Null hypothesis
p-value

Chi-square test
G-test

t-test

Non-parametric tests

ANOVA

Statistical power

Multiple test corrections

Null hypothesis
p-value

WRONG

t-test

Chi-square test
G-test

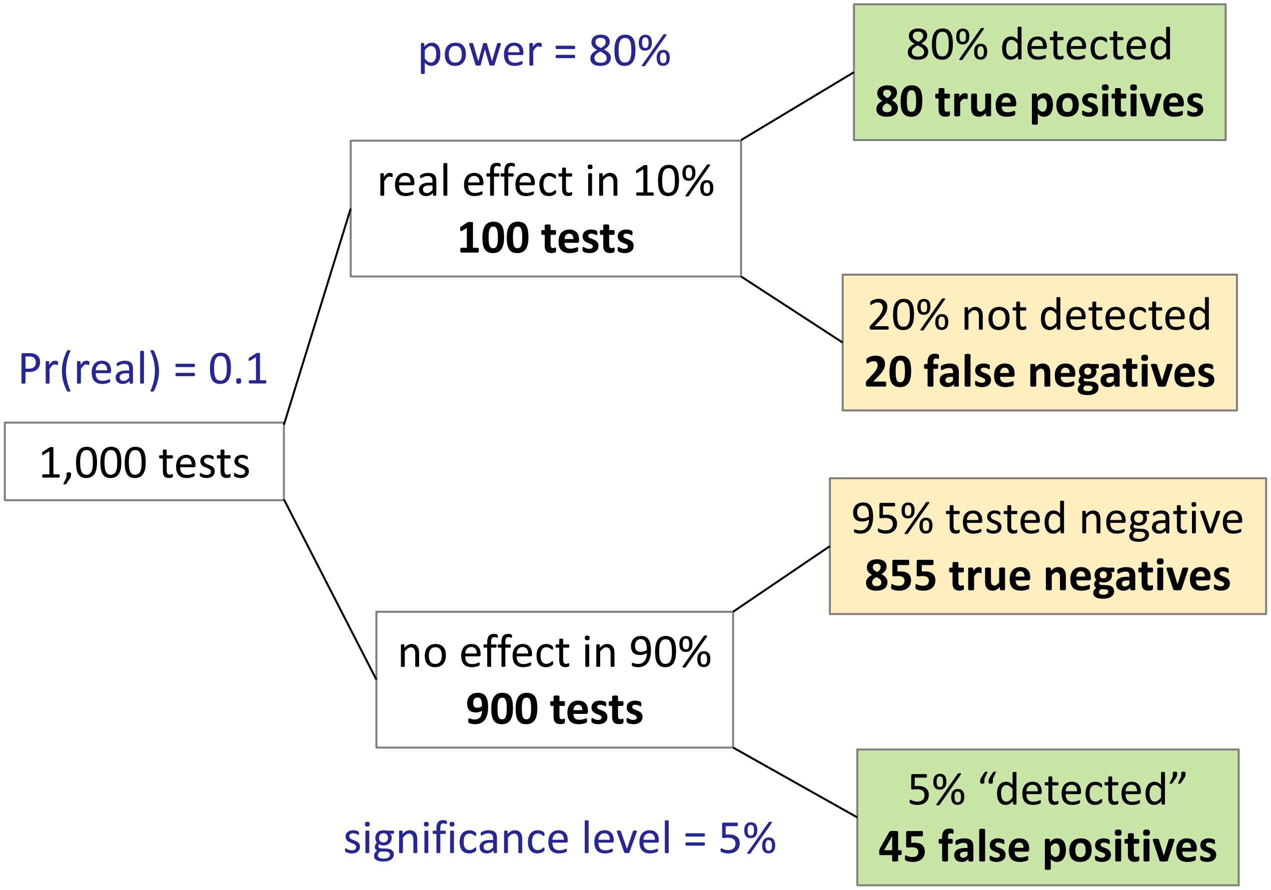
Non-parametric tests

ANOVA

Statistical power

WRONG

Multiple test corrections



1,000 tests

Pr(real) = 0.1

real effect in 10%
100 tests

power = 80%

80% detected
80 true positives

20% not detected
20 false negatives

no effect in 90%
900 tests

significance level = 5%

95% tested negative
855 true negatives

5% “detected”
45 false positives

False positive rate

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

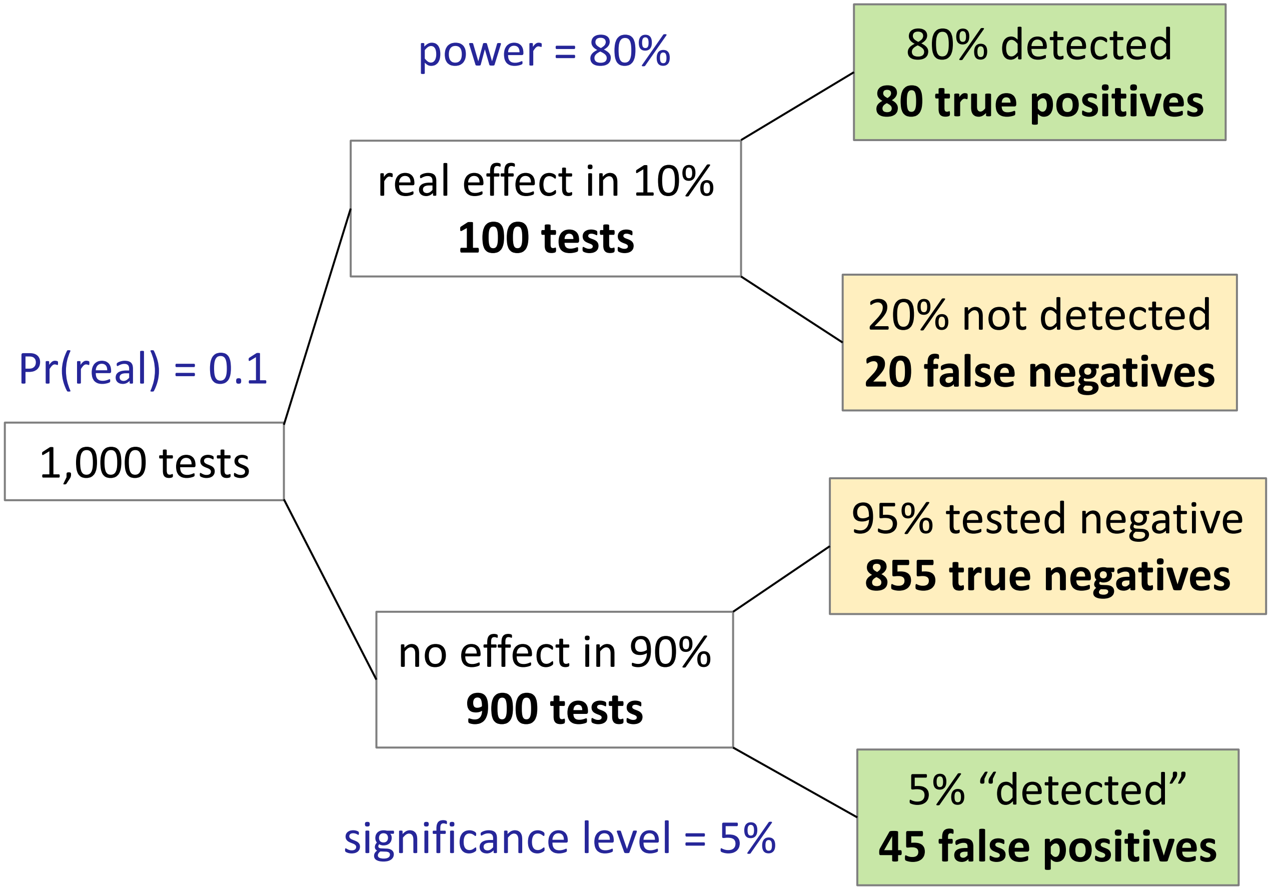
$$FPR = \frac{45}{900} = 0.05$$

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.



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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.

What’s wrong with p-values?

Marek Gierliński
Division of Computational Biology

Hand-outs available at http://is.gd/statlec

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

hypothesis being true is 5%

A p-value of 0.005 implies much more significant result than does a p-value of 0.05 ✗

than does a p-value of 0.05

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

chance

Statistical testing

Statistical model

Null hypothesis

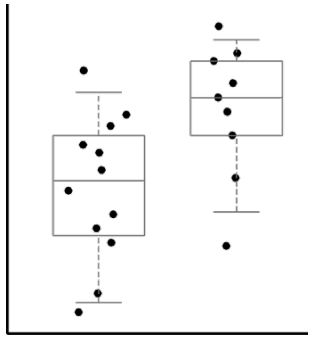
H_0: no effect

All other assumptions

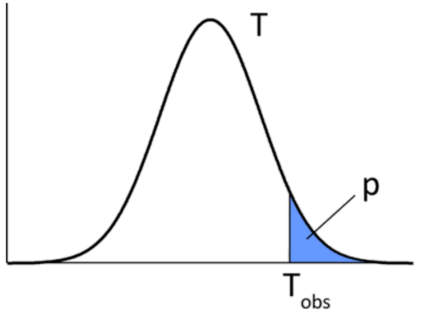
Significance level

$\alpha = 0.05$

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:

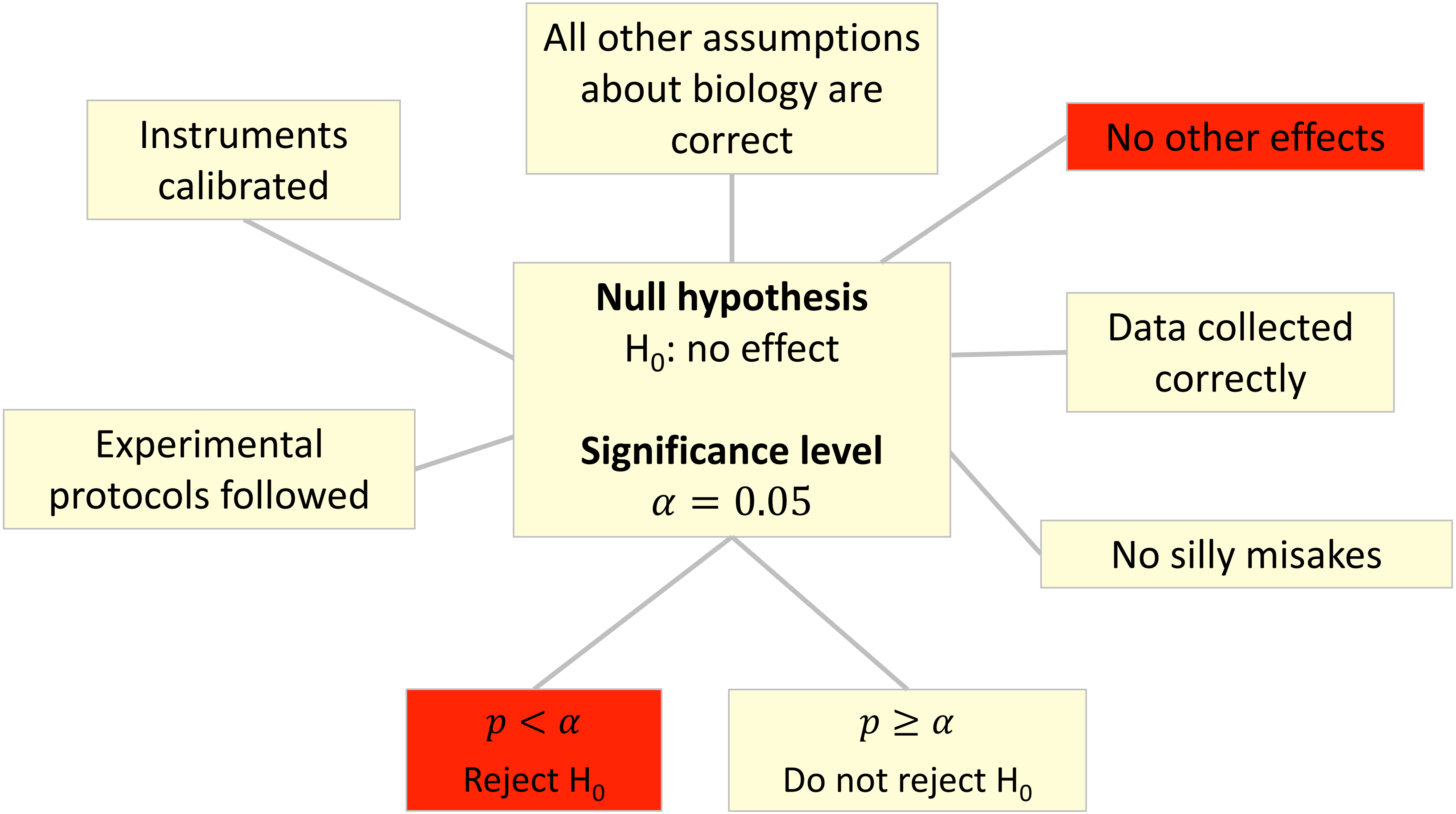
Given that H_0 is true, the probability of observed, or more extreme, data

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”



All other assumptions about biology are correct

Instruments calibrated

No other effects

Null hypothesis

H_0: no effect

Significance level

$\alpha = 0.05$

Data collected correctly

Experimental protocols followed

No silly misakes

$p < \alpha$

Reject H_0

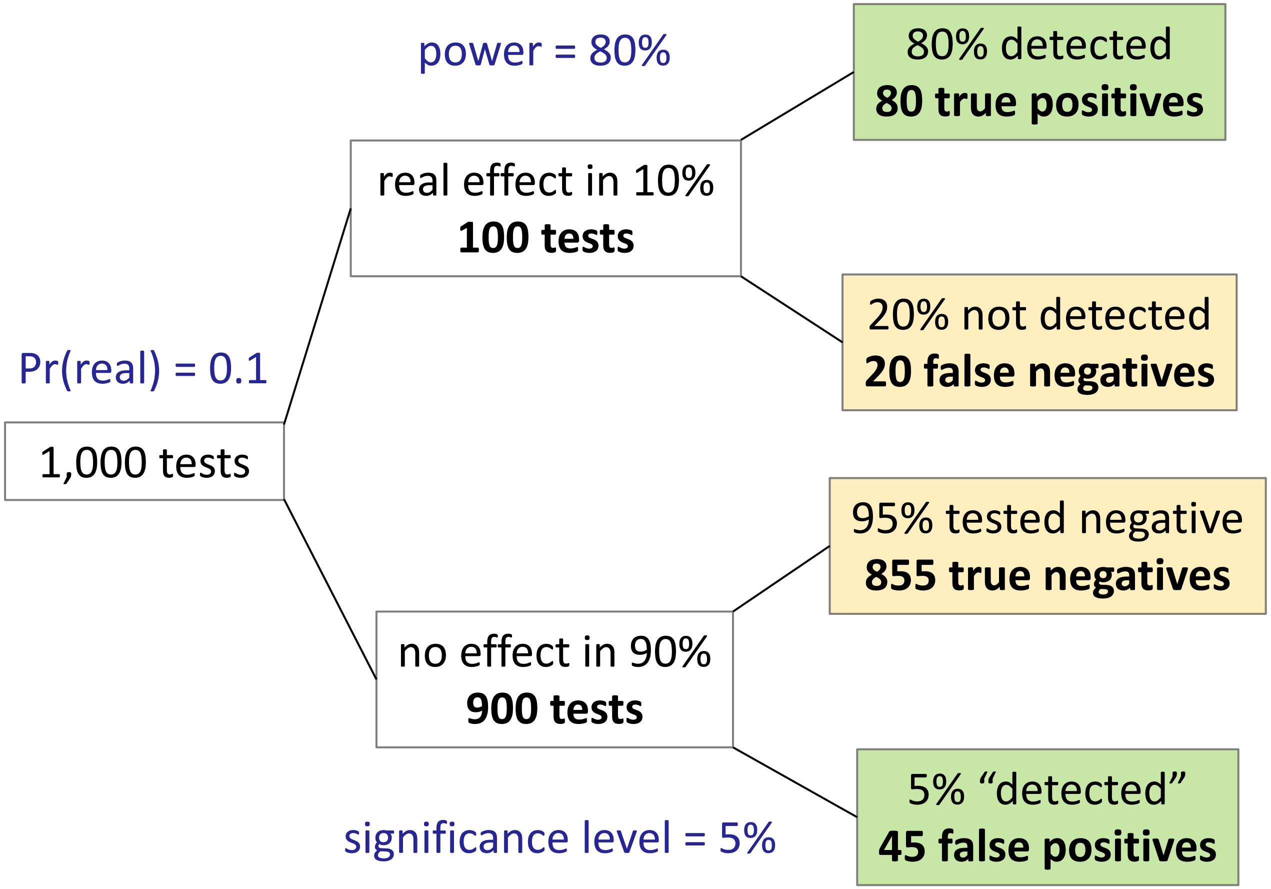
$p \geq \alpha$

Do not reject H_0

1

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

Why large false discovery rate?



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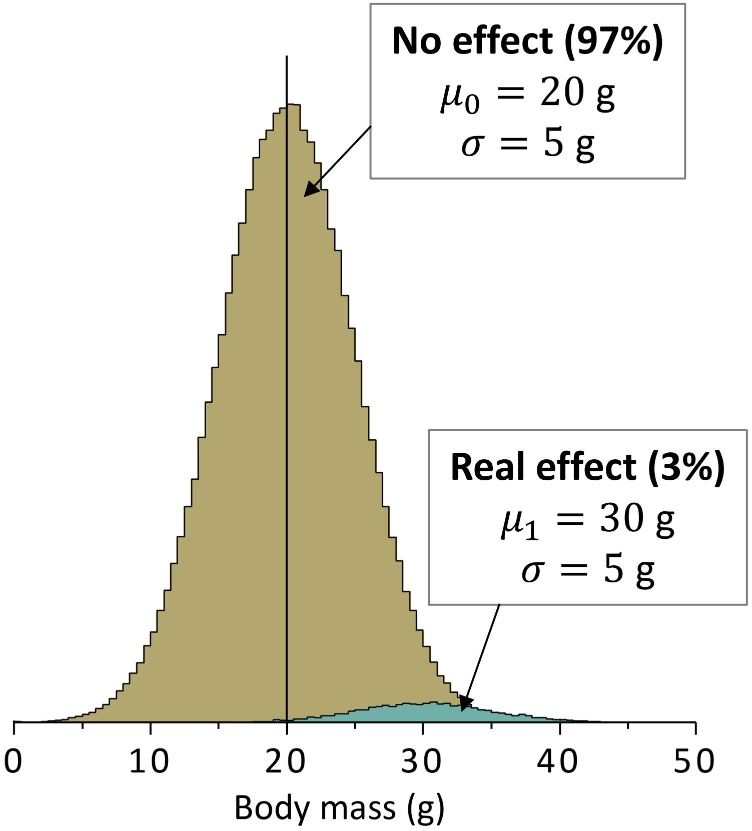
significance level = 5%

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

Simulated population of mice



No effect (97%)
$\mu_0 = 20\ \mathrm{g}$
$\sigma = 5\ \mathrm{g}$

Real effect (3%)
$\mu_1 = 30\ \mathrm{g}$
$\sigma = 5\ \mathrm{g}$

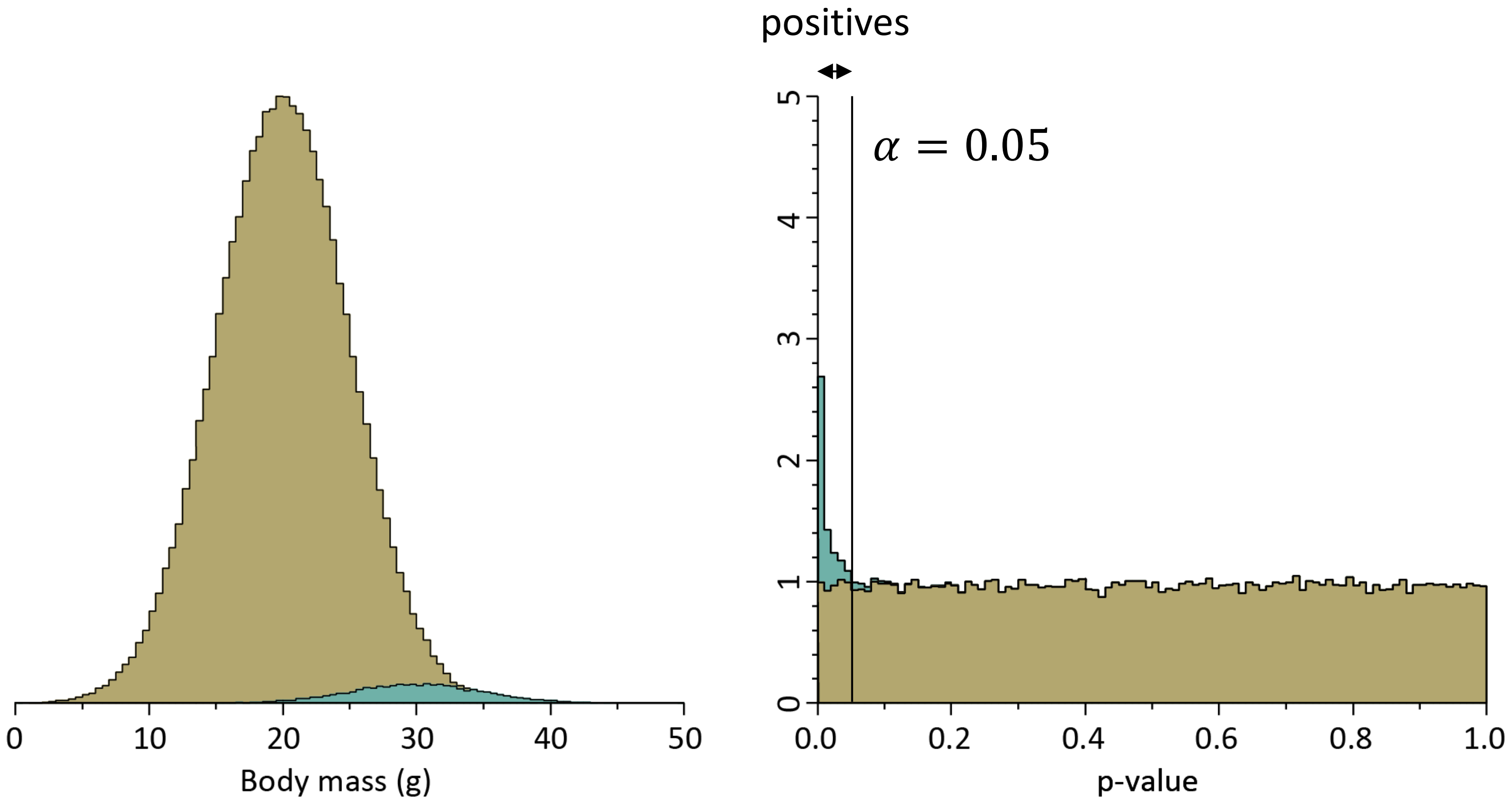
Null hypothesis H_0: $\mu = 20\ \mathrm{g}$

