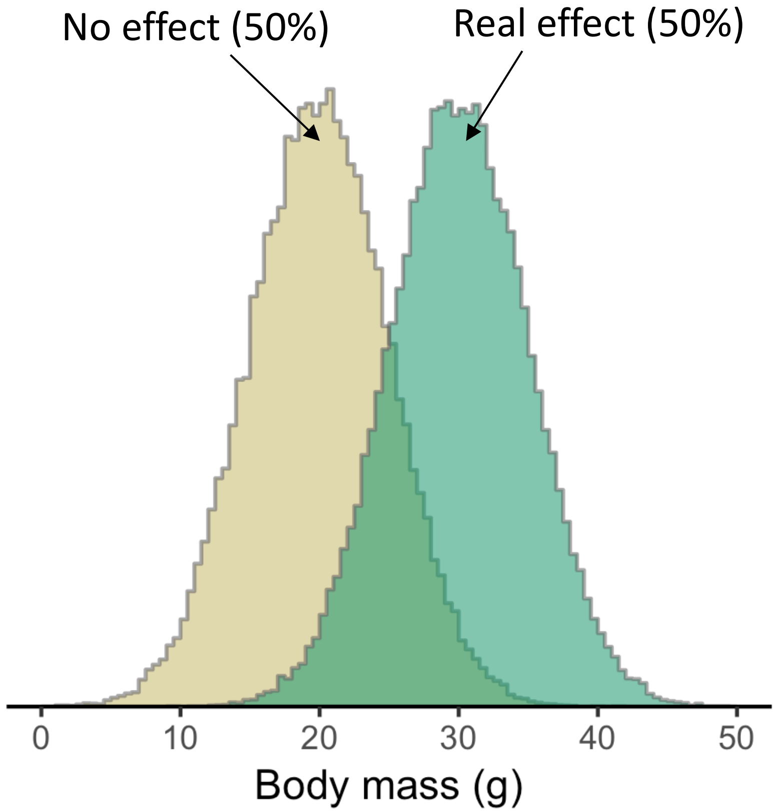
$$FDR \approx 0.05$$



3

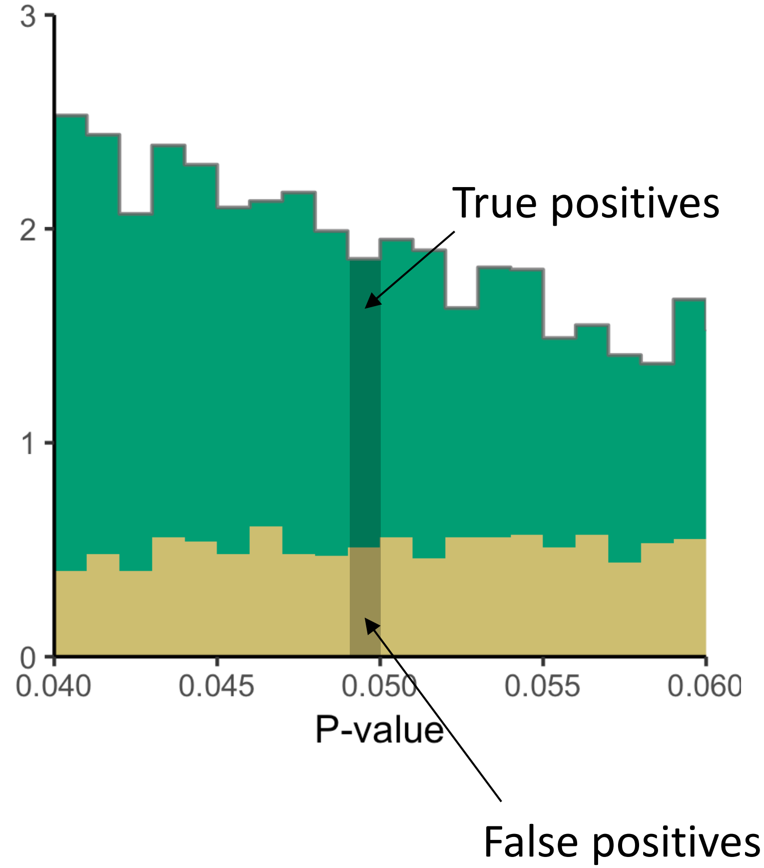
When the effect is rare,
FDR is high

What does a p-value ~ 0.05 really mean?



$$\alpha \sim 0.05$$

$$FDR = 0.21$$



Bayesian approach: consider all prior distributions

Berger & Selke
(Bayesian approach)

$$p \sim 0.05 \;\Rightarrow\; FDR \geq 0.3$$

3-sigma approach

$$p \sim 0.003 \;\Rightarrow\; FDR \geq 0.04$$

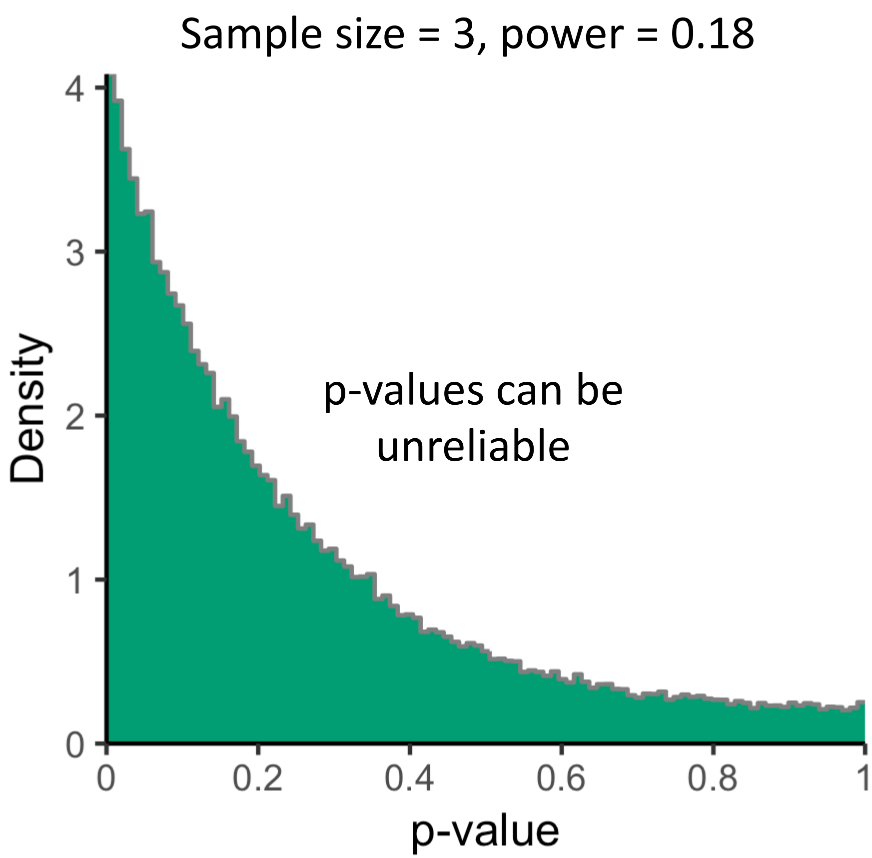
Berger J.O, Selke T., “Testing a point null hypothesis: the irreconcilability of P values and evidence”, 1987, *JASA*, **82**, 112-122

