Slides of this talk available at
http://is.gd/statlec

We collaborate on various types of projects

Anything involving data analysis

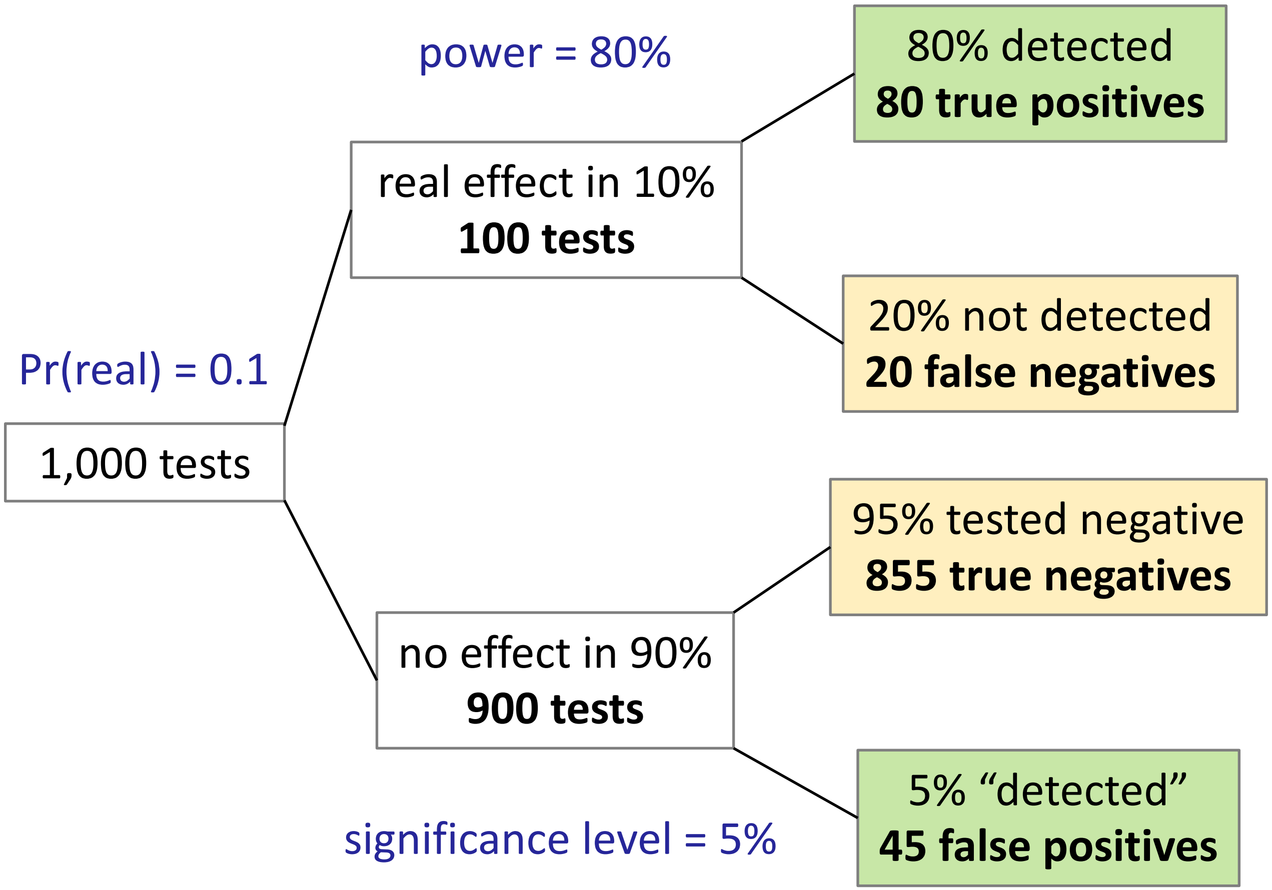
Marek Gierliński

James Abbott

http://www.compbio.dundee.ac.uk/dag.html

Lies
damn lies
statistics

Marek Gierliński
Division of Computational Biology



False positive rate

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

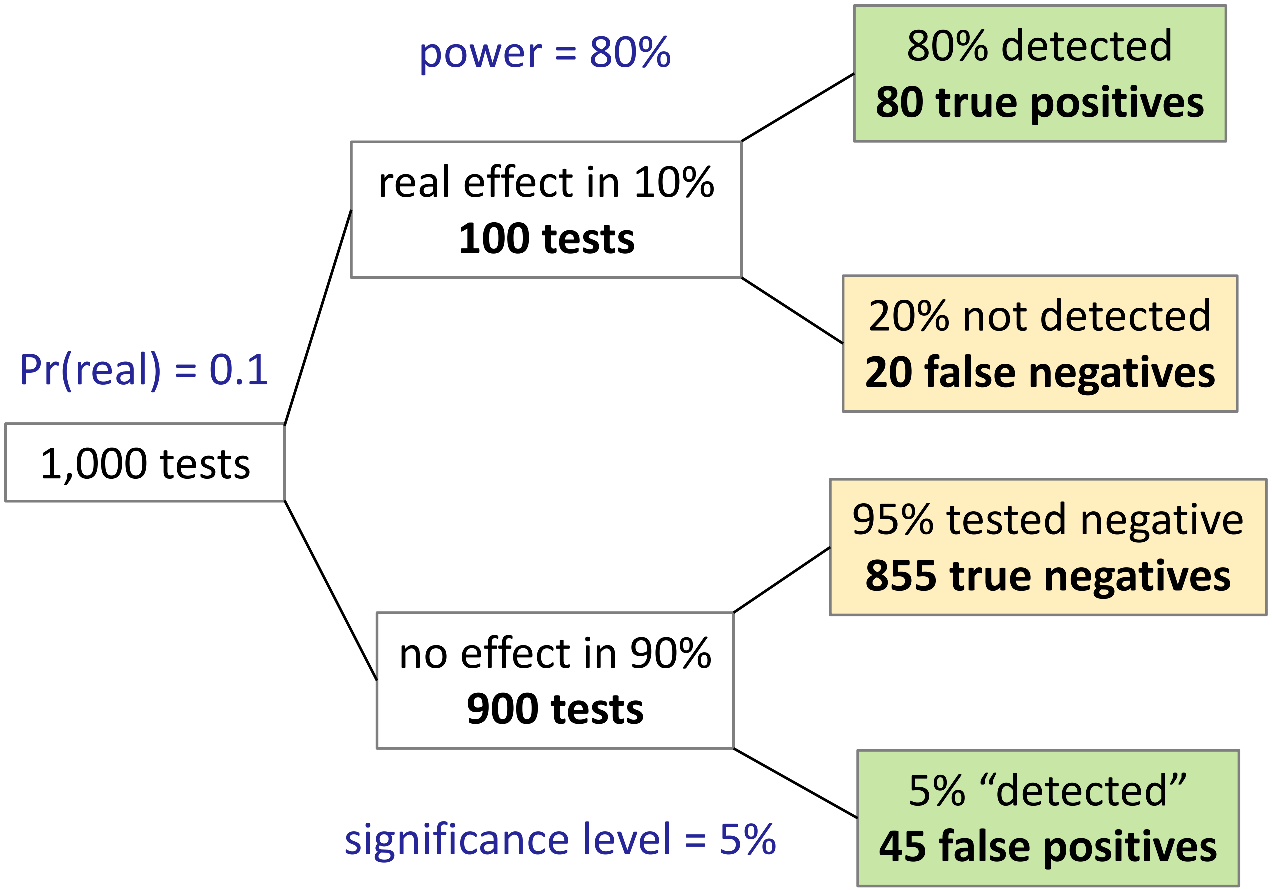
$$FPR = \frac{45}{900} = 0.05$$

False discovery rate

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

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

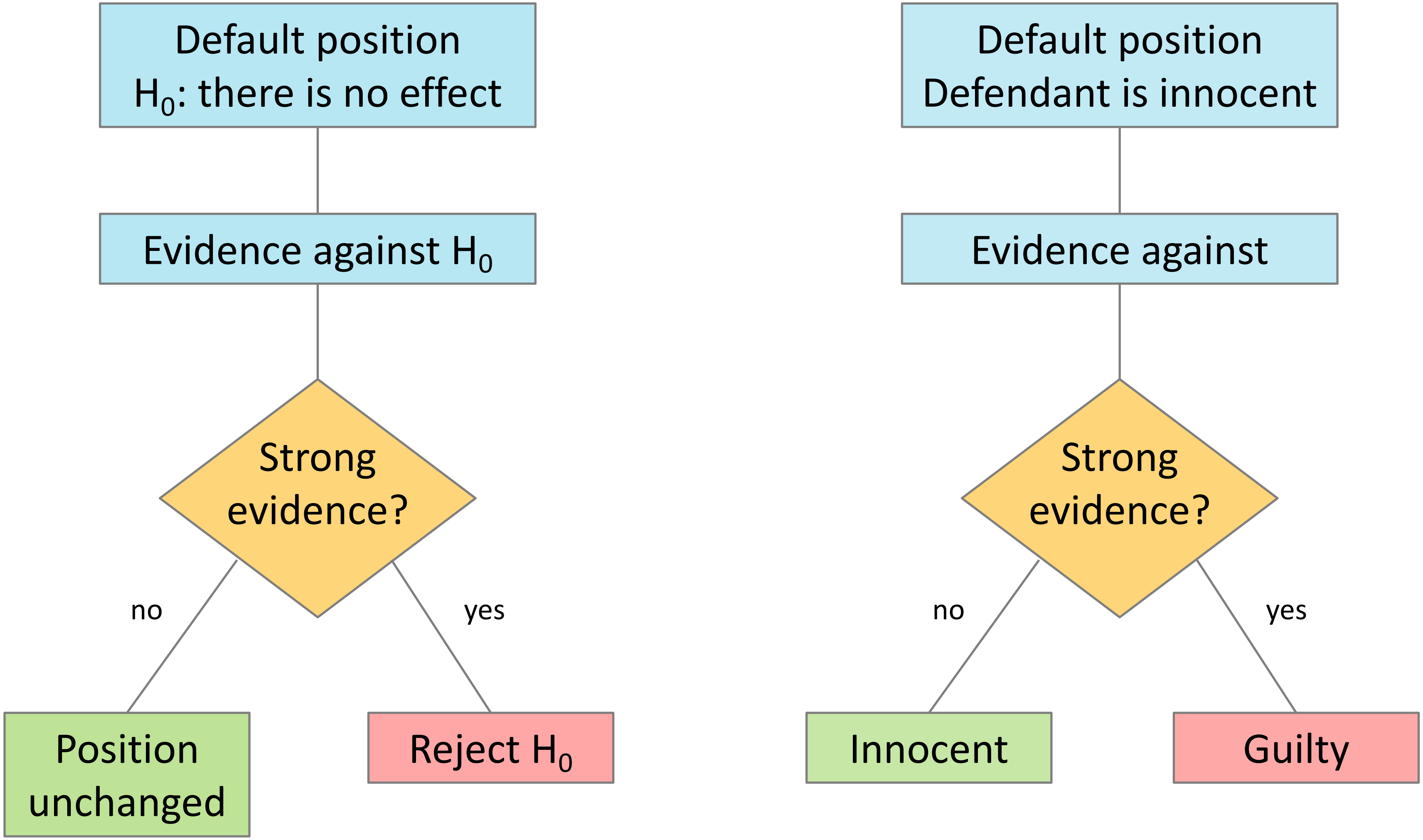
Colquhoun D., 2014, “An investigation of the false discovery rate and the misinterpretation of *p*-values”, *R. Soc. open sci.* **1**: 140216.