one-sample t-test

Power analysis

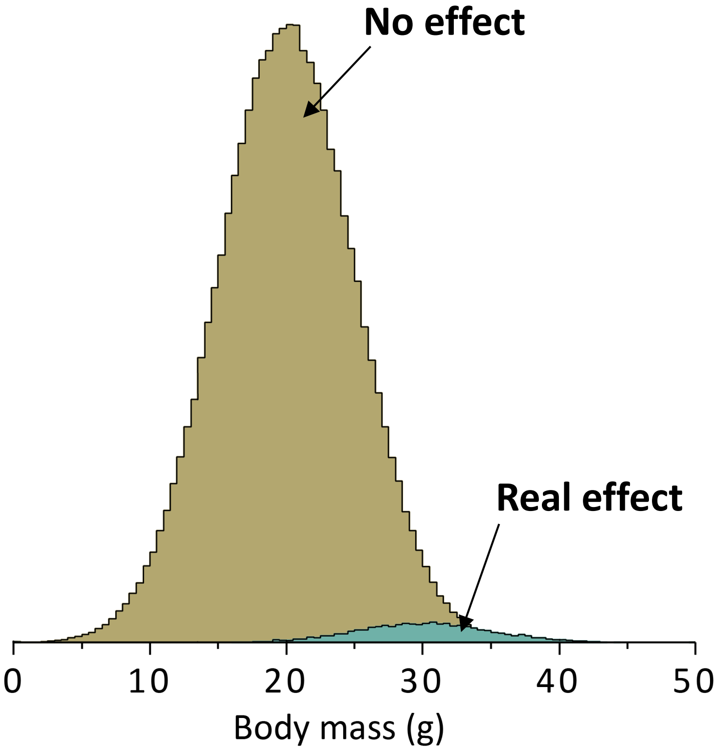
effect size	$\Delta m = 10\ \mathrm{g}$
power	$\mathcal{P} = 0.9$
significance level	$\alpha = 0.05$
sample size	$n = 5$

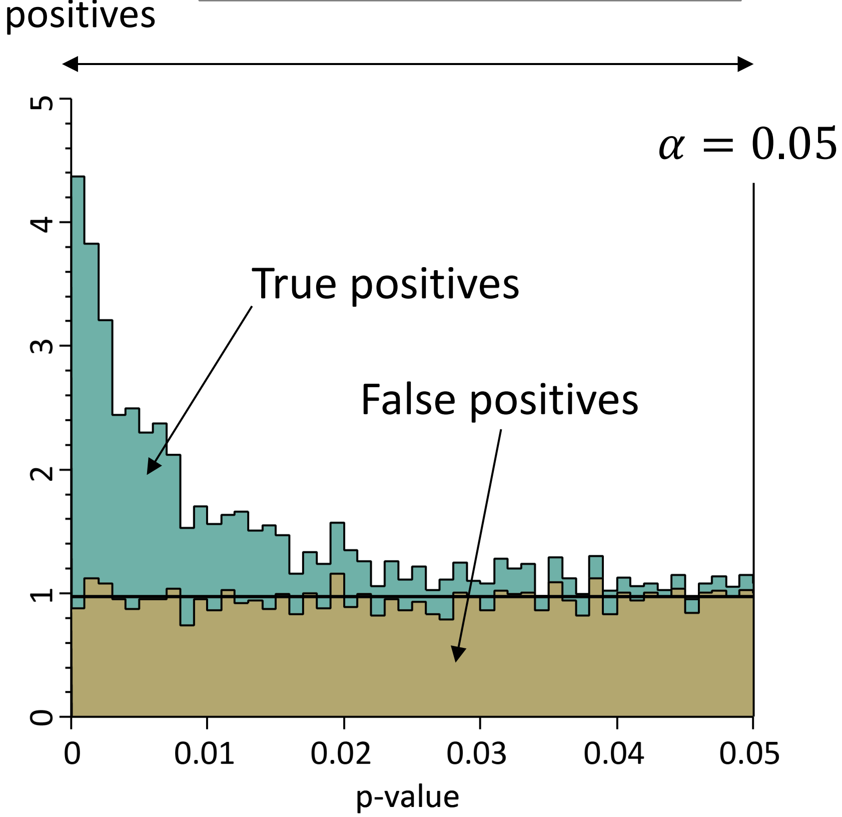
Gedankenexperiment: distribution of p-values



Gedankenexperiment: “significant” p-values

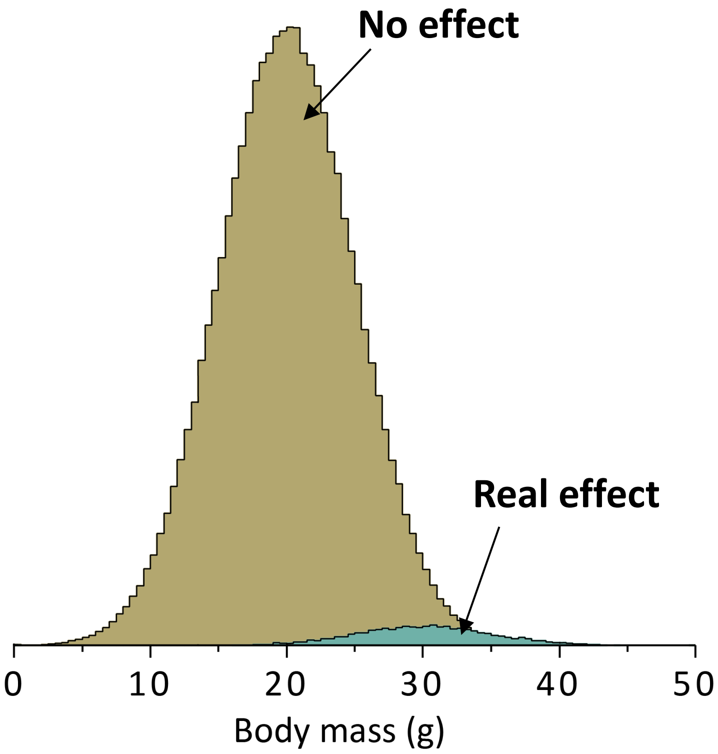
$$FDR = \frac{FP}{FP + TP} \approx 0.63$$