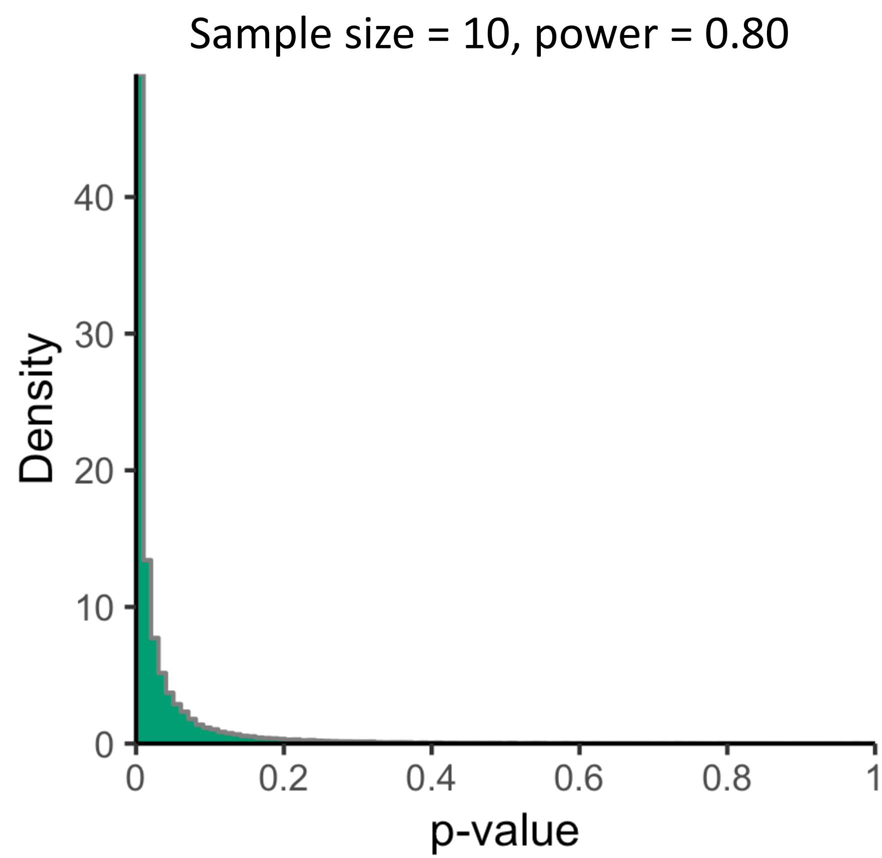
4

When you get a $p \sim 0.05$,
FDR is high

Gedankenexperiment: reliability of p-values

Normal population, 100% real effect (d = 1)
One-sample t-test

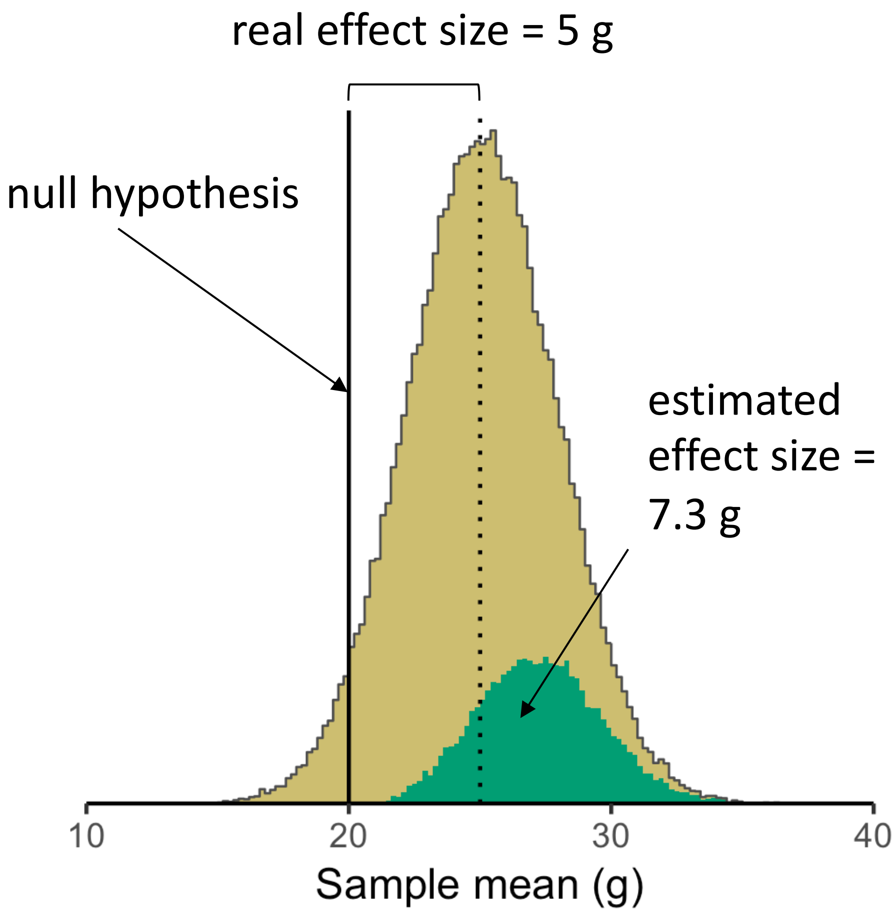


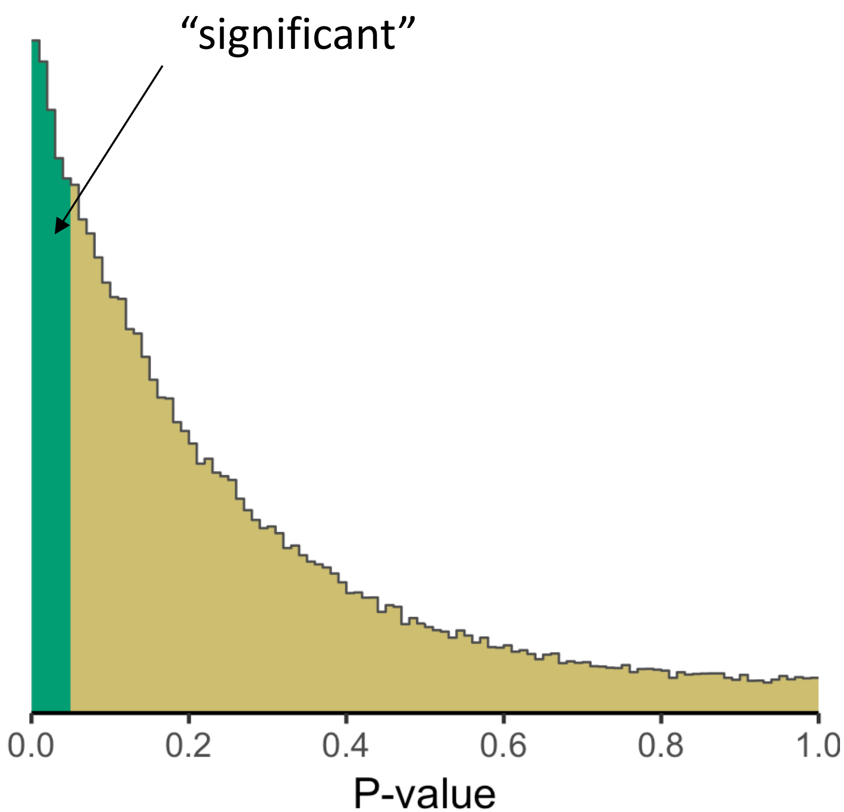


Underpowered studies lead to unreliable p-values

Inflation of the effect size