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.

Null hypothesis



Statistical testing

Statistical model

Null hypothesis

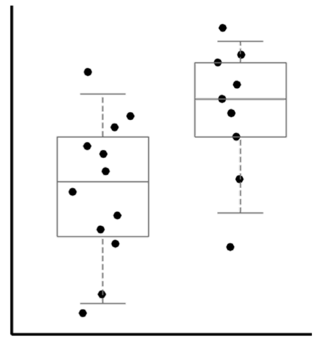
H_0: no effect

All other assumptions

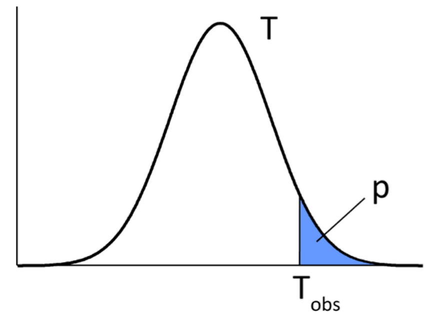
Significance level

$\alpha = 0.05$

Data



Statistical test against H_0



p-value: probability that the observed effect is random

$p < \alpha$

Reject H_0

(at your own risk)

Effect is real

$p \geq \alpha$

Insufficient evidence

p-value:

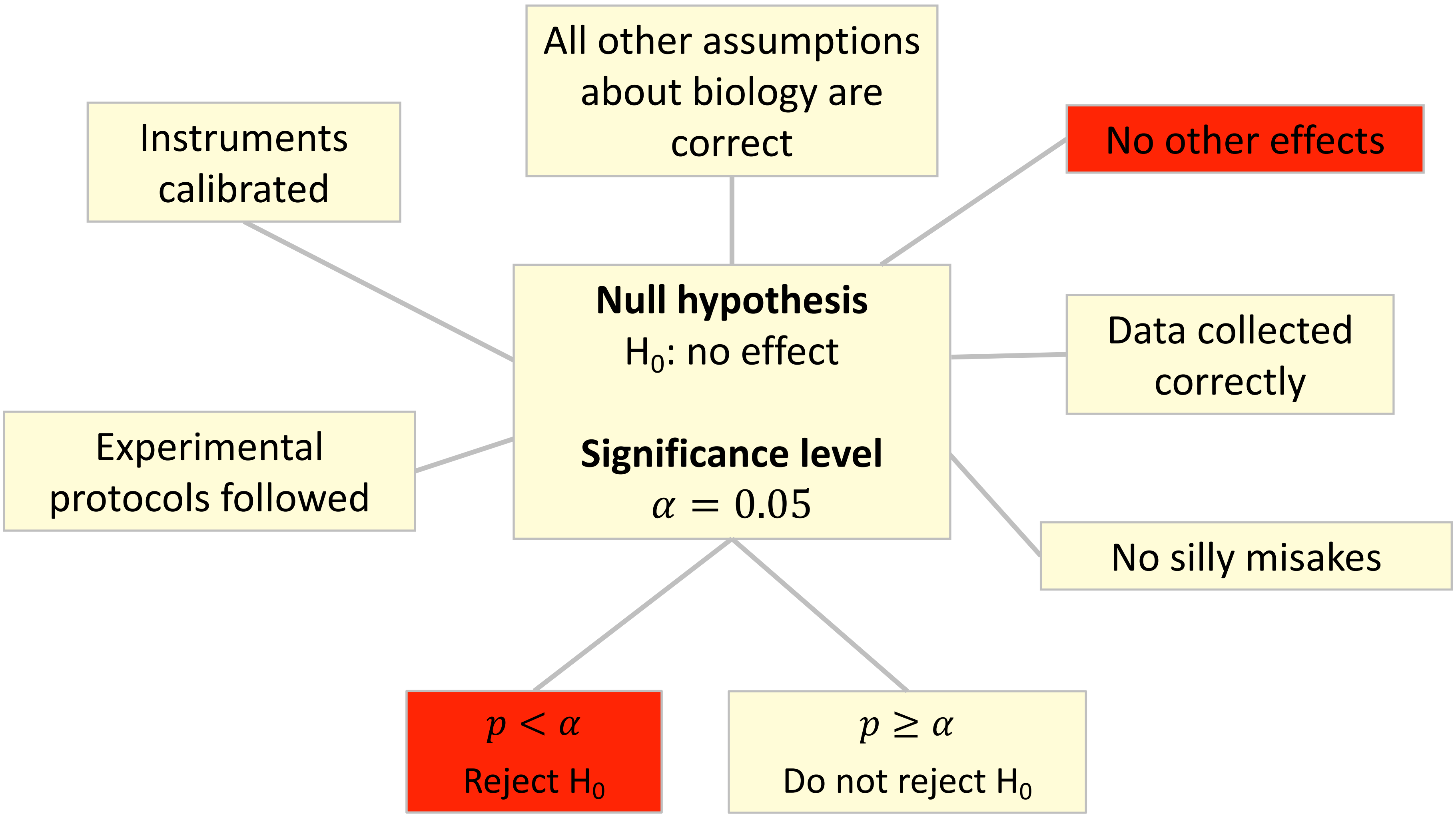
Given that H_0 is true, the probability of observed, or more extreme, data

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

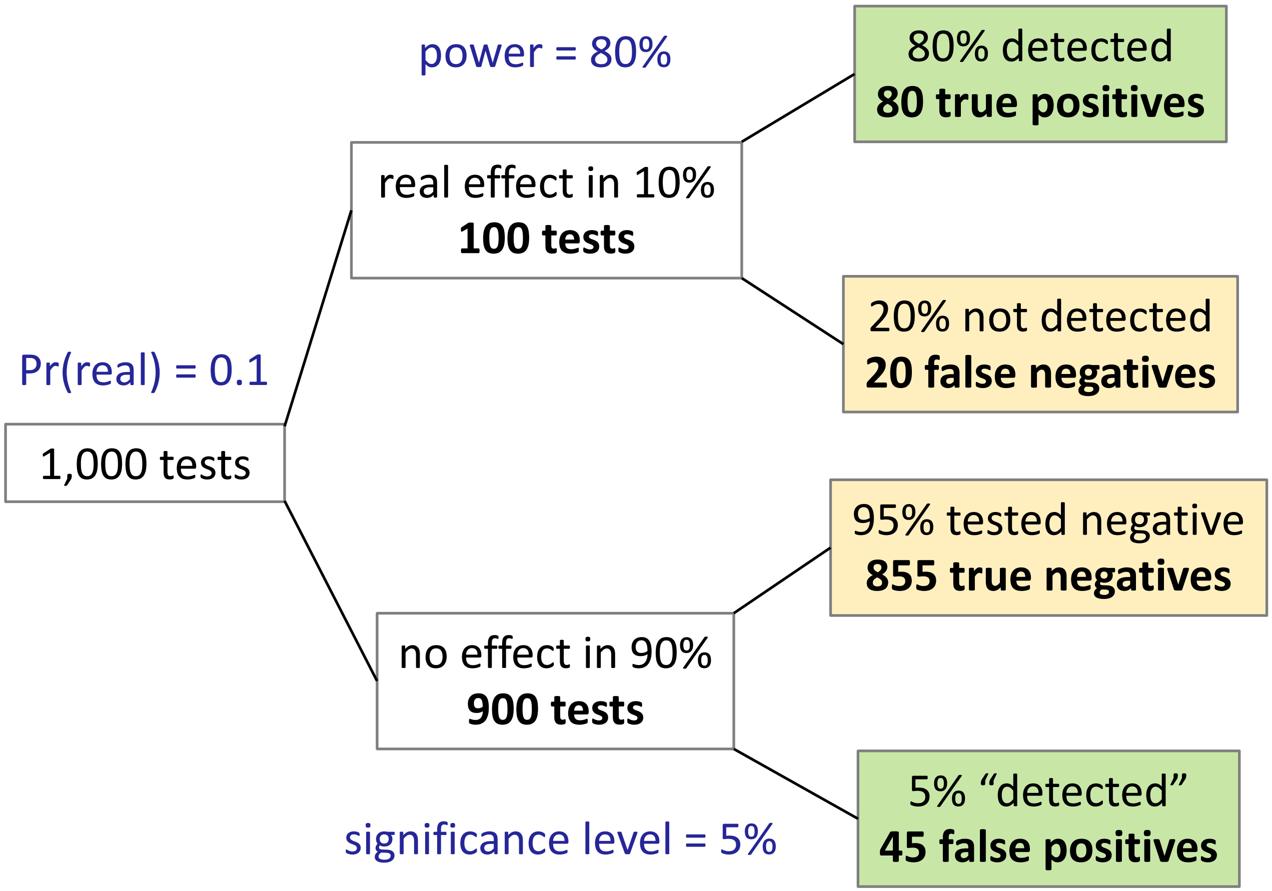
"All other assumptions"



1

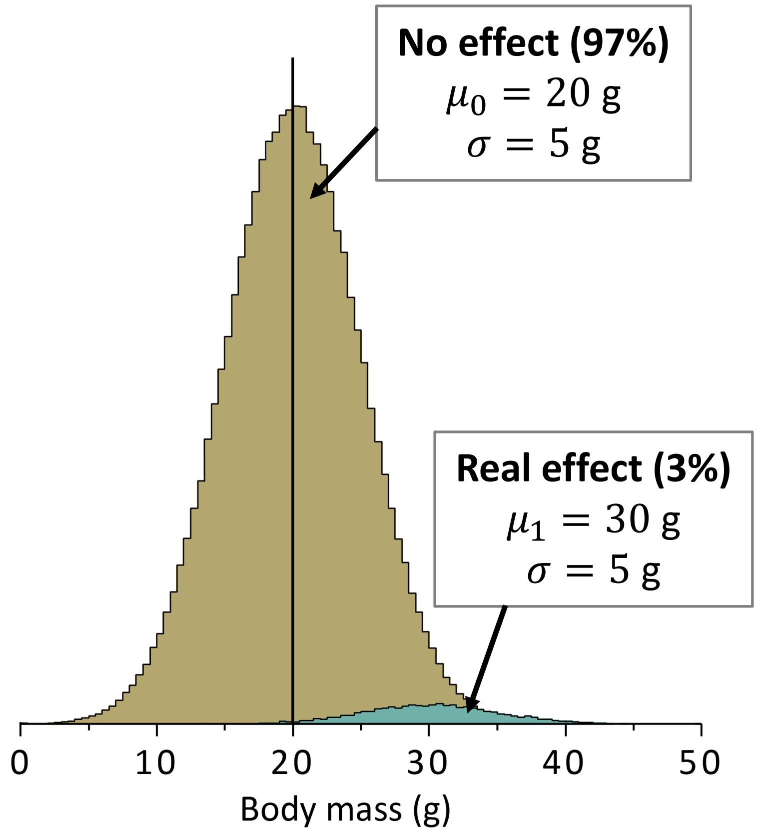
p-values test not only the null hypothesis, but everything else in the experiment

Why large false discovery rate?