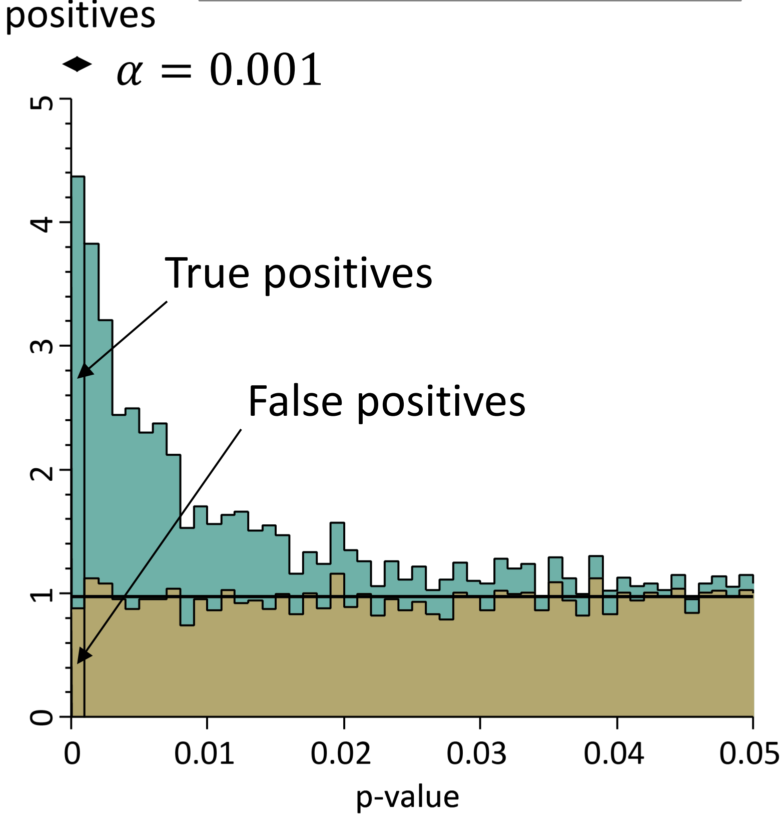




Small α doesn't help

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





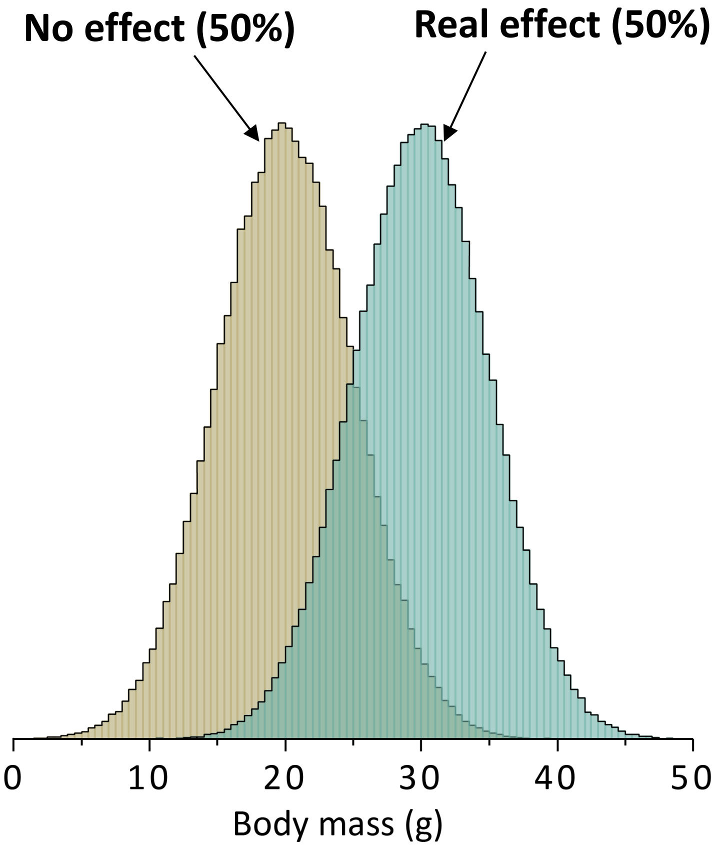
2

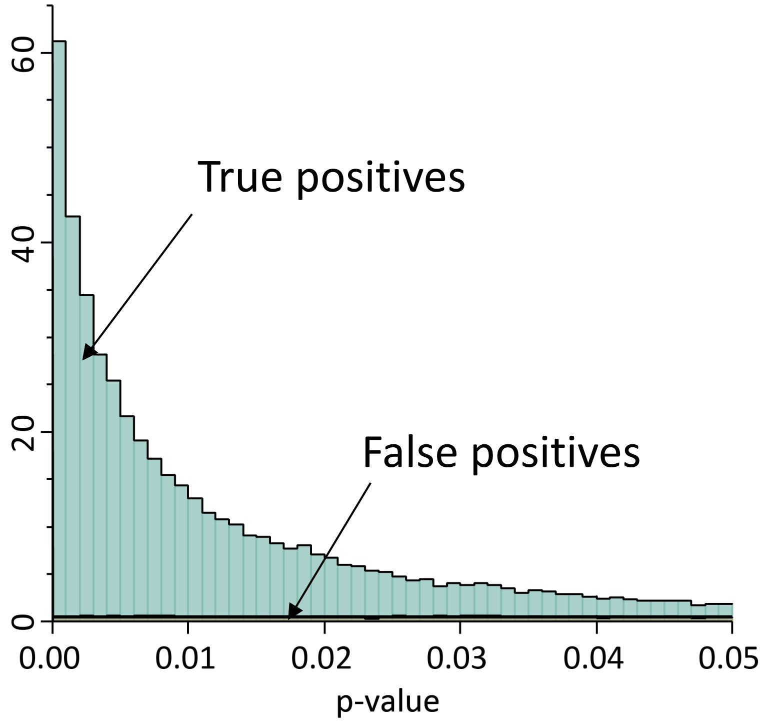
The chance of making a fool of yourself is much larger than $\alpha = 0.05$

FDR depends on the probability of real effect

$\alpha = 0.05$

$FDR \approx 0.05$





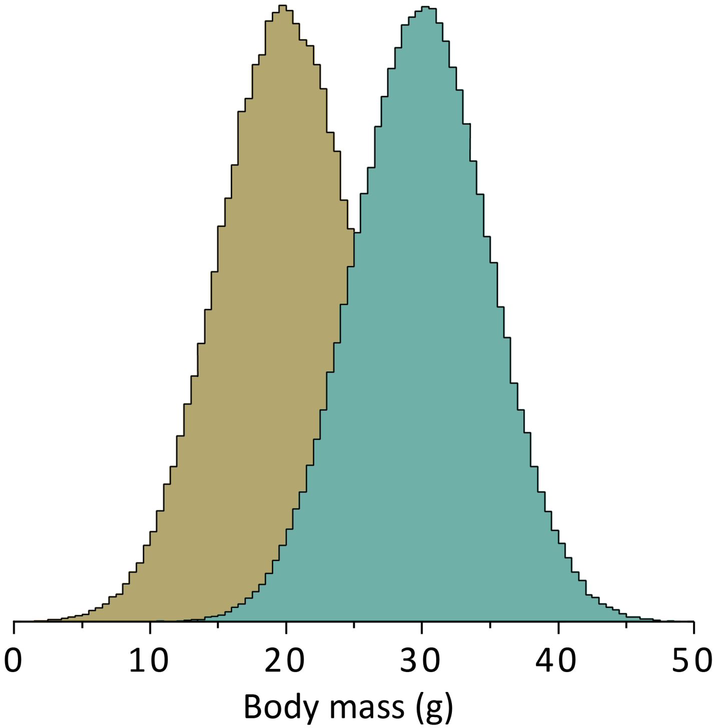
3

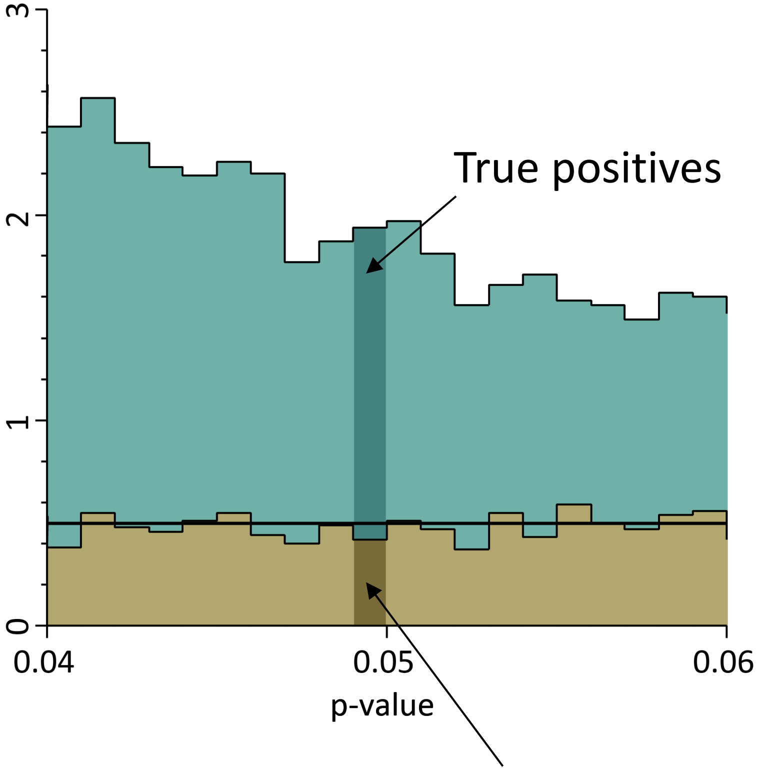
When the effect is rare,
you are screwed

What does a p-value ~ 0.05 really mean?

$$\alpha \sim 0.05$$

$$FDR = 0.21$$

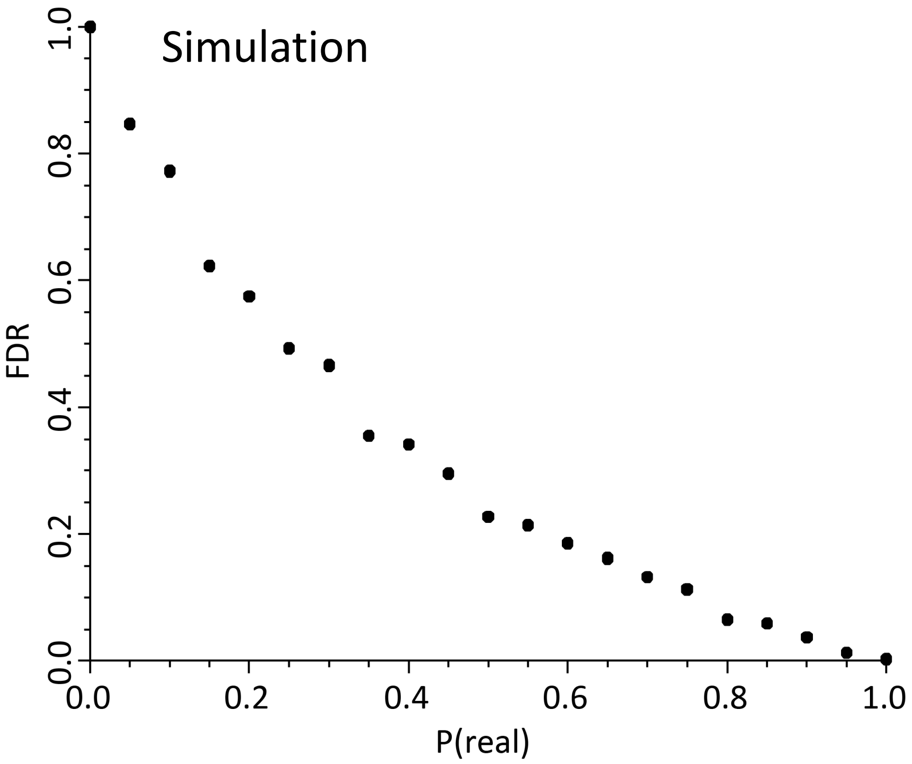




True positives

False positives

Bayesian approach: consider all prior distributions



Berger & Selke
(Bayesian approach)

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

3-sigma approach
$p \sim 0.003 \;\Rightarrow\; FDR \geq 0.04$

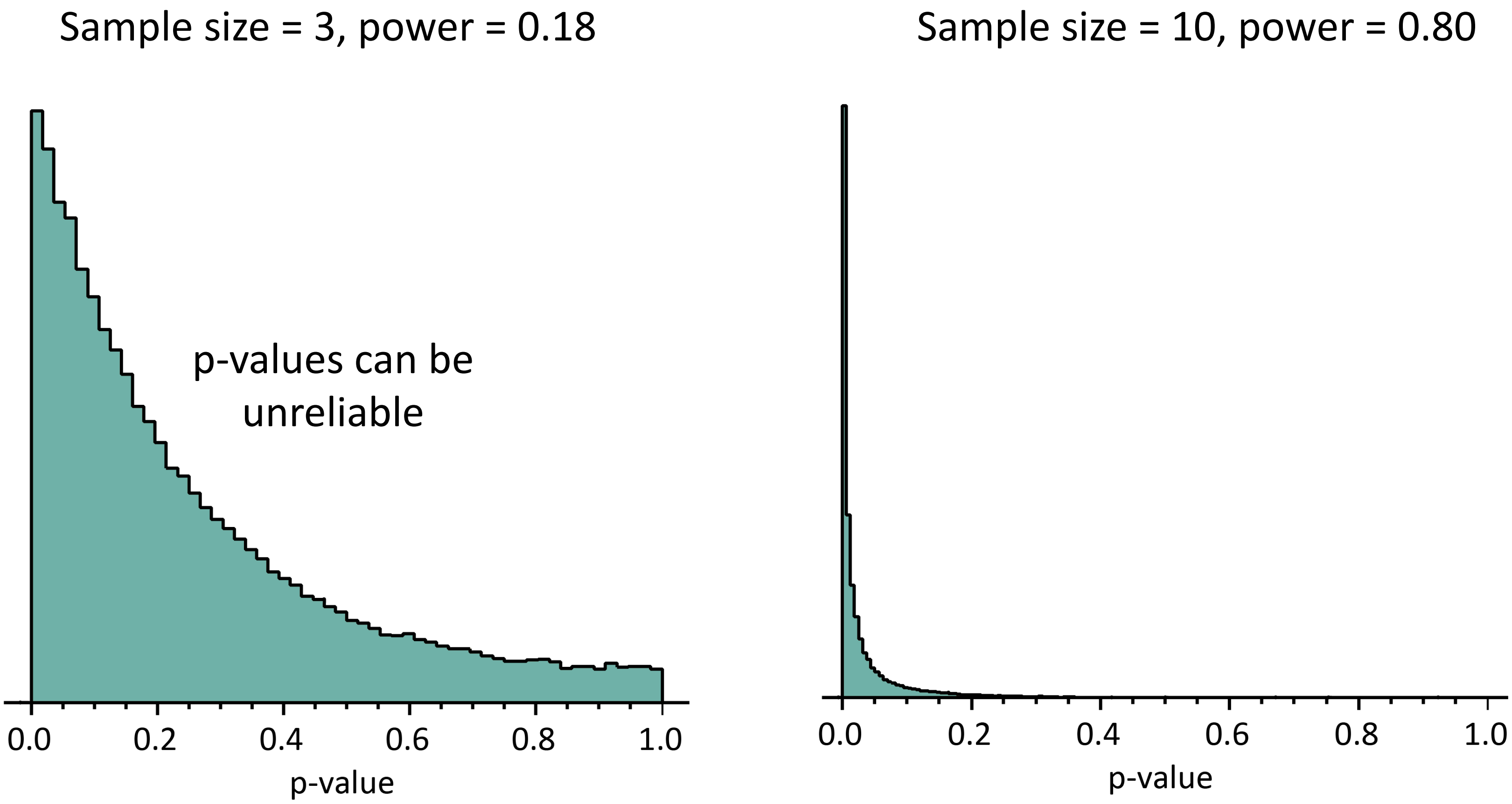
Berger J.O, Selke T., “Testing a point null hypothesis: the irreconcilability of P values and evidence”, 1987, *JASA*, **82**, 112-122