Gedankenexperiment: draw 100,000 samples of size $n = 3$ from normal population with effect size of 5 g. One-sample t-test against $\mu = 20$ g. "Significant" results inflate the effect size.





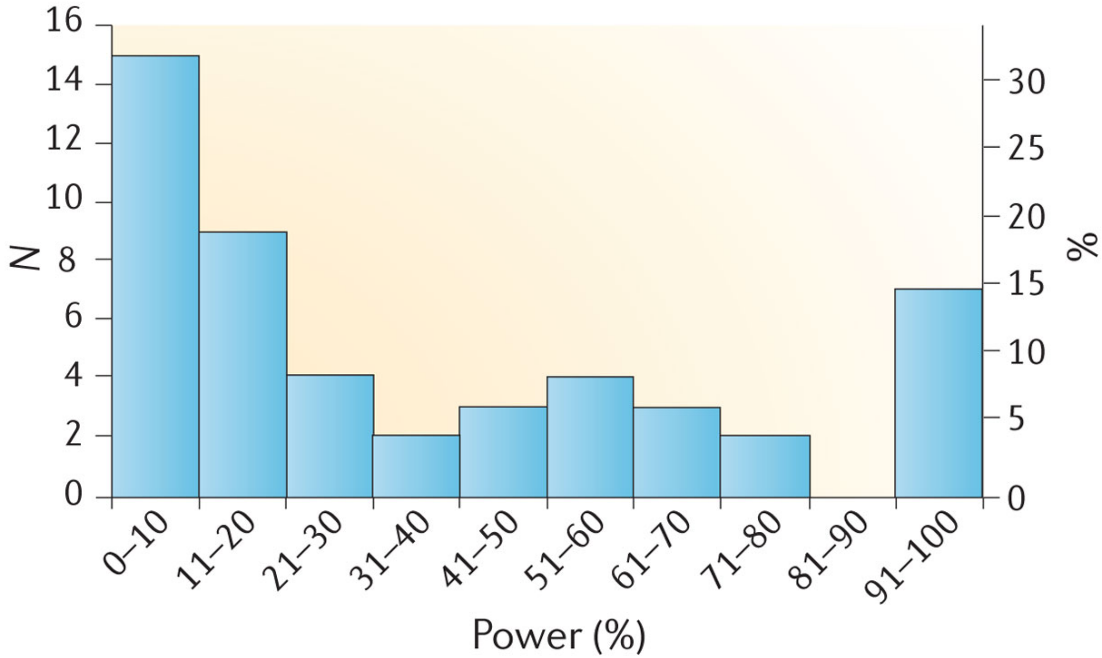
Underpowered studies lead to unreliable p-values

Underpowered studies lead to overestimated effect size

5

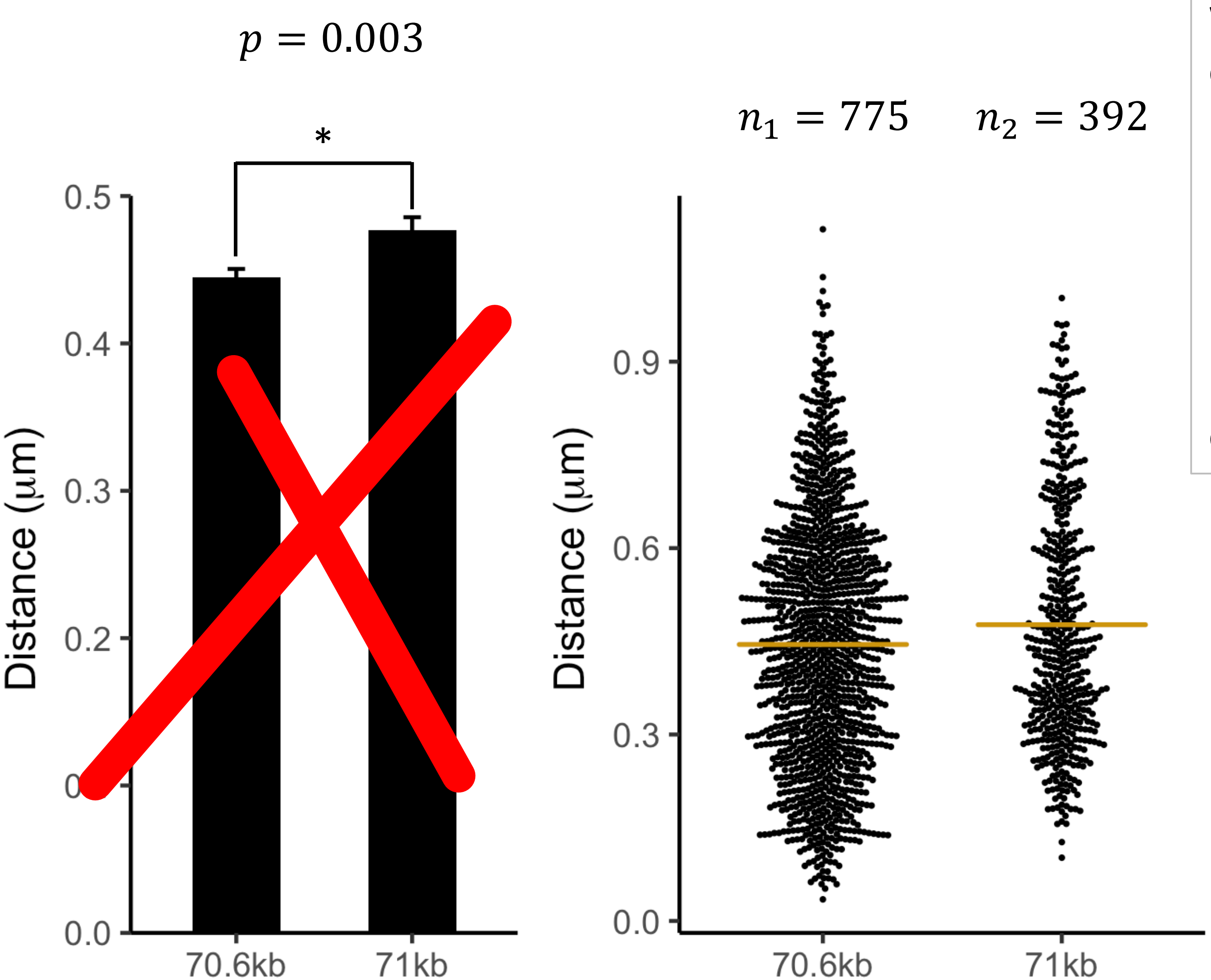
When your experiment is underpowered,
you are screwed