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

Simulated population of mice



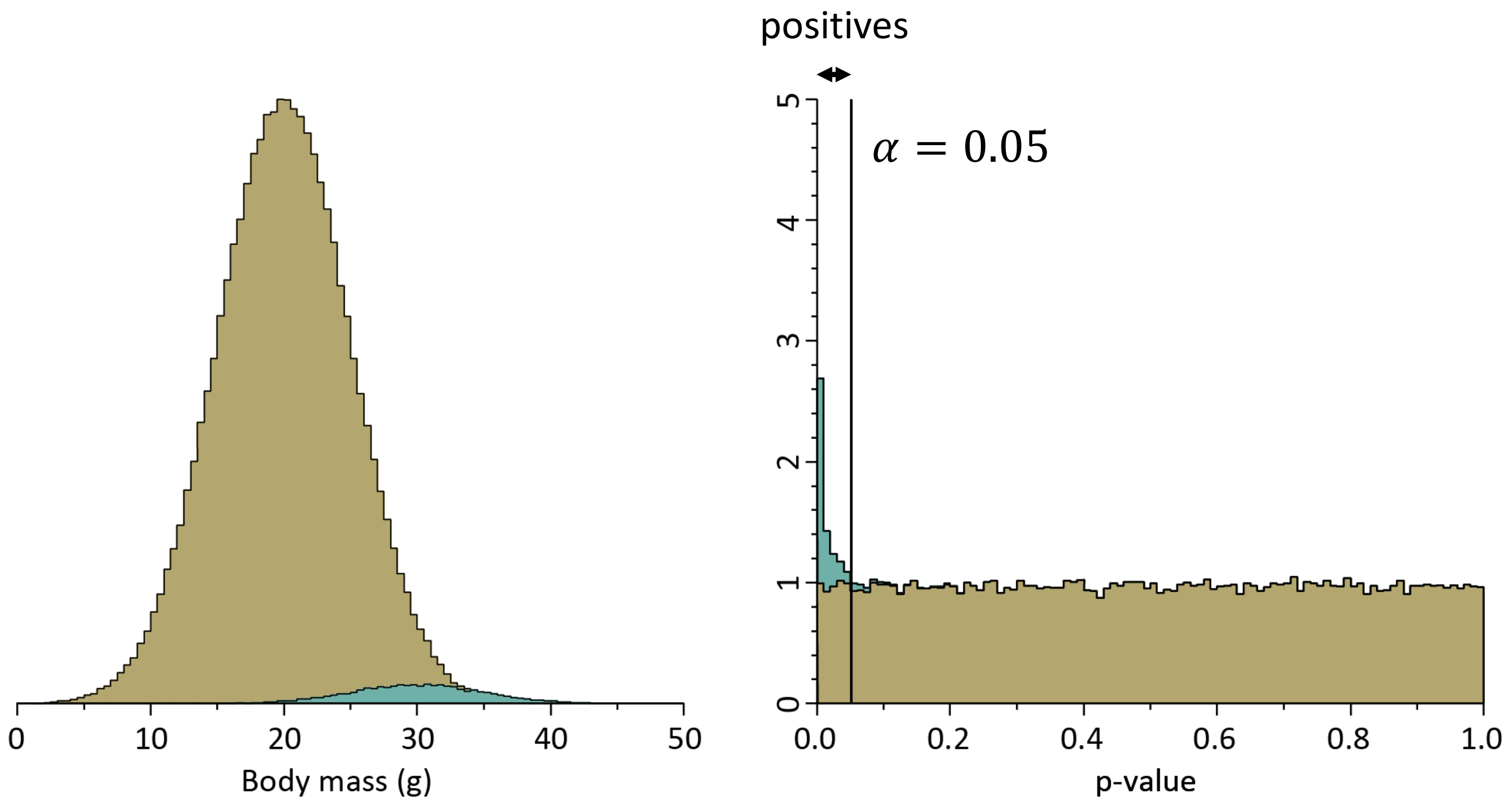
Null hypothesis H_0: $\mu = 20$ g

one-sample t-test

Power analysis

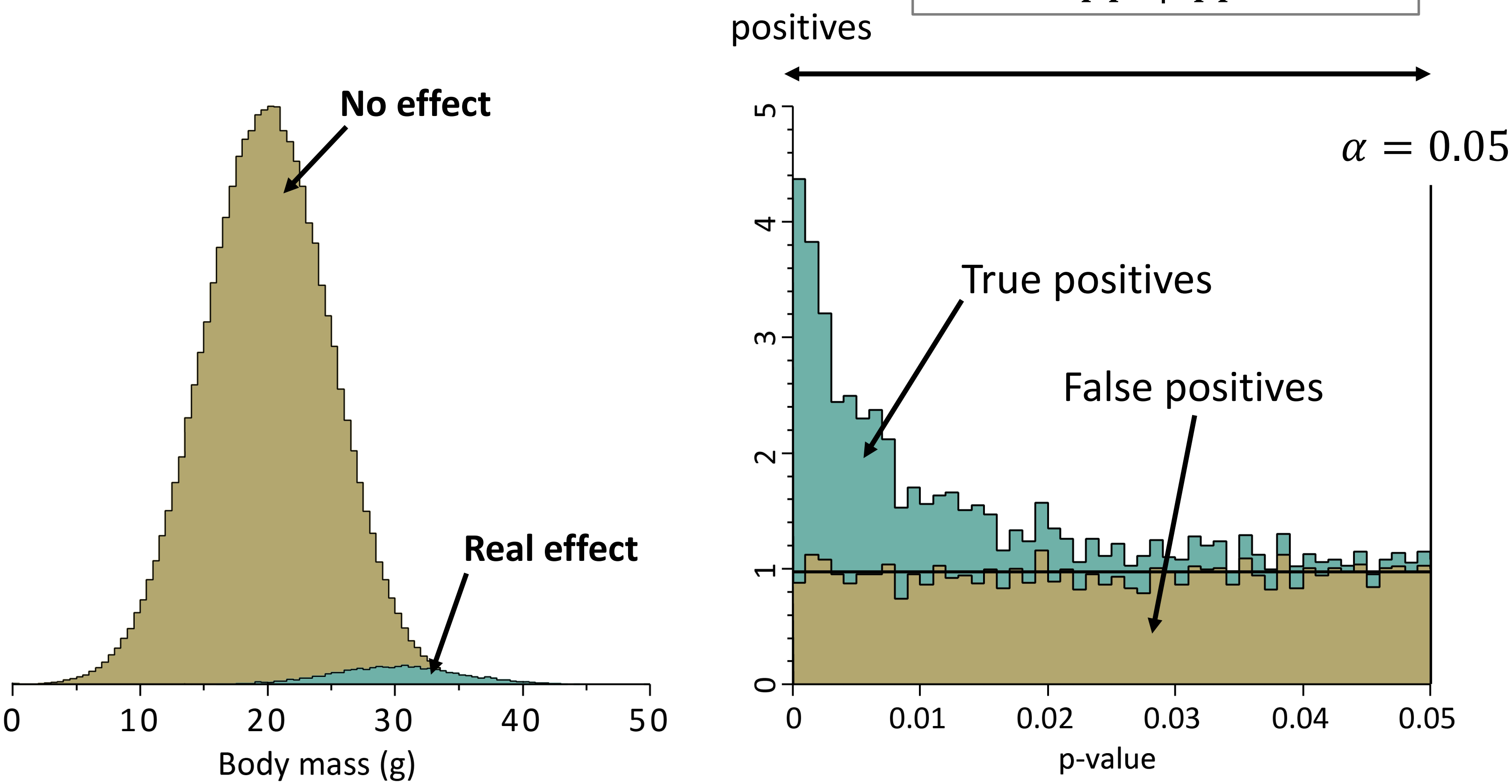
effect size	$\Delta m = 10$ g
power	$\mathcal{P} = 0.9$
significance level	$\alpha = 0.05$
sample size	$n = 5$