4

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

Gedankenexperiment: reliability of p-values

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



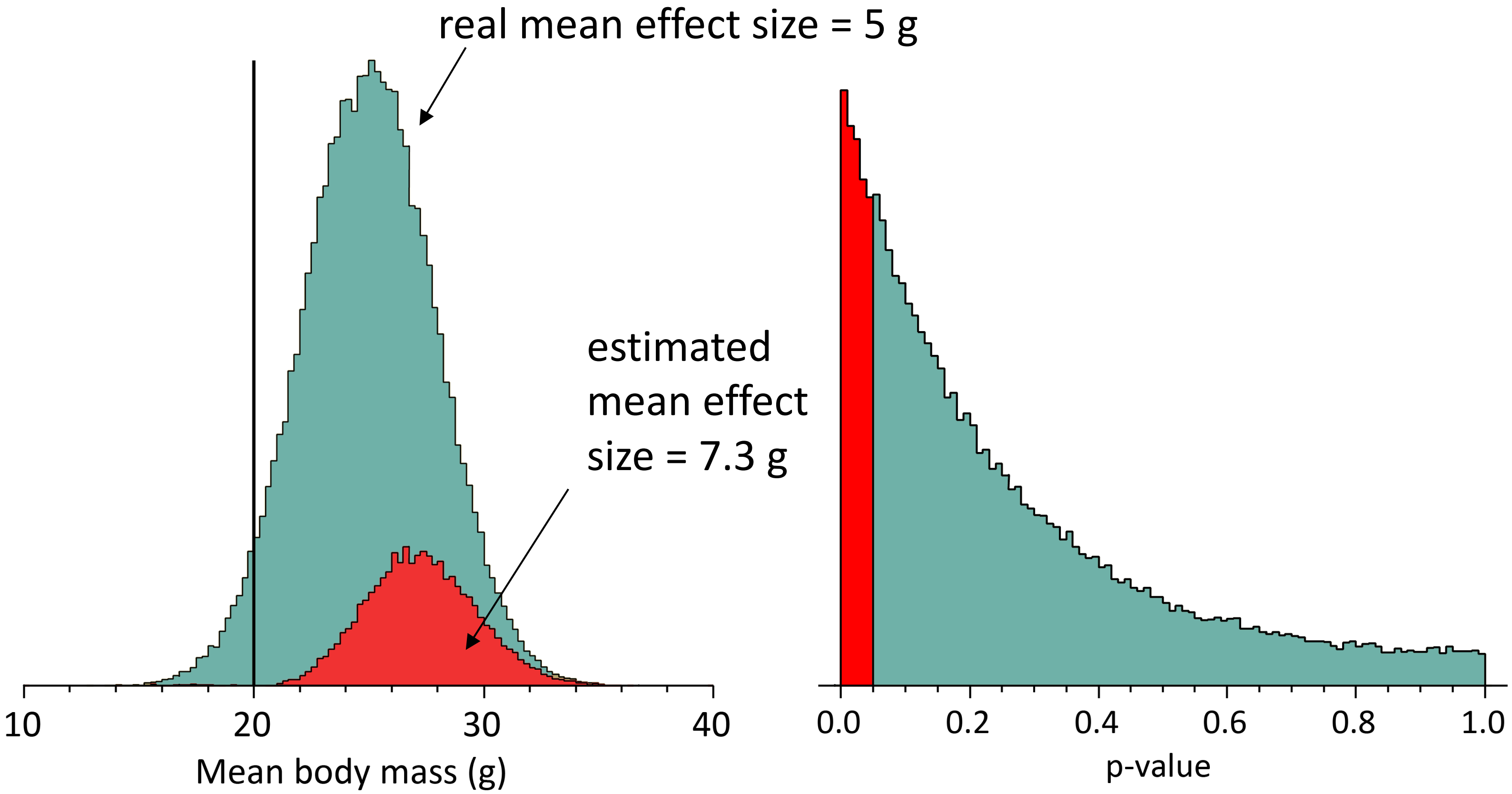
Sample size = 3, power = 0.18

Sample size = 10, power = 0.80

p-values can be unreliable

Underpowered studies lead to unreliable p-values

Inflation of the effect size



real mean effect size = 5 g

estimated mean effect size = 7.3 g

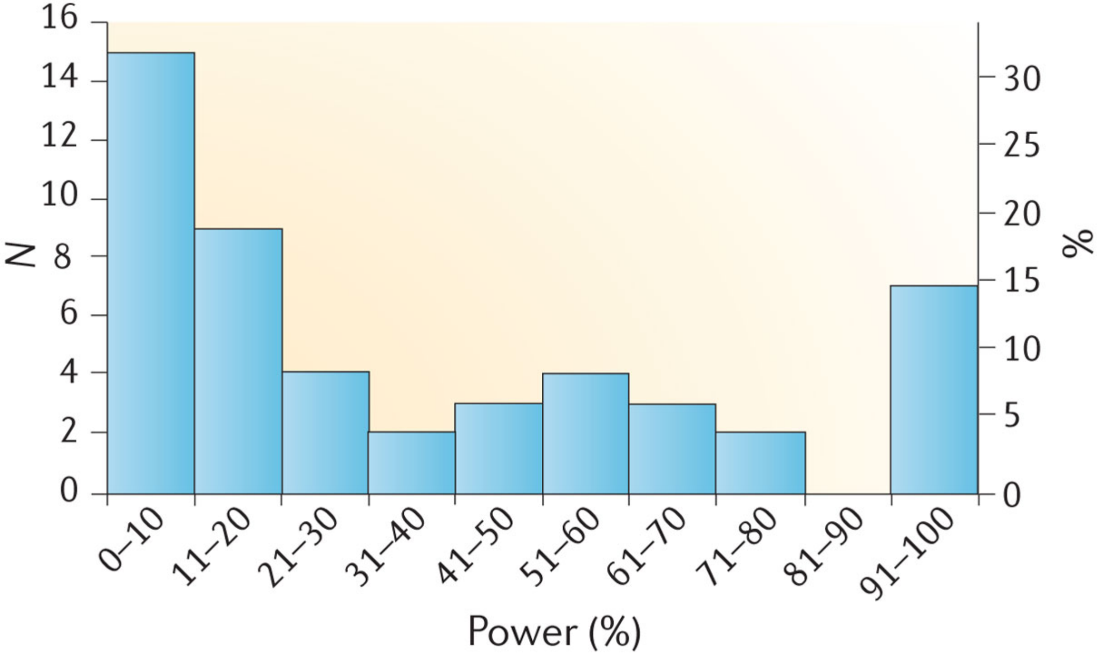
Underpowered studies lead to unreliable p-values

Underpowered studies lead to overestimated effect size

5

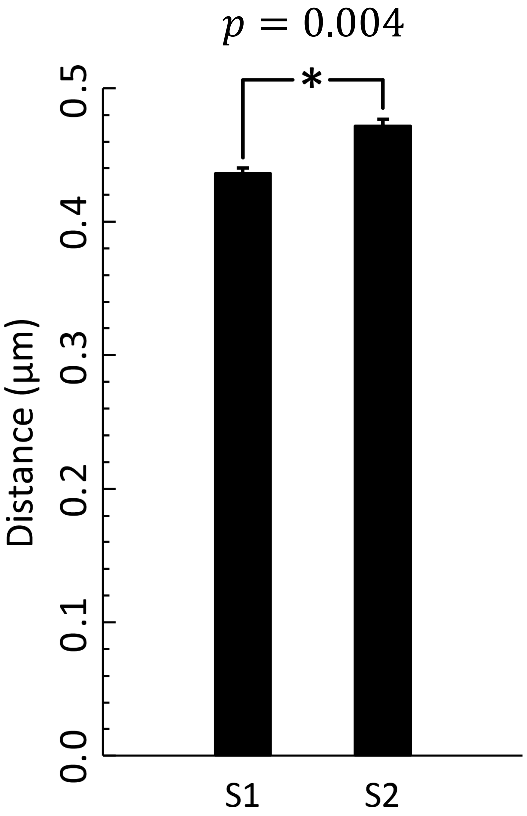
When your experiment is underpowered,
you are screwed

Neuroscience: most studies underpowered

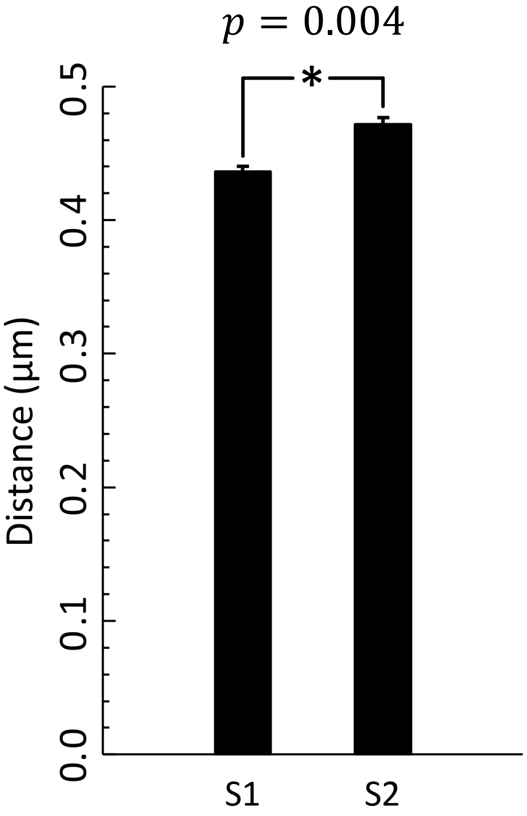


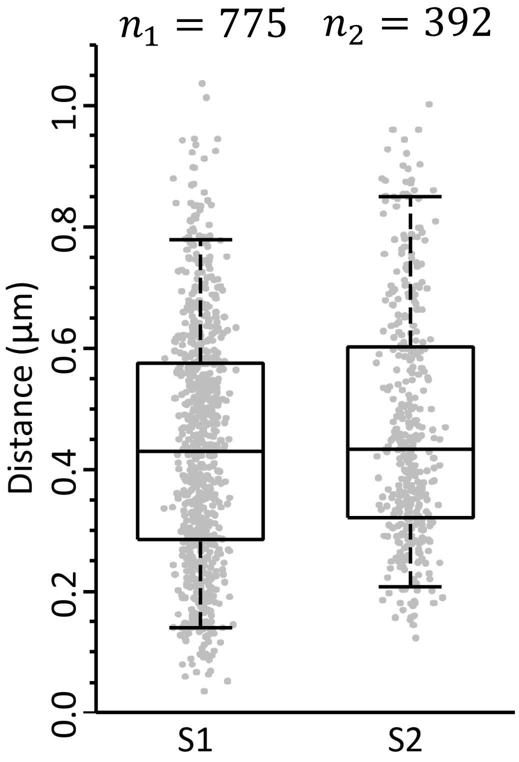
Button et al. (2013) "Power failure: why small sample size undermines the reliability of neuroscience", *Nature Reviews Neuroscience* **14**, 365-376