Neuroscience: most studies underpowered



Button et al. (2013) “Power failure: why small sample size undermines the reliability of neuroscience”, *Nature Reviews Neuroscience* **14**, 365-376

The effect size



With sample size large enough everything is "significant"

Effect size is more important

Looking at whole data is even more important

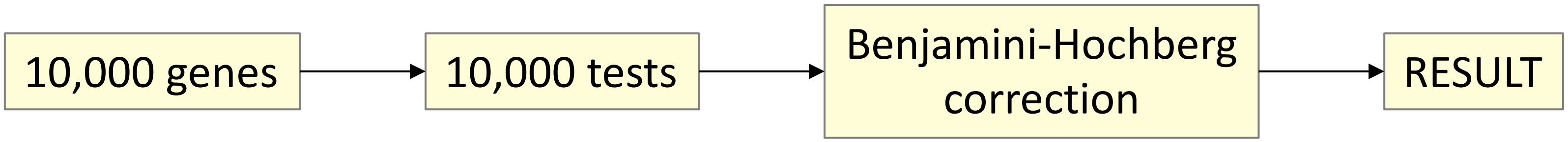
6

When you have lots of replicates, p-values are useless

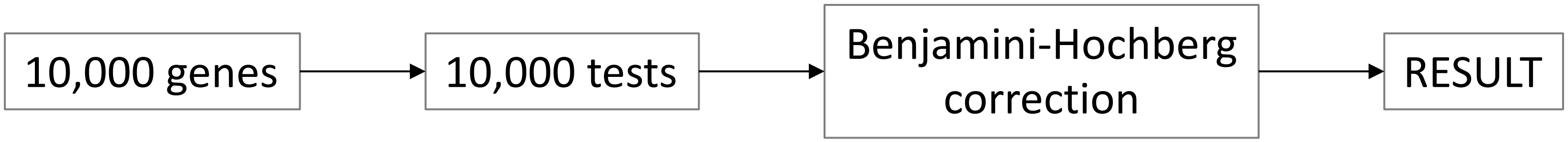
7

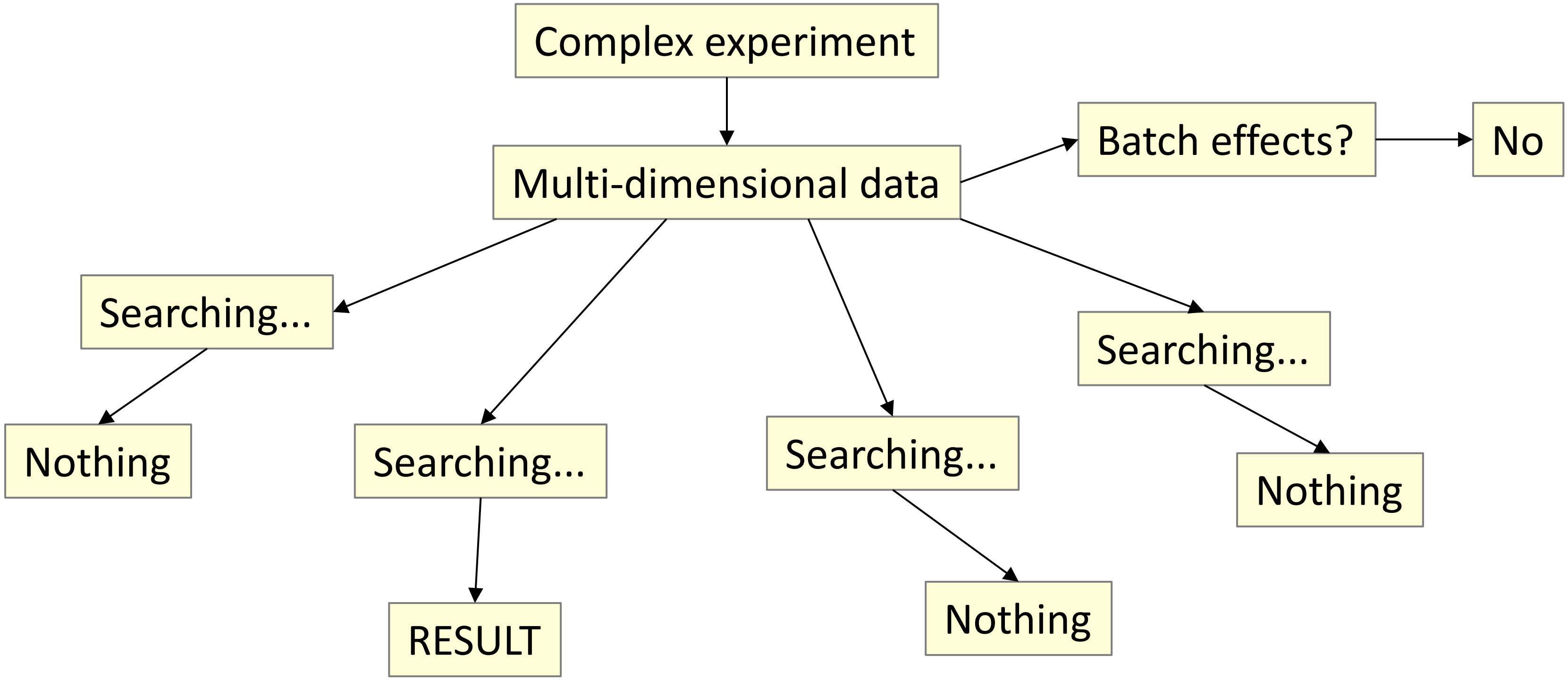
Statistical significance does not imply biological relevance

Multiple test corrections can be tricky



Multiple test corrections can be tricky





8

It is not always obvious how to correct p-values

What’s wrong with p-values?