Gedankenexperiment: distribution of p-values

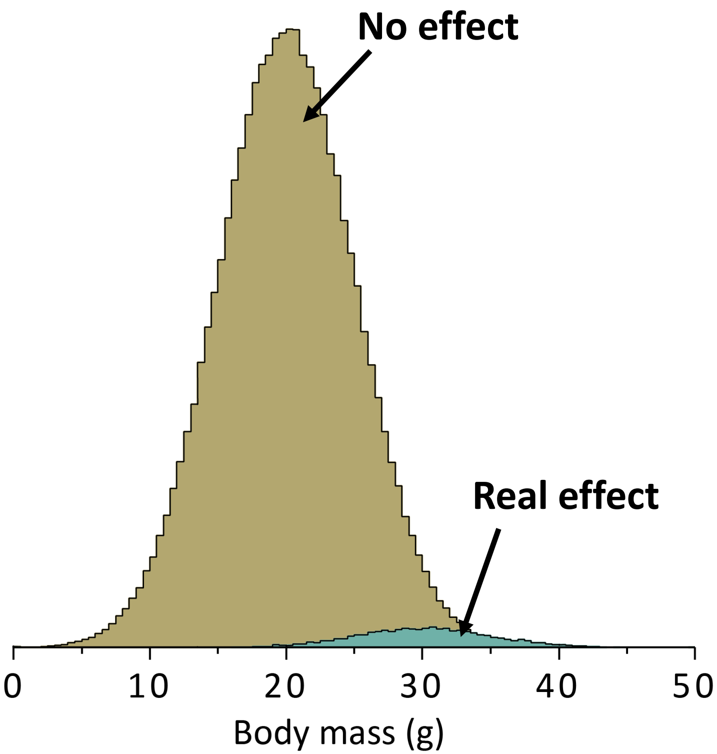


Gedankenexperiment: "significant" p-values

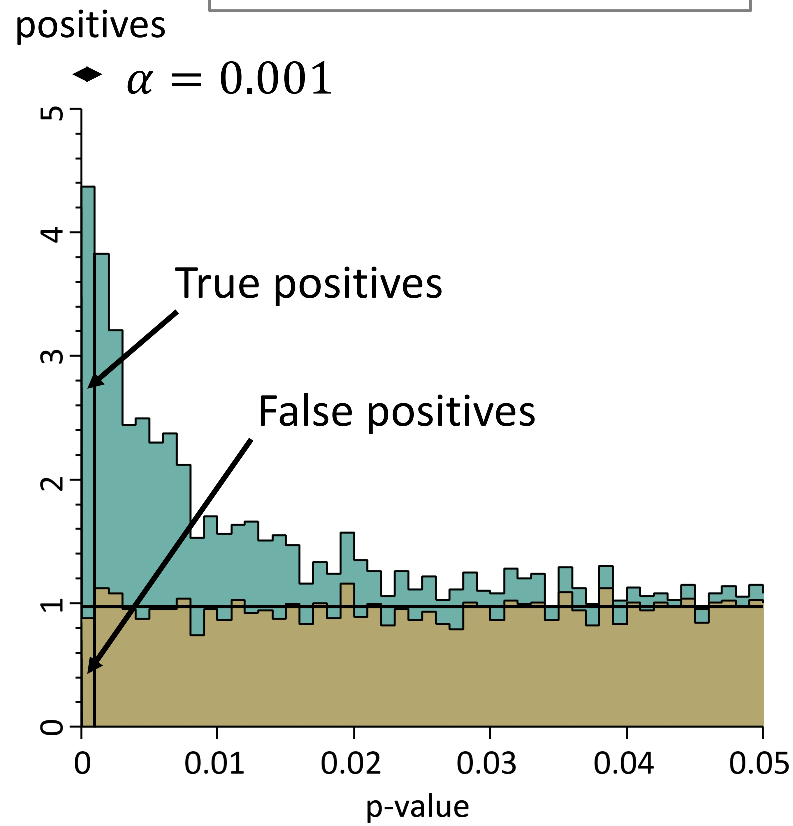
$$FDR = \frac{FP}{FP + TP} \approx 0.63$$



Small α doesn't help



$$FDR = \frac{FP}{FP + TP} \approx 0.20$$



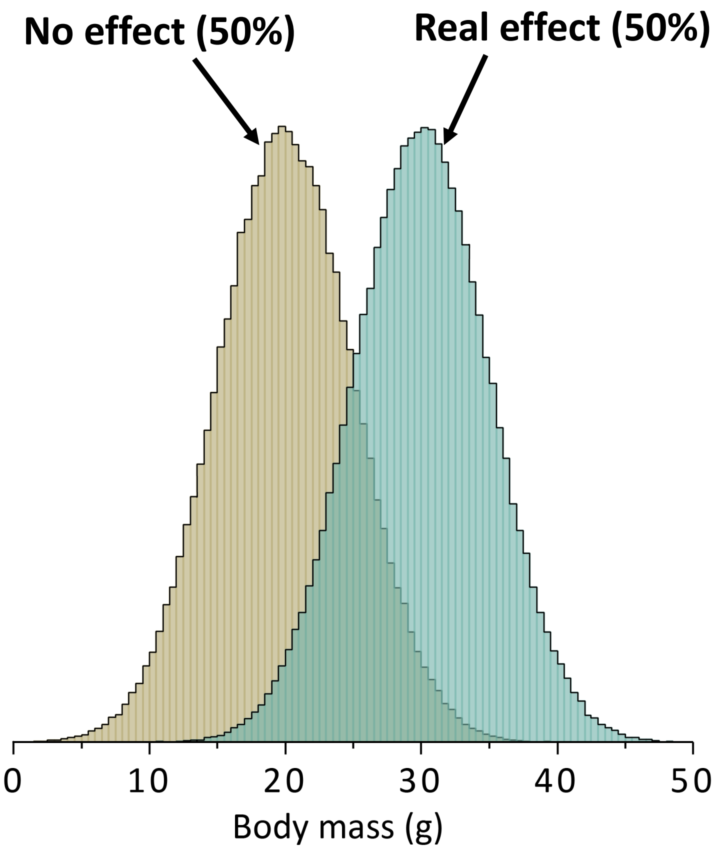
2

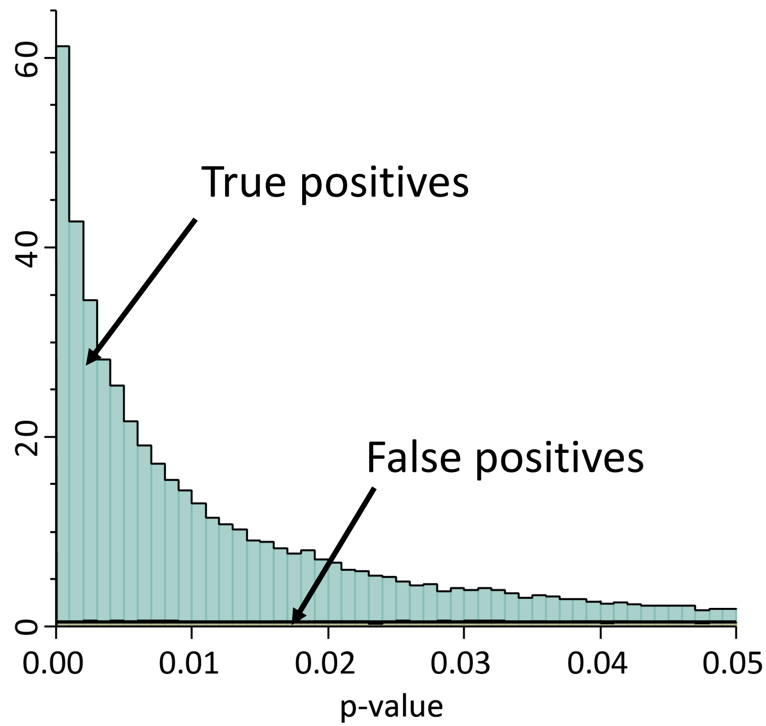
The chance of making a fool of yourself is much larger than $\alpha = 0.05$

FDR depends on the probability of real effect

$\alpha = 0.05$

$FDR \approx 0.05$





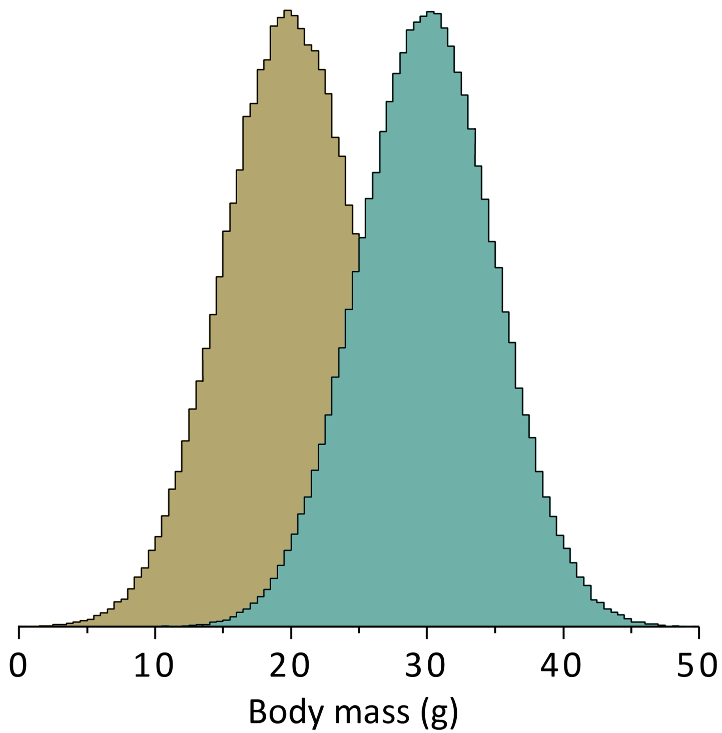
3

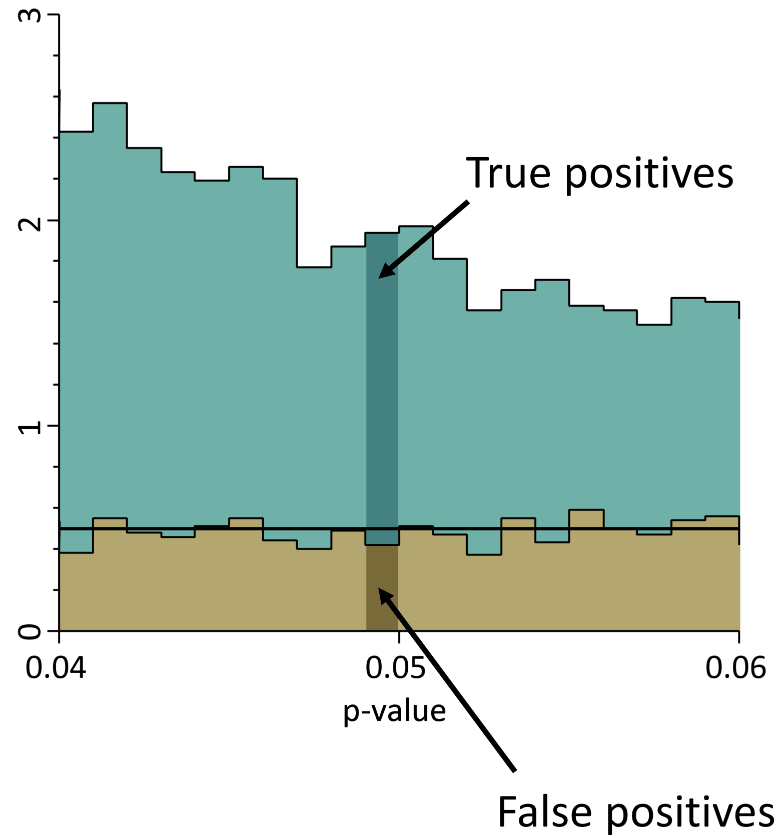
When the effect is rare,
you are screwed

What does a p-value ~ 0.05 really mean?