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

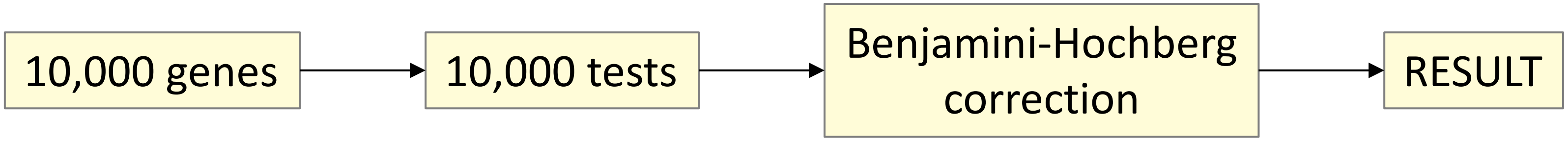
6

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

7

Statistical significance does not imply biological relevance

Multiple test corrections can be tricky



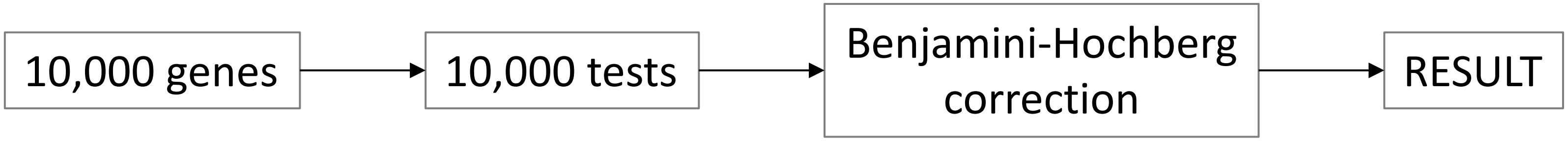
10,000 genes

10,000 tests

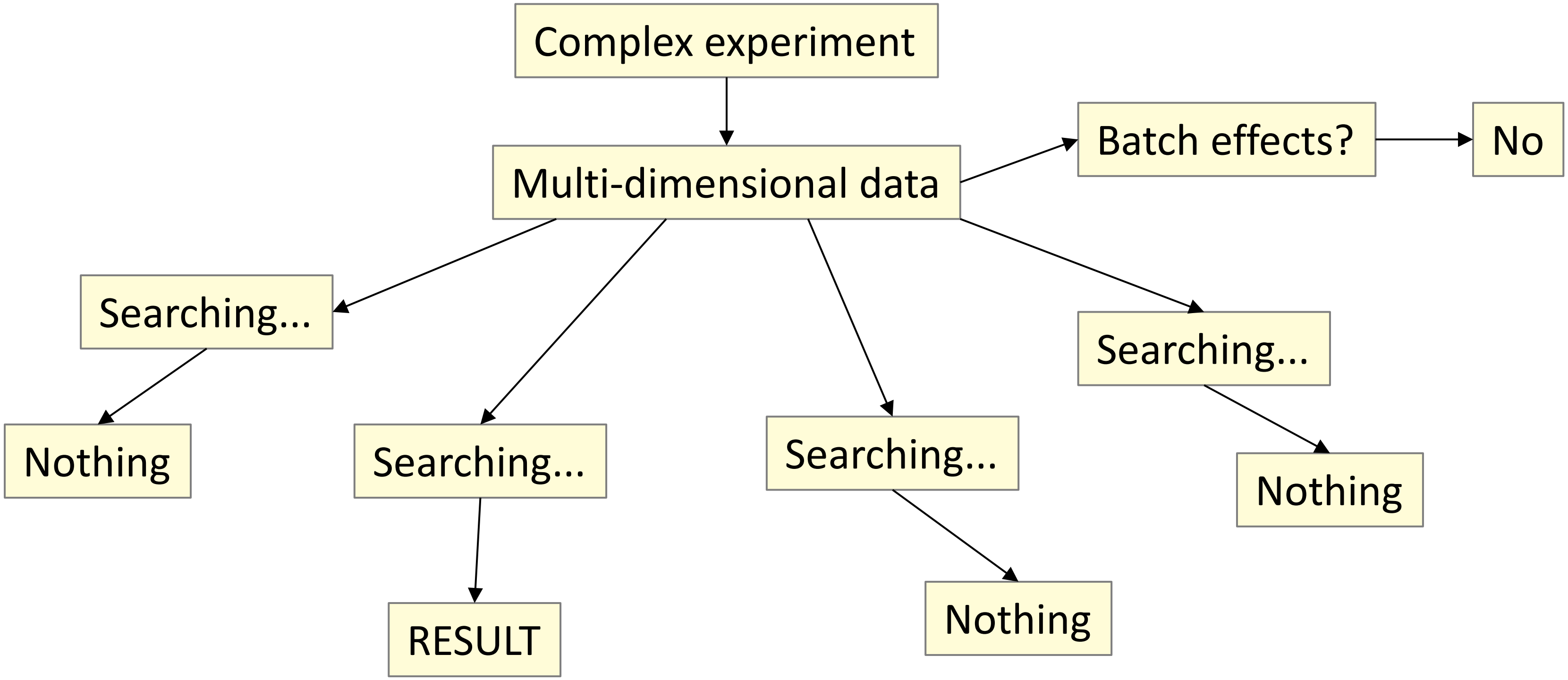
Benjamini-Hochberg correction

RESULT

Multiple test corrections can be tricky



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



Complex experiment

Multi-dimensional data

Batch effects?

No

Searching...

Nothing

Searching...

RESULT

Searching...

Nothing

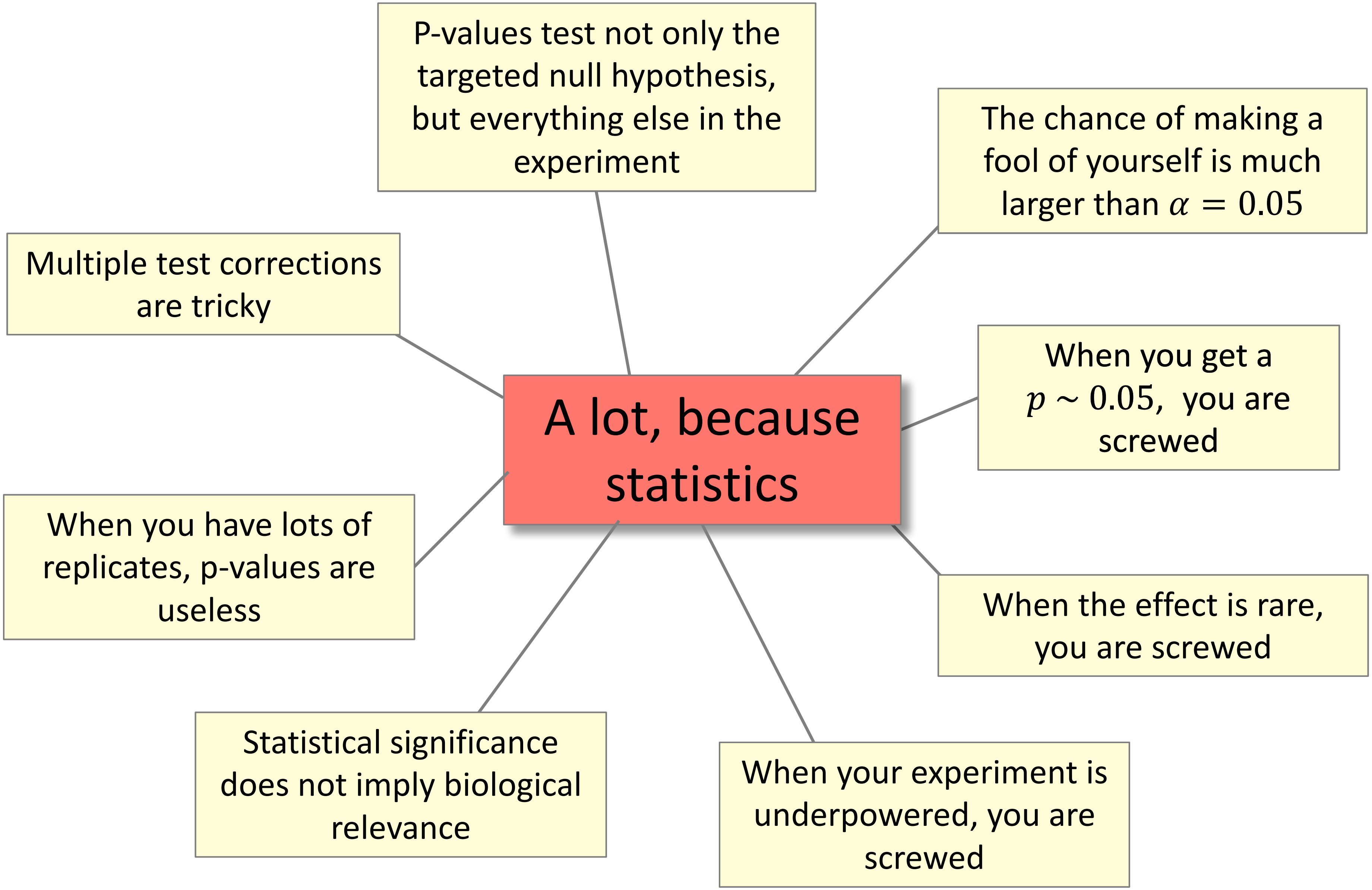
Searching...