A lot, because statistics

- P-values test not only the targeted null hypothesis, but everything else in the experiment
- The chance of making a fool of yourself is much larger than $\alpha = 0.05$
- When you get a $p \sim 0.05$, FDR is high
- When the effect is rare, FDR is high
- When your experiment is underpowered, you are screwed
- Statistical significance does not imply biological relevance
- When you have lots of replicates, p-values are useless
- Multiple test corrections are tricky

P-Values: Misunderstood and Misused

Bertie Vidgen and Taha Yasseri *

frontiers in Physics

MINI REVIEW
published: 04 March 2016
doi: 10.3389/fphy.2016.00006

The fickle *P* value generates irreproducible results

Lewis G Halsey, Douglas Curran-Everett, Sarah L Vowler & Gordon B Drummond

NATURE METHODS | VOL.12 NO.3 | MARCH 2015 | 179

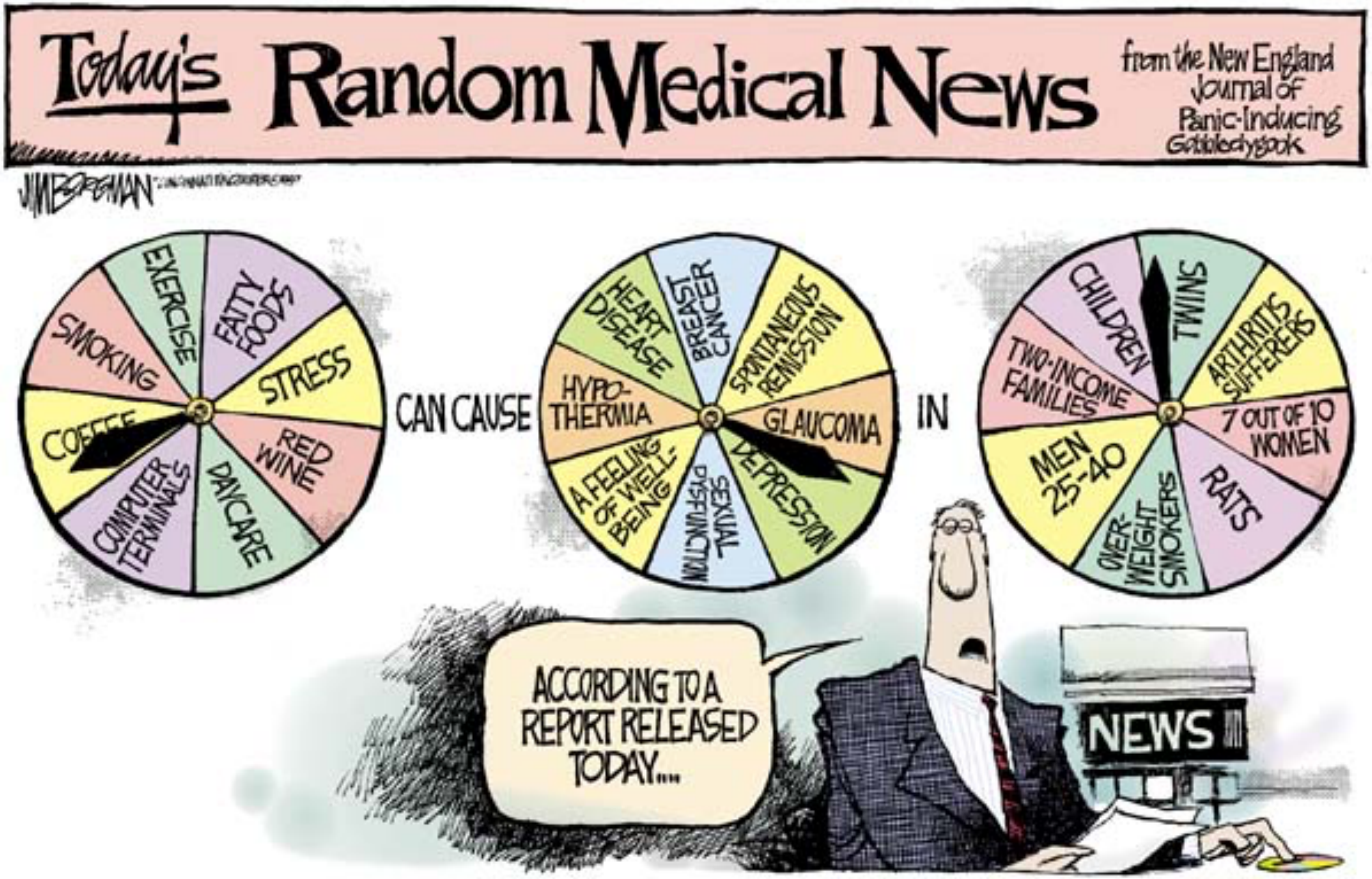
Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

PLoS Medicine | www.plosmedicine.org 0696 August 2005 | Volume 2 | Issue 8 | e124



By Jim Borgman, first published by the Cincinnati Inquirer 27 April 1997

What’s wrong with us?