$$p \sim 0.05$$

$$FDR = 0.21$$





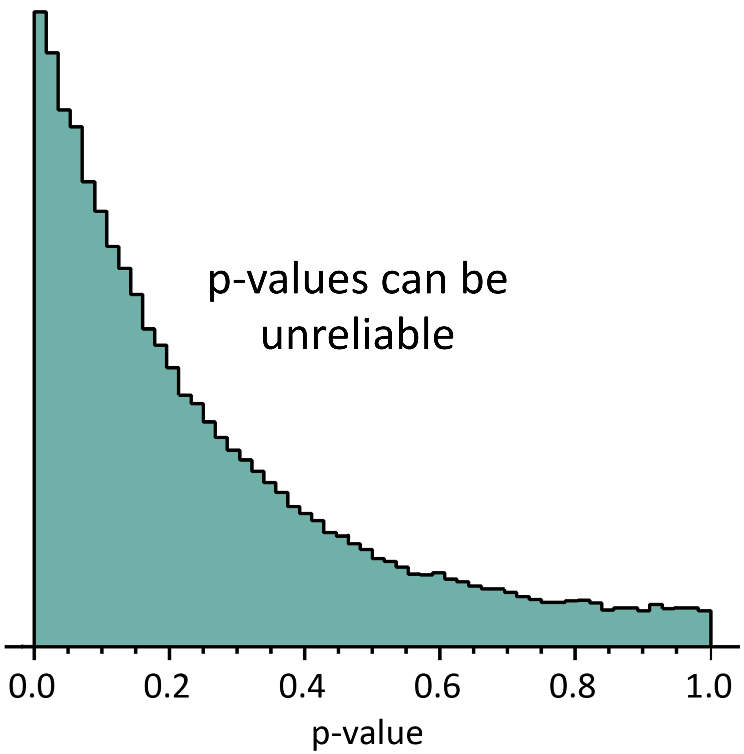
4

When you get a $p \sim 0.05$,
you are screwed

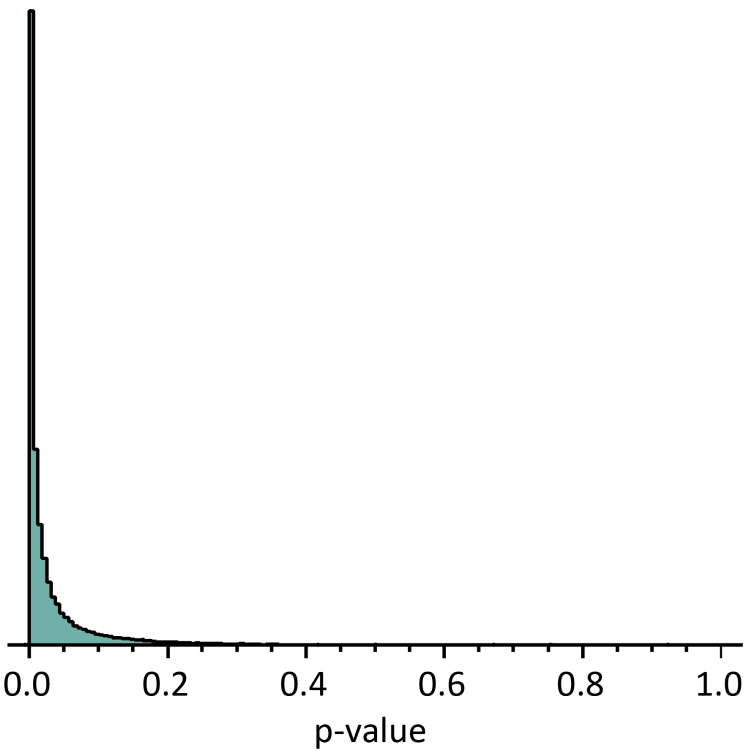
Gedankenexperiment: reliability of p-values

Normal population, 100% real effect
One-sample t-test

Sample size = 3, power = 0.18

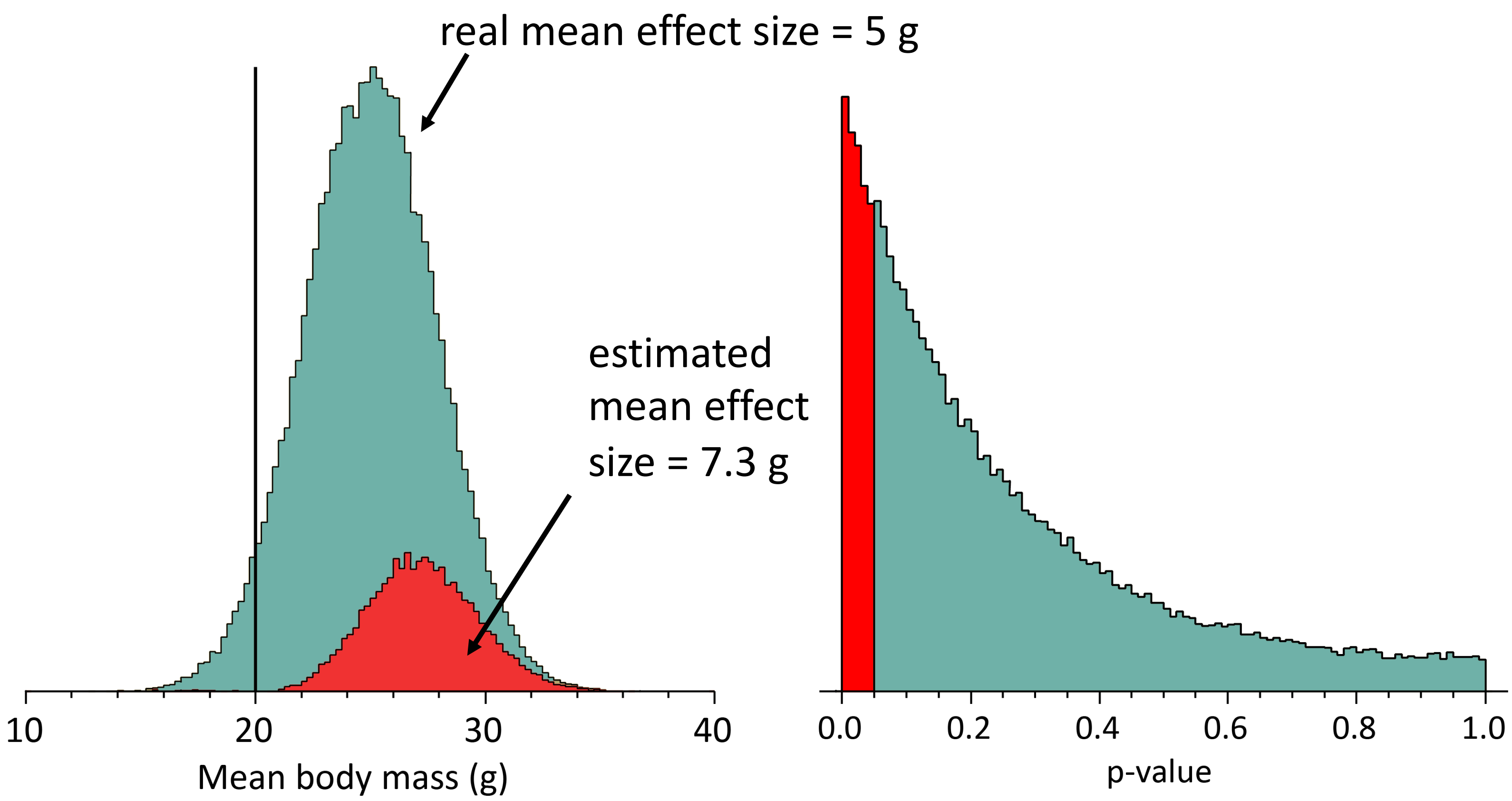


Sample size = 10, power = 0.80



Underpowered studies lead to unreliable p-values

Inflation of the effect size



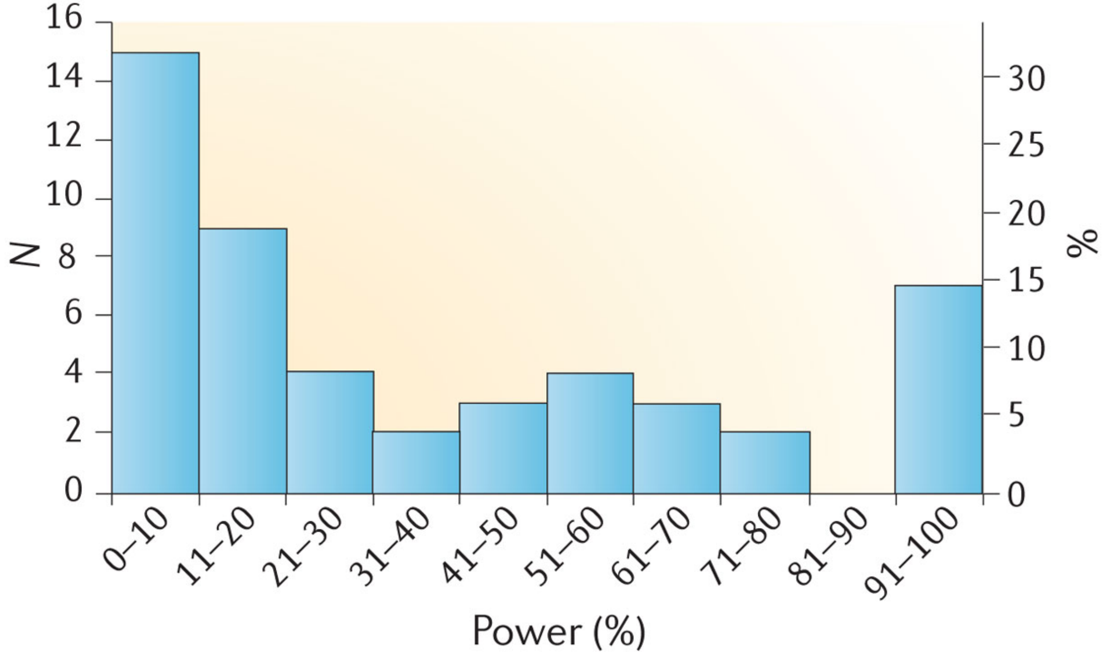
Underpowered studies lead to unreliable p-values

Underpowered studies lead to overestimated effect size

5

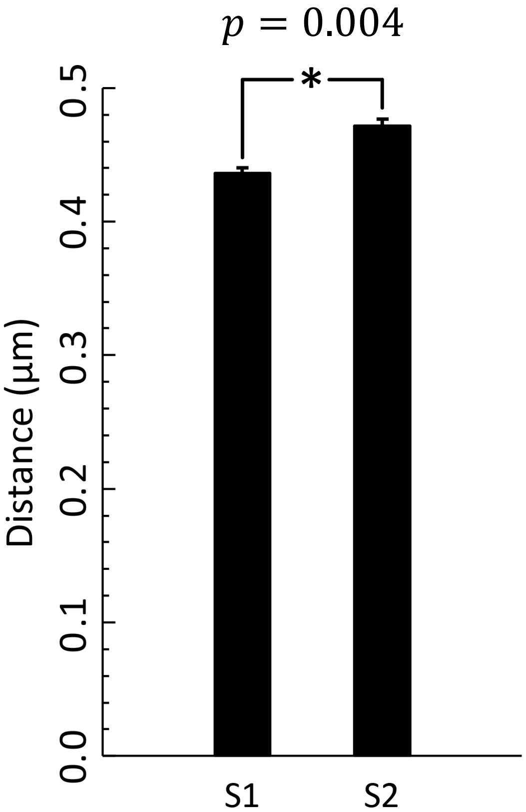
When your experiment is underpowered,
you are screwed