Nothing

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 $p \sim 0.05$, you are screwed

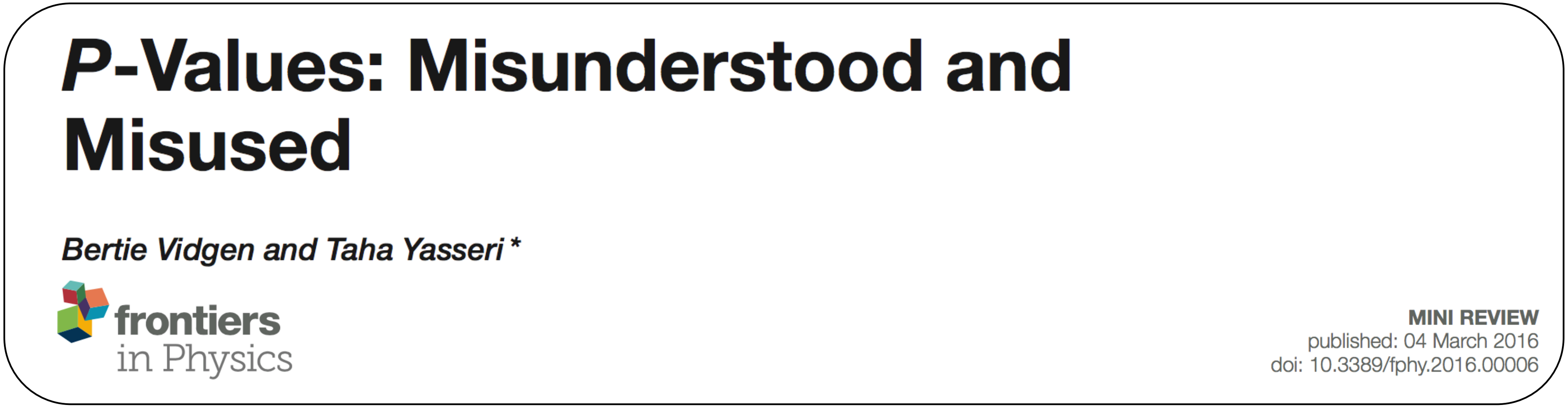
When the effect is rare, you are screwed

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

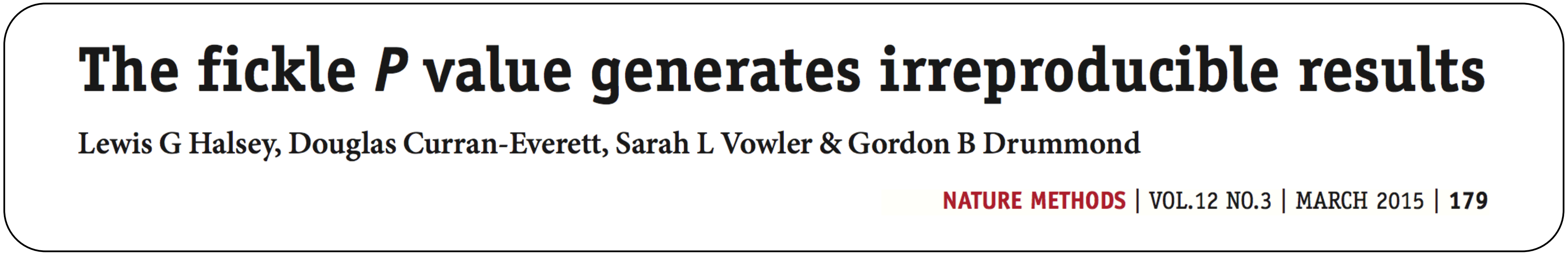


P-Values: Misunderstood and Misused

Bertie Vidgen and Taha Yasseri *

frontiers in Physics

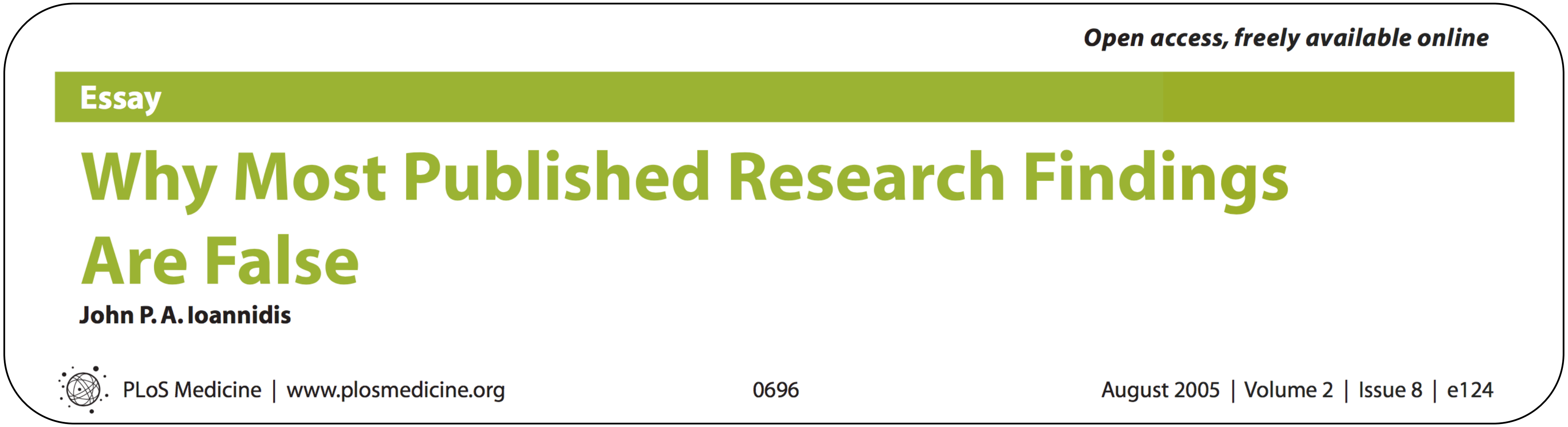
MINI REVIEW
published: 04 March 2016
doi: 10.3389/fphy.2016.00006



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.

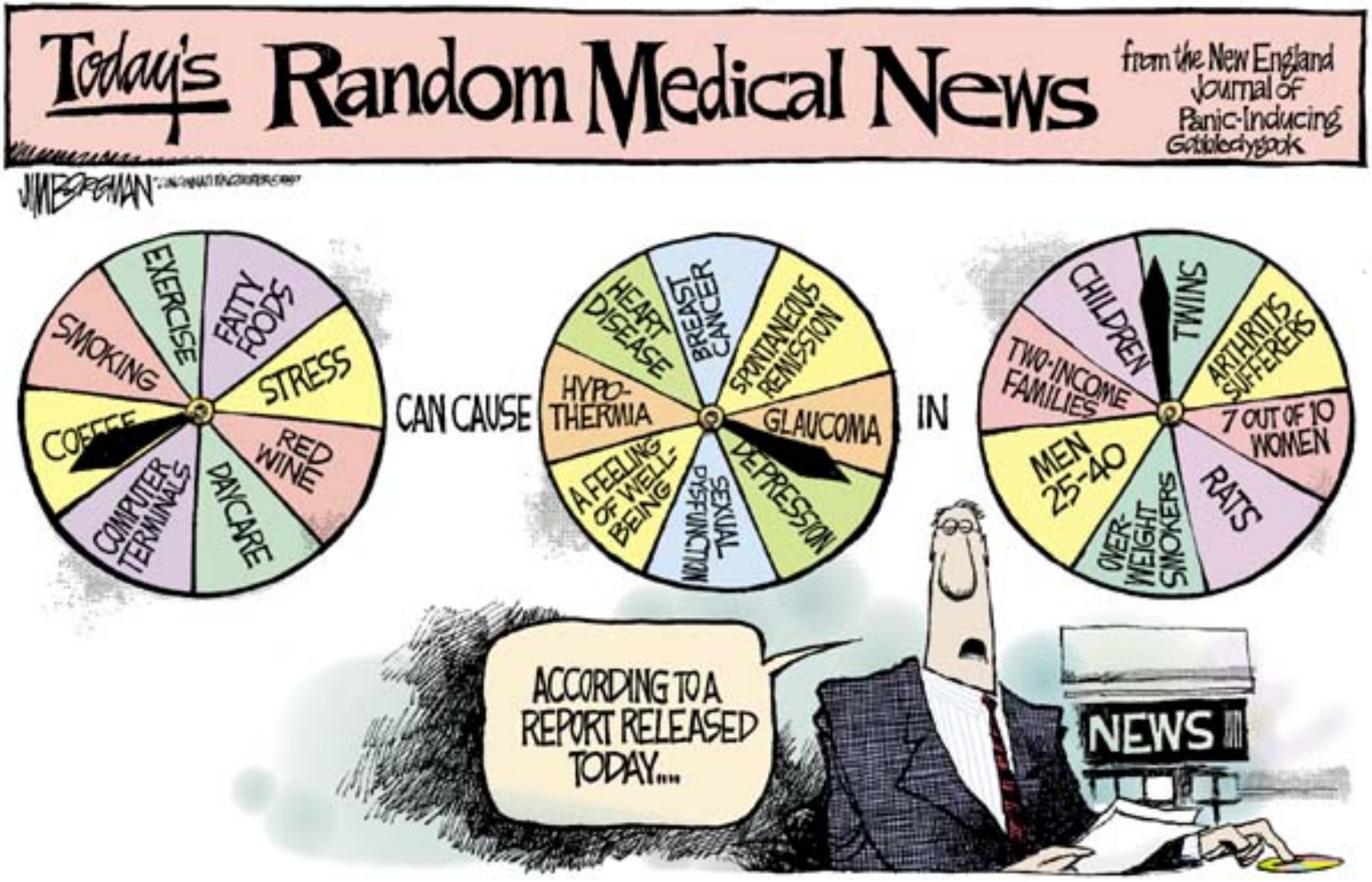
Paul Meehl, 1967, *Philosophy of Science*, 34, 103-115

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.

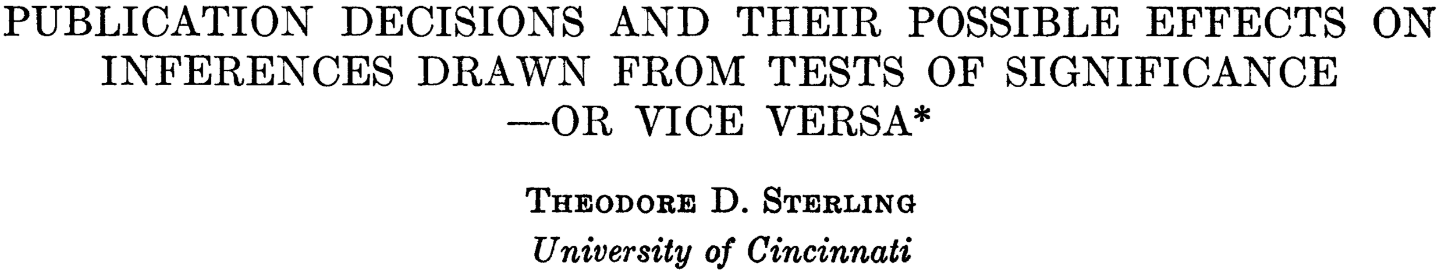
ASA statement on statistical significance and p-values (2016)



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 [...].”



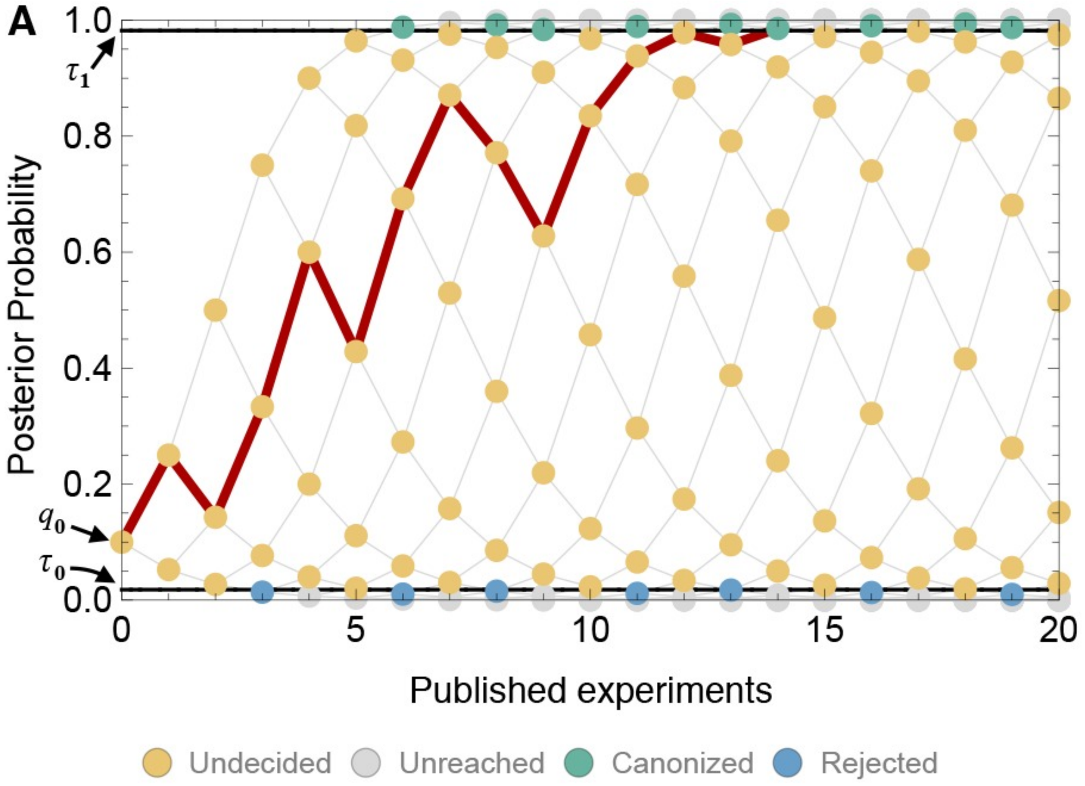
PUBLICATION DECISIONS AND THEIR POSSIBLE EFFECTS ON INFERENCES DRAWN FROM TESTS OF SIGNIFICANCE —OR VICE VERSA*

THEODORE D. STERLING

University of Cincinnati

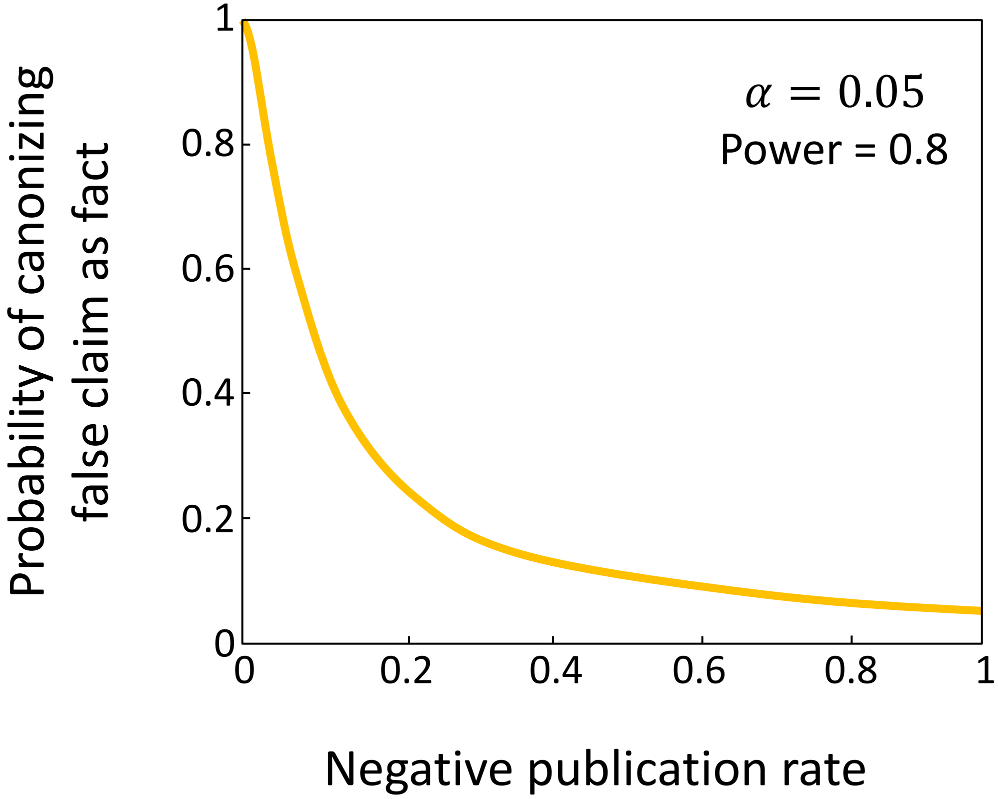
Journal of the American Statistical Association,
Vol. 54, No. 285 (Mar., 1959), pp. 30-34

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

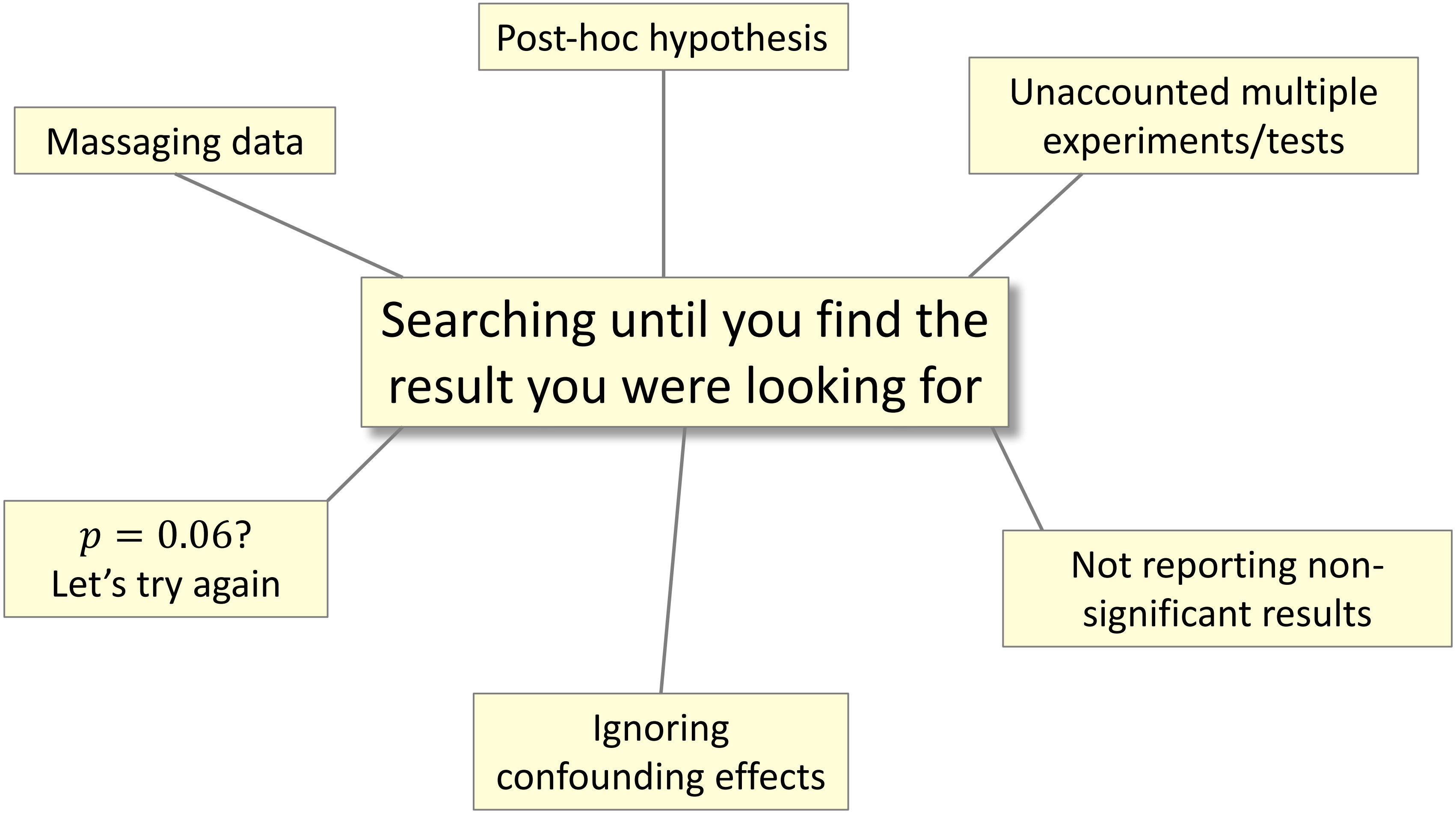


Nissen S.B., et al., “Research: Publication bias and the canonization of false facts”, eLife 2016;5:e21451

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



Searching until you find the result you were looking for

Post-hoc hypothesis

Unaccounted multiple experiments/tests

Massaging data

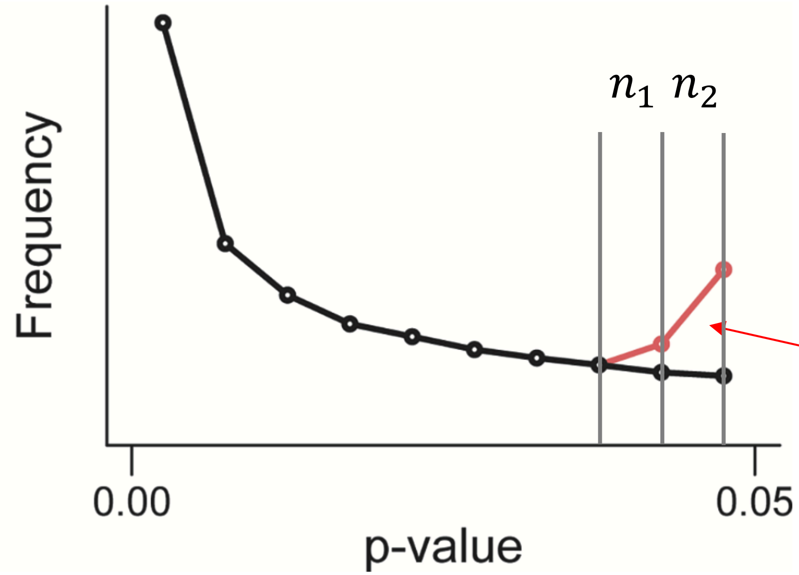
$p = 0.06$?
Let’s try again

Not reporting non-significant results

Ignoring confounding effects

Evidence of p-hacking

Distribution of p-values reported in publications