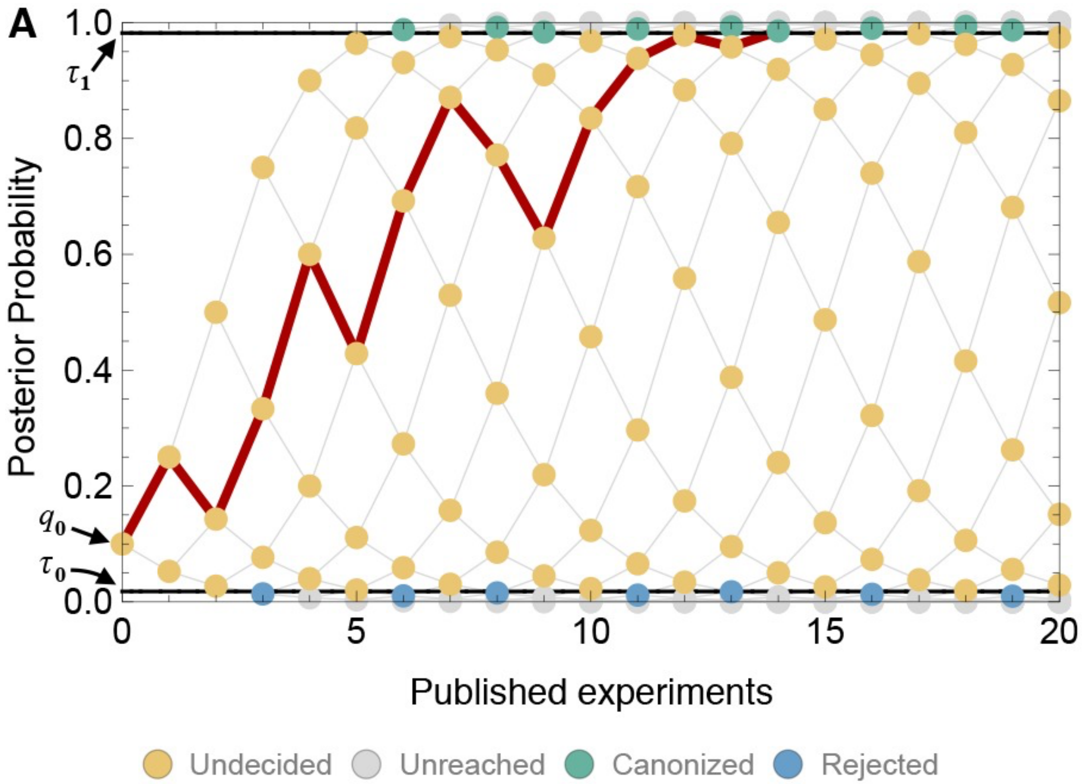
“There is some evidence that [...] research which yields nonsigificant results is not published. Such research being unknown to other investigators may be repeated independently until eventually by chance a significant result occurs [...] The possibility thus arises that the literature [...] consists in substantial part of false conclusions [...].”

PUBLICATION DECISIONS AND THEIR POSSIBLE EFFECTS ON INFERENCES DRAWN FROM TESTS OF SIGNIFICANCE —OR VICE VERSA*

THEODORE D. STERLING
University of Cincinnati

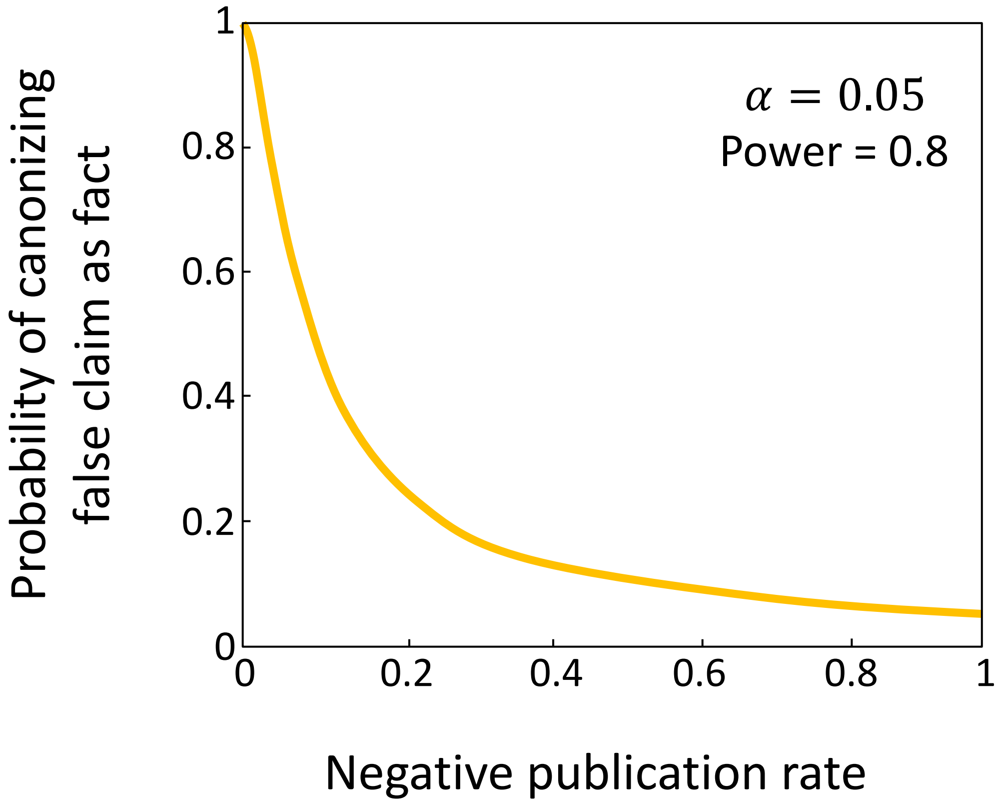
Journal of the American Statistical Association,
Vol. 54, No. 285 (Mar., 1959), pp. 30-34

Canonization of false facts



Nissen S.B., et al., “Research: Publication bias and the canonization of false facts”, eLife 2016;5:e21451

Canonization of false facts



Nissen S.B., et al., “Research: Publication bias and the canonization of false facts”, eLife 2016;5:e21451

If you don’t publish negative results, science is screwed

but…

there is a thin line between “negative result” and “no result”