Neuroscience: most studies underpowered

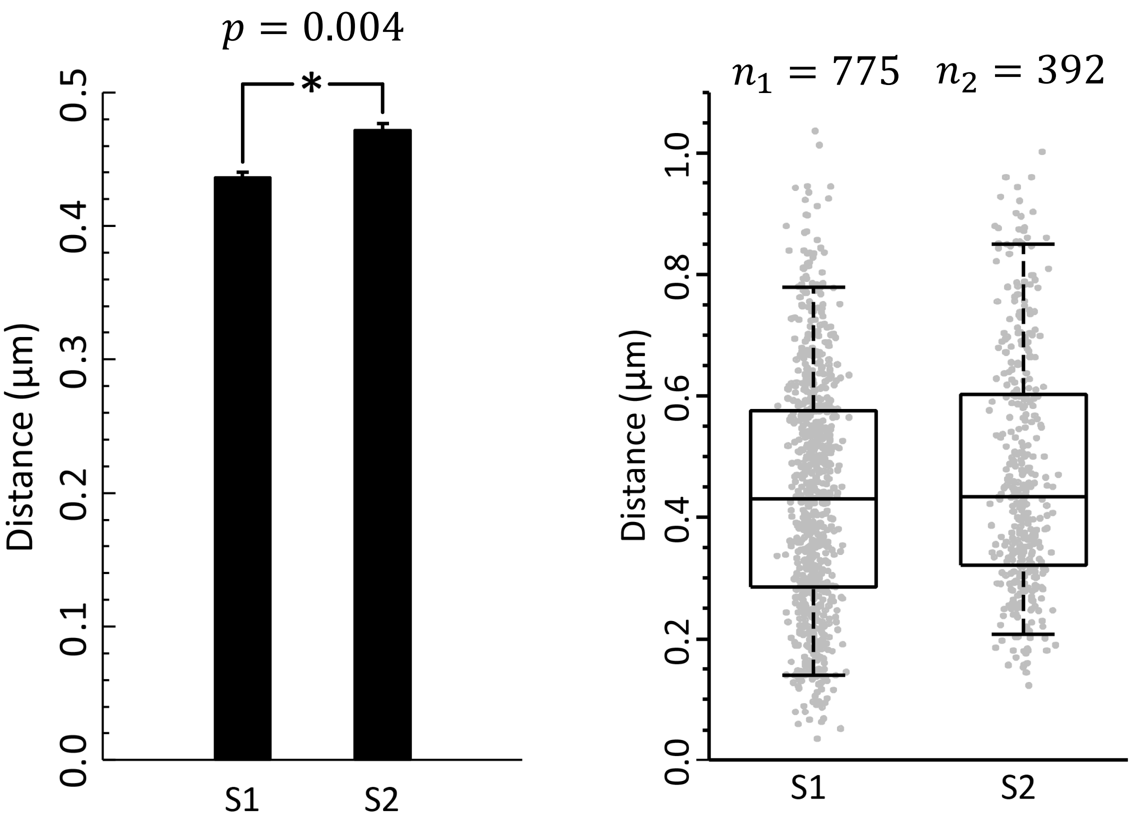


Button et al. (2013) "Power failure: why small sample size undermines the reliability of neuroscience", *Nature Reviews Neuroscience* **14**, 365-376

The effect size



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

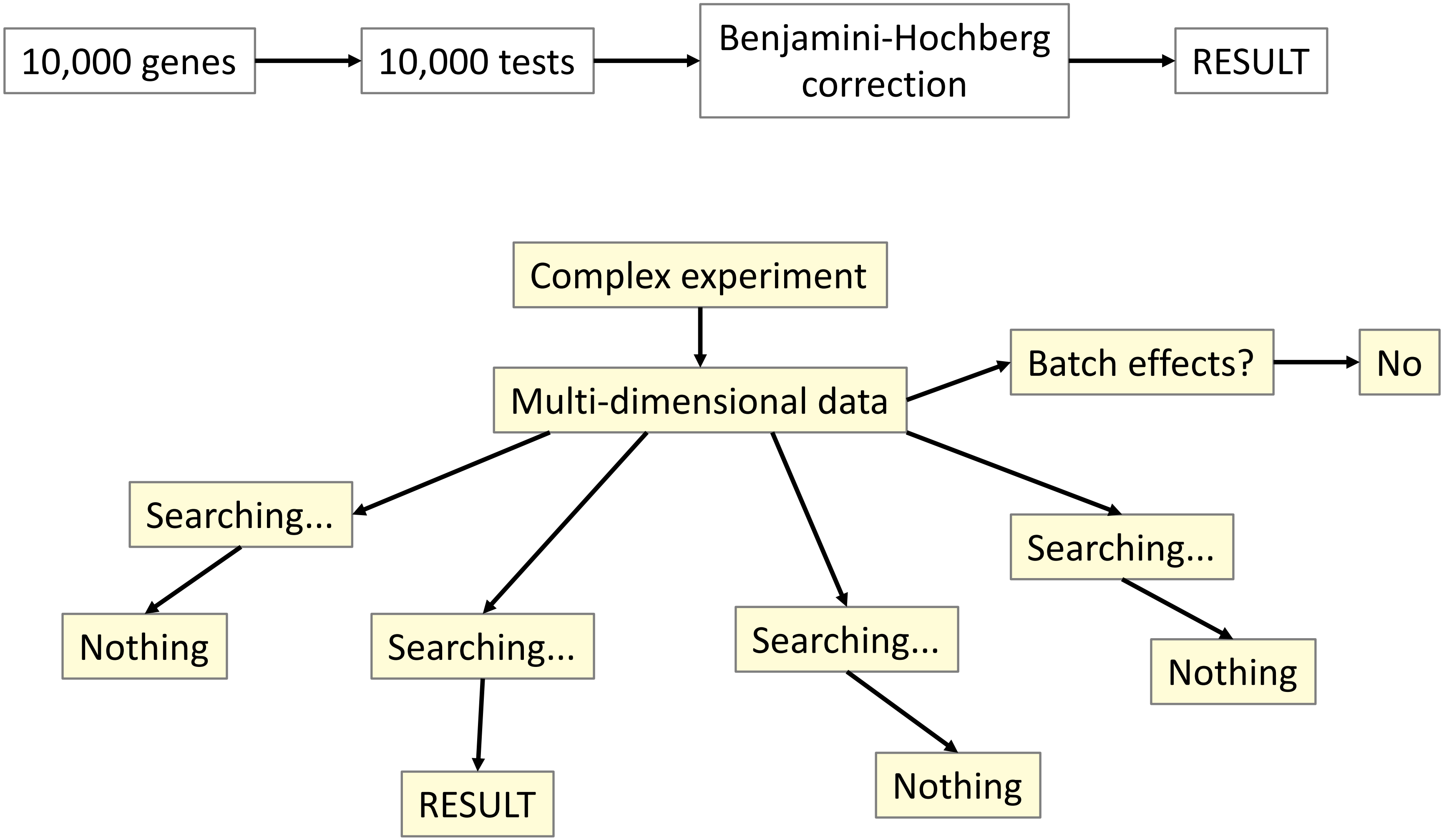
7

Statistical significance does not imply biological relevance

Multiple test corrections can be tricky

10,000 genes → 10,000 tests → Benjamini-Hochberg correction → RESULT

Multiple test corrections can be tricky



8

It is not always obvious how to do multiple-test corrections

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 $p \sim 0.05$, you are screwed
- When the effect is rare, you are screwed
- 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

Null hypothesis significance testing is a potent but sterile intellectual rake who leaves in his merry path a long train of ravished maidens but no viable scientific offspring.

Paul Meehl, 1967, *Philosophy of Science*, 34, 103-115

The plain fact is that 70 years ago Ronald Fisher gave scientists a mathematical machine for turning baloney into breakthroughs, and flukes into funding. It is time to pull the plug.

Robert Matthews, *Sunday Telegraph*, 13 September 1998.

The widespread use of "statistical significance" as a license for making a claim of a scientific finding leads to considerable distortion of the scientific process.

ASA statement on statistical significance and p-values (2016)

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

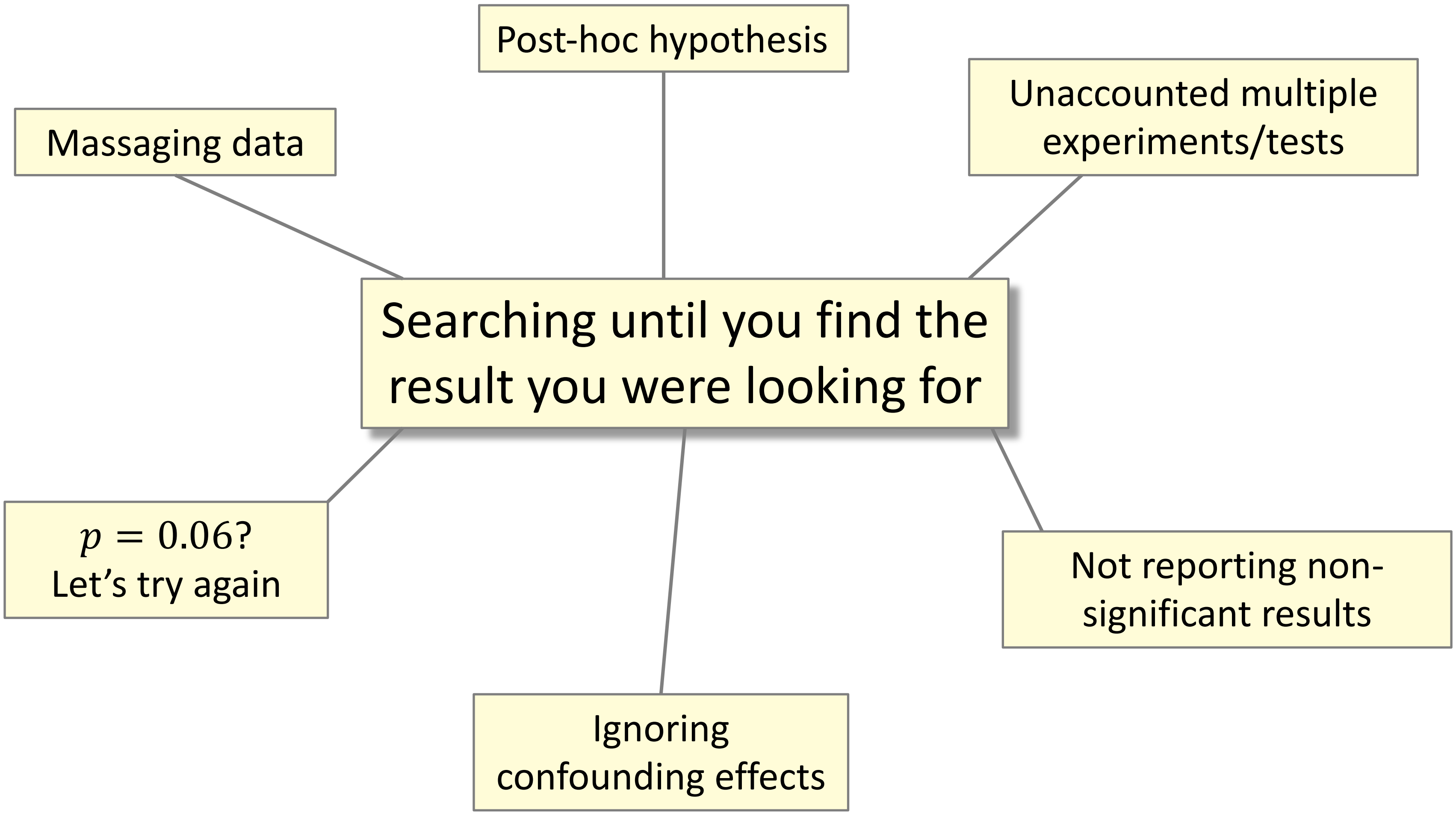
Journal of the American Statistical Association,
Vol. 54, No. 285 (Mar., 1959), pp. 30-34

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

but…

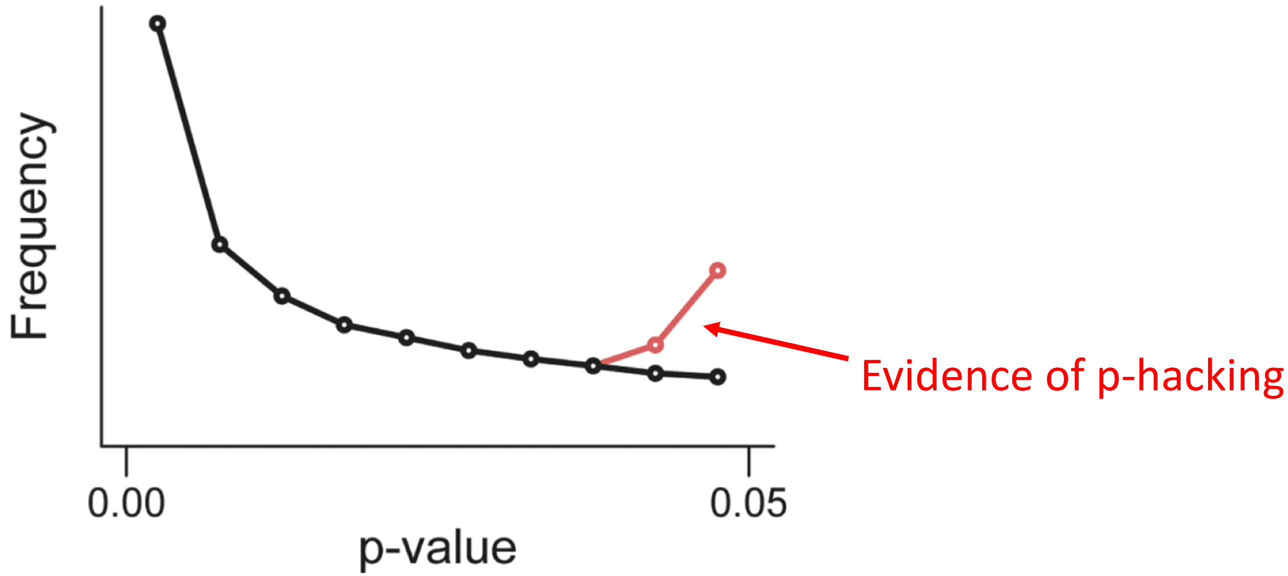
there is a thin line between “negative result” and “no result”

Data dredging, p-hacking



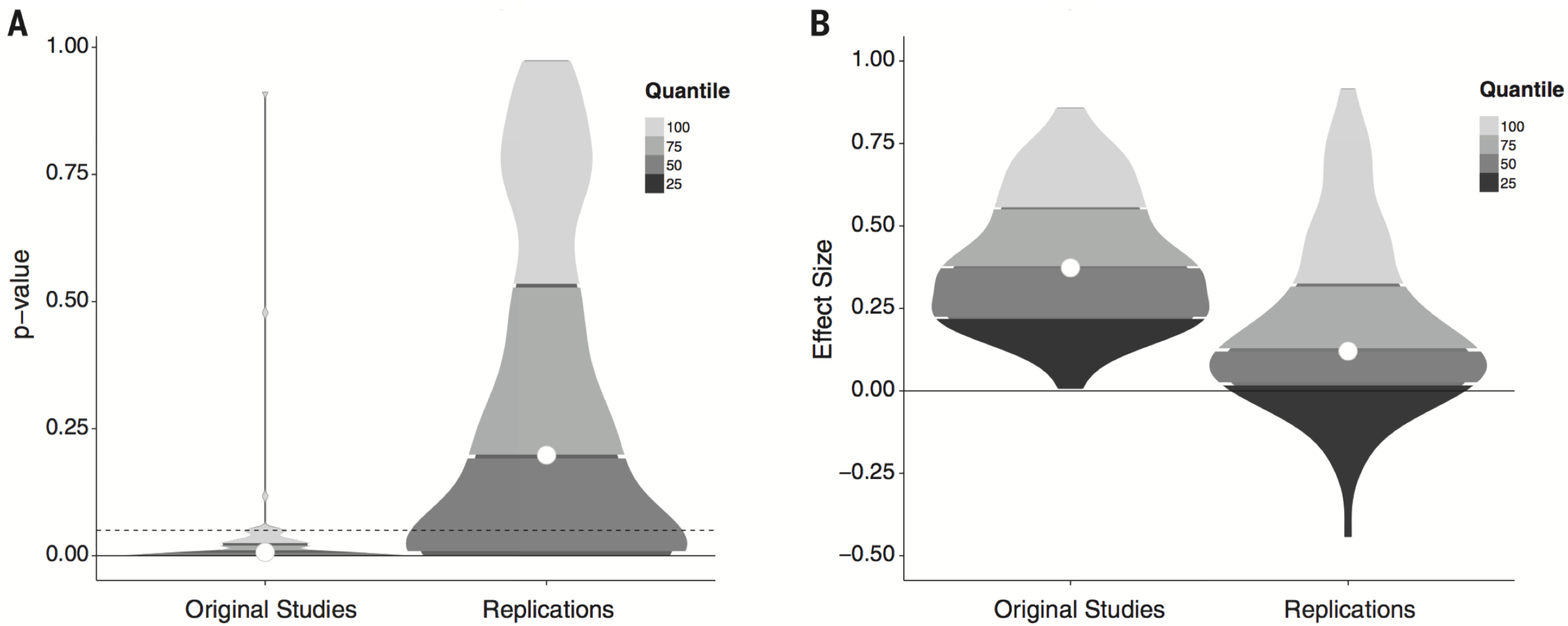
Evidence of p-hacking

Distribution of p-values reported in publications



Head M.L., et al. “The Extent and Consequences of P-Hacking in Science”, PLoS Biol 13, e1002106 (2015)

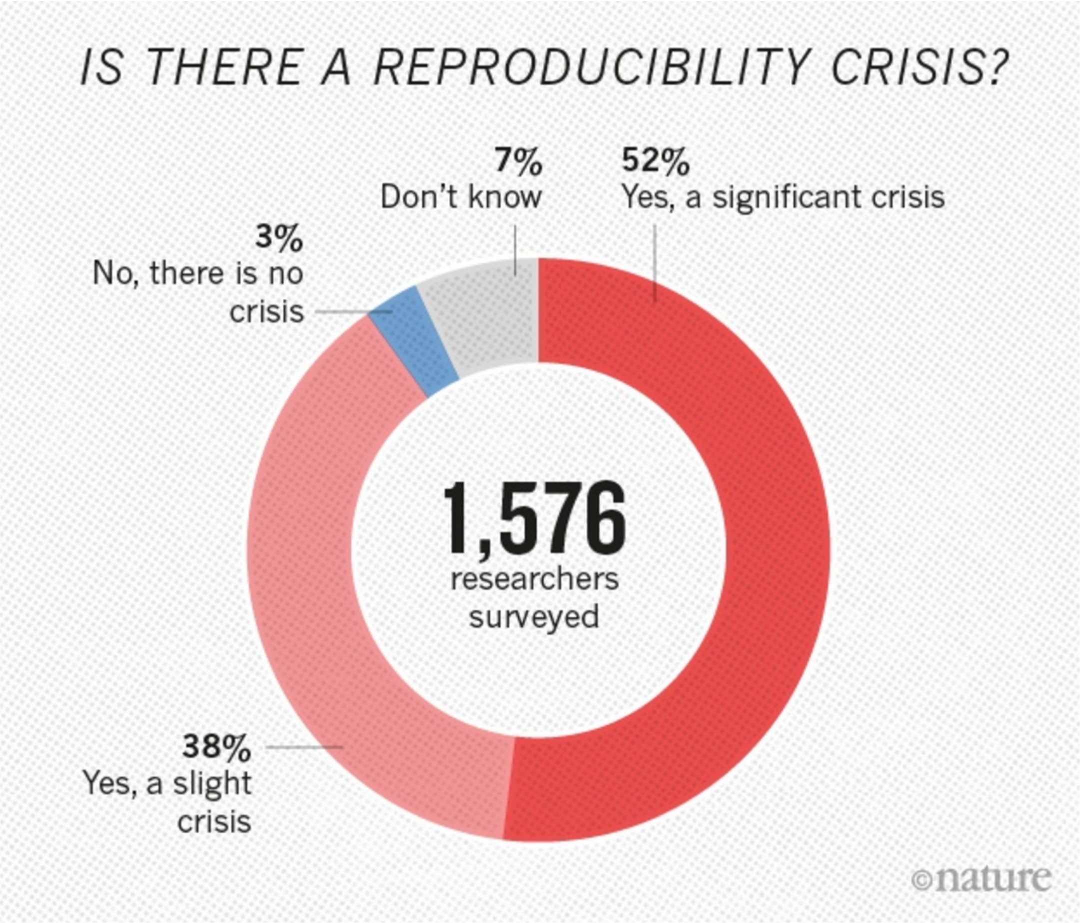
Reproducibility crisis



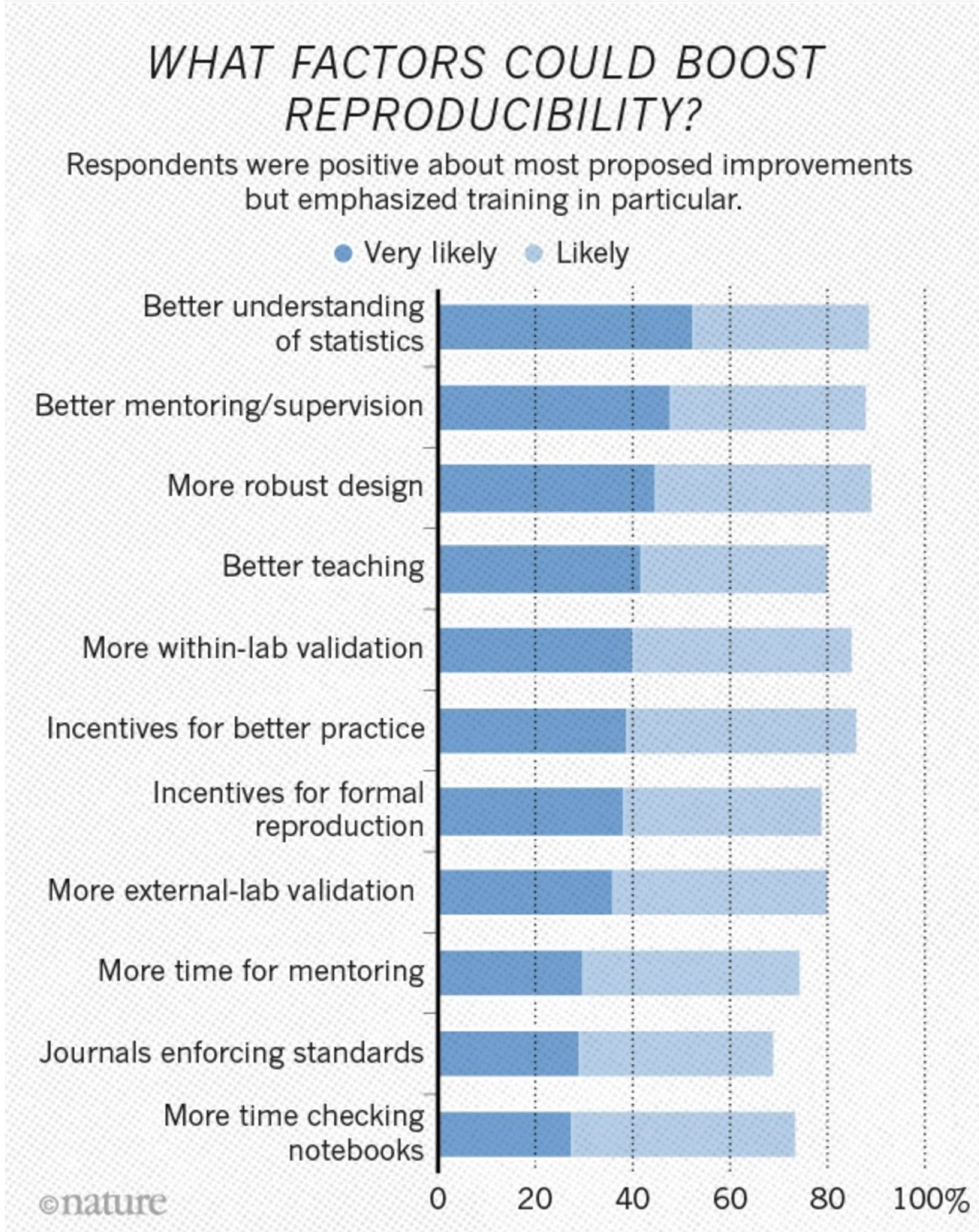
Open Science Collaboration, “Estimating the reproducibility of psychological science”, *Science*, **349** (2015)

Managed to reproduce only 39% results

Reproducibility crisis



Nature's survey of 1,576 researchers


WHAT FACTORS COULD BOOST REPRODUCIBILITY?
Respondents were positive about most proposed improvements but emphasized training in particular.
Very likely
Likely
Better understanding of statistics
Better mentoring/supervision
More robust design
Better teaching
More within-lab validation
Incentives for better practice
Incentives for formal reproduction
More external-lab validation
More time for mentoring
Journals enforcing standards
More time checking notebooks
0
20
40
60
80
100%
©nature

The great reproducibility experiment

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

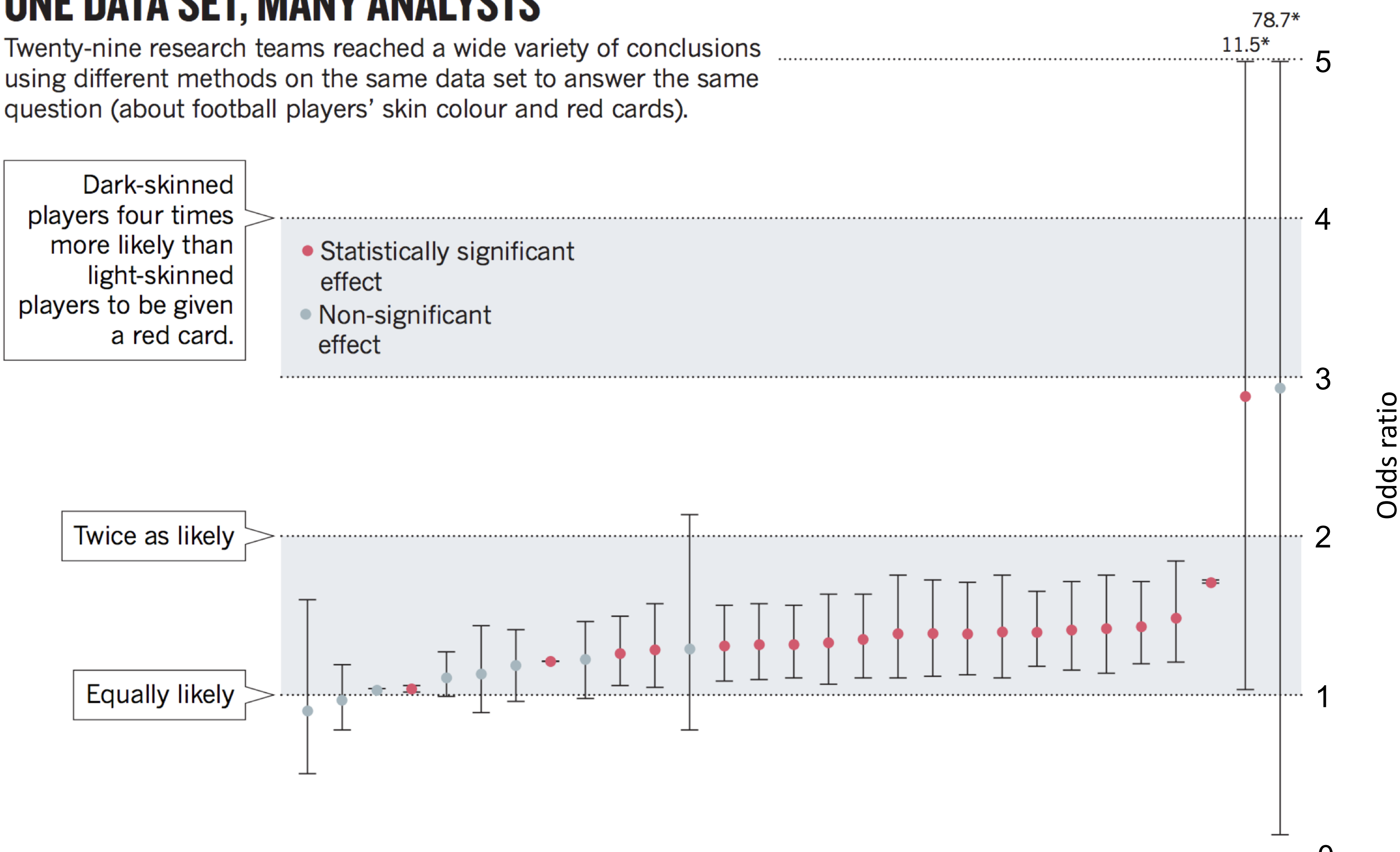

Mario Balotelli, playing for Manchester City, is shown a red card during a match against Arsenal.

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).



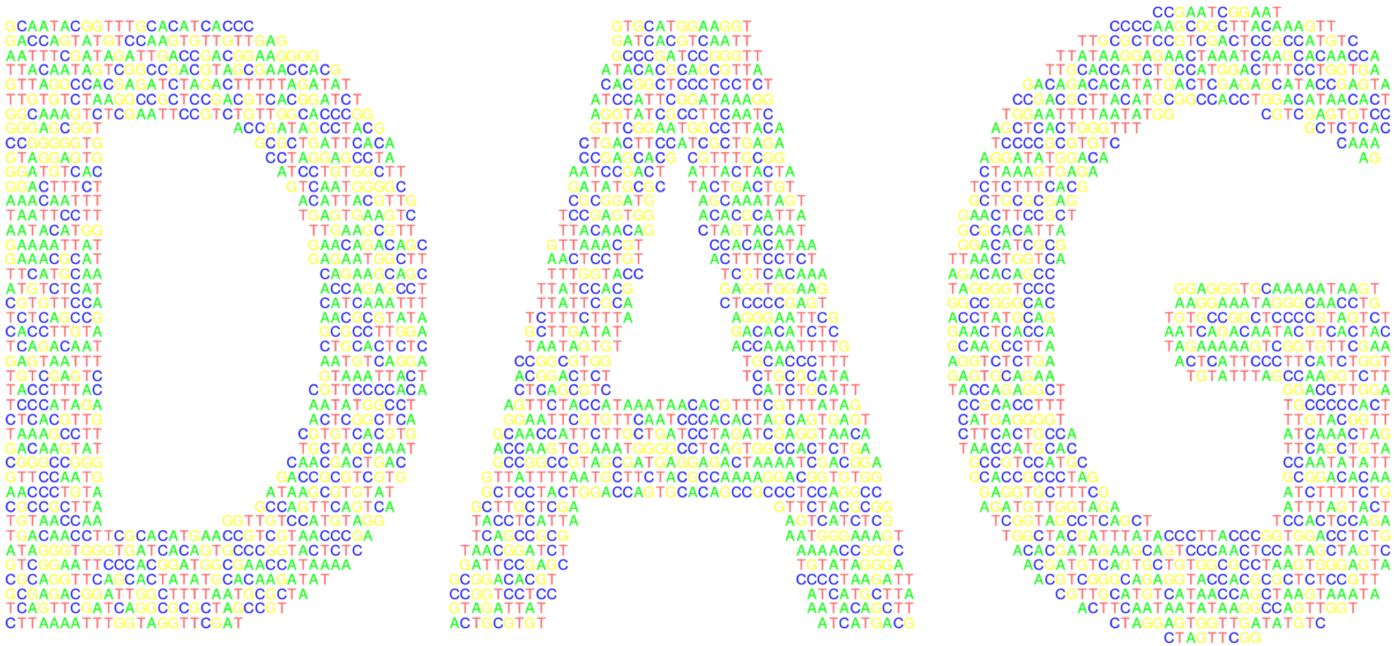
Point estimates and 95% confidence intervals. *Truncated upper bounds.

Science is 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

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http://is.gd/statlec