Data dredging, p-hacking

Post-hoc hypothesis

Massaging data

Unaccounted multiple experiments/tests

Searching until you find the result you were looking for

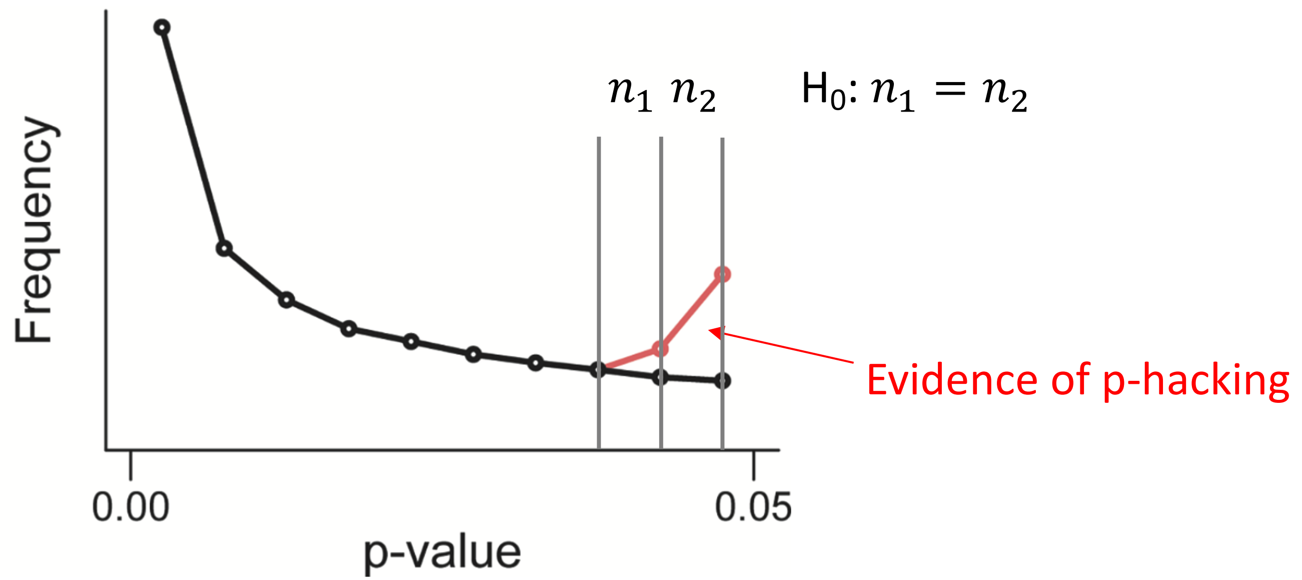
$p = 0.06$?
Let's try again

Not reporting non-significant results

Ignoring confounding effects

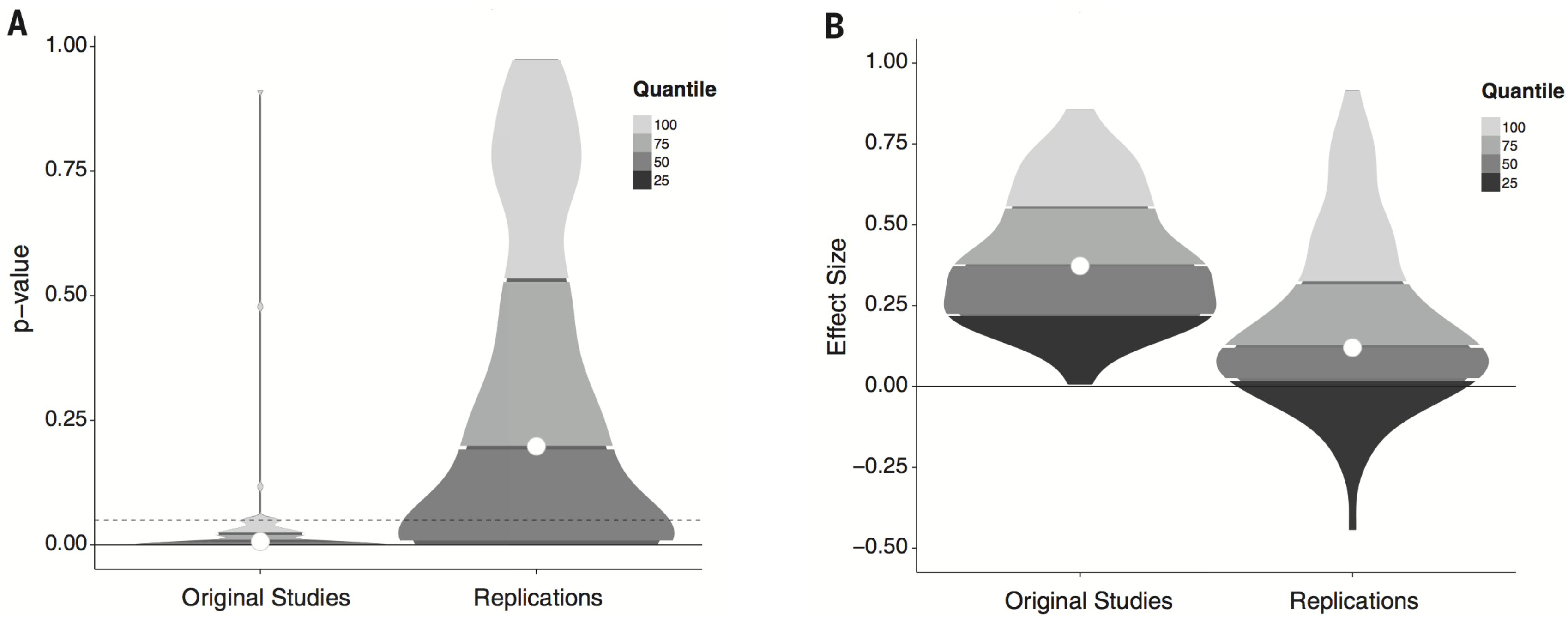
Evidence of p-hacking

Distribution of p-values reported in publications



Head M.L., et al. "The Extent and Consequences of P-Hacking in Science", PLoS Biol 13(3)

Reproducibility crisis



Open Science Collaboration, "Estimating the reproducibility of psychological science", *Science*, **349** (2015)

Tried to reproduce 100 published experiments

Managed to reproduce only 39% results

The great reproducibility experiment

Are referees more likely to give red cards to black players?

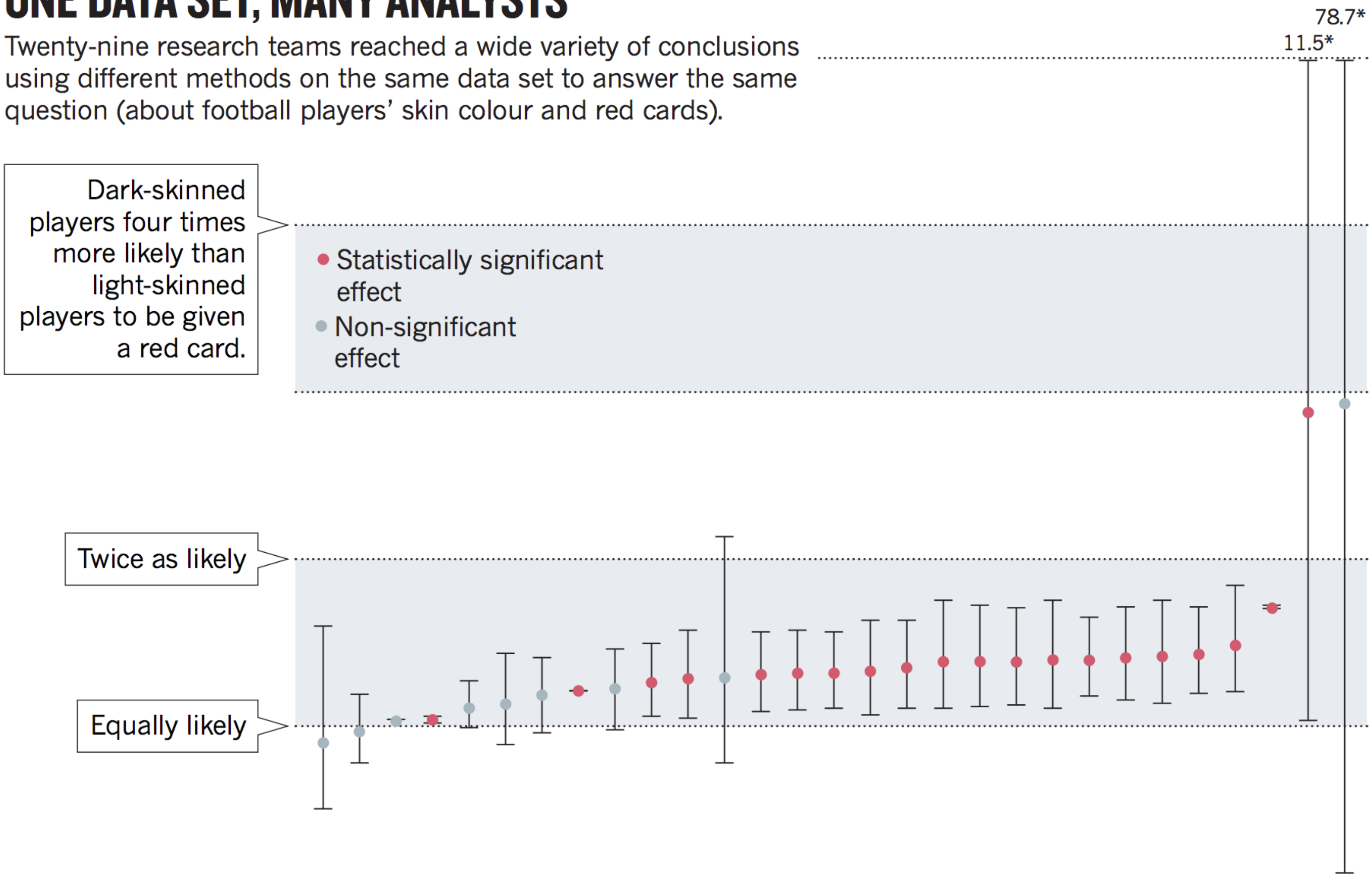

Mario Balotelli, playing for Manchester City, is shown a red card during a match against Arsenal.

Silberzahn et al., “Many analysts, one dataset: Making transparent how variations in analytical choices affect results” (2018) doi:10.1177/2515245917747646

- one data set
- 29 teams
- 61 scientists
- task: find odds ratio

ONE DATA SET, MANY ANALYSTS

Twenty-nine research teams reached a wide variety of conclusions using different methods on the same data set to answer the same question (about football players' skin colour and red cards).



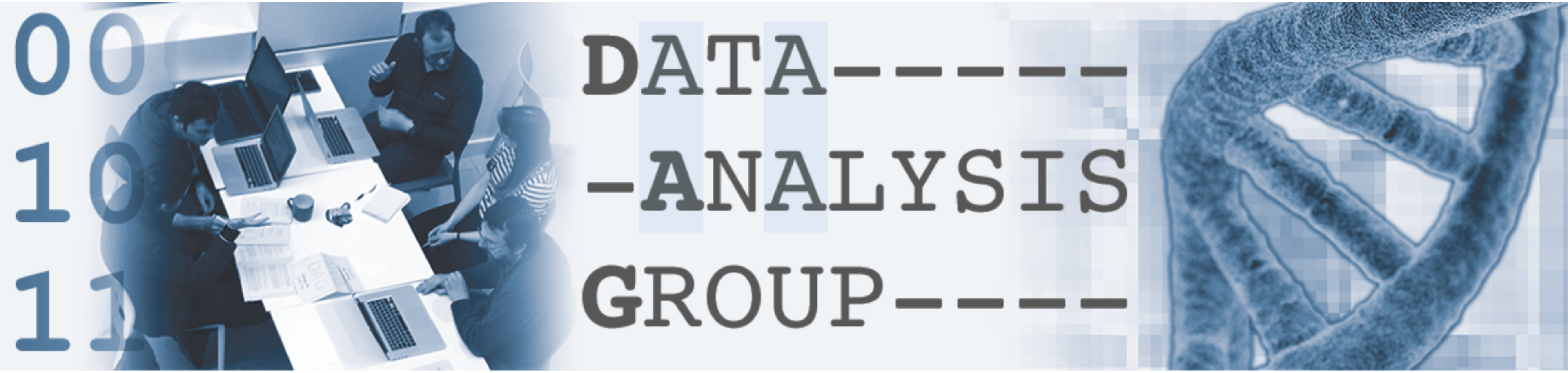
Point estimates and 95% confidence intervals. *Truncated upper bounds.

P-values are broken

We are broken

What do we do?

Before you do the experiment



talk to us

The Data Analysis Group
http://www.compbio.dundee.ac.uk/dag.html

Specify the null hypothesis

Design the experiment

- randomization
- statistical power

Quality control

some crap comes out in statistics

Ditch the α limit

use p-values as a continuous measure of data incompatibility with H_0

$p \sim 0.05$ only means '**worth a look**'

Reporting a discovery based only on $p < 0.05$ is **wrong**

We assumed the null hypothesis

Never, ever say that large p supports H_0

Use the three-sigma rule

that is $p < 0.003$, to demonstrate a discovery

Reporting

- Always report the effect size and its confidence limits
- Show data (not dynamite plots)
- Don't use the word 'significant'
- Don't use asterisks to mark 'significant' results in figures

Validation

Follow-up experiments to confirm discoveries

Publication

Publish negative results

ASA Statement on Statistical Significance and P-Values

1. P-values can indicate how incompatible the data are with a specified statistical model
2. P-values do not measure the probability that the studied hypothesis is true, or the probability that the data were produced by random chance alone
3. Scientific conclusions and business or policy decisions should not be based only on whether a p-value passes a specific threshold
4. Proper inference requires full reporting and transparency
5. A p-value, or statistical significance, does not measure the size of an effect or the importance of a result
6. By itself, a p-value does not provide a good measure of evidence regarding a model or hypothesis

https://is.gd/asa_stat

Propensity to misuse or misunderstand a tool should not necessarily lead us to prohibit its use

Clarice R. Weinberg

Hand-outs available at
https://dag.compbio.dundee.ac.uk/training/Statistics_lectures.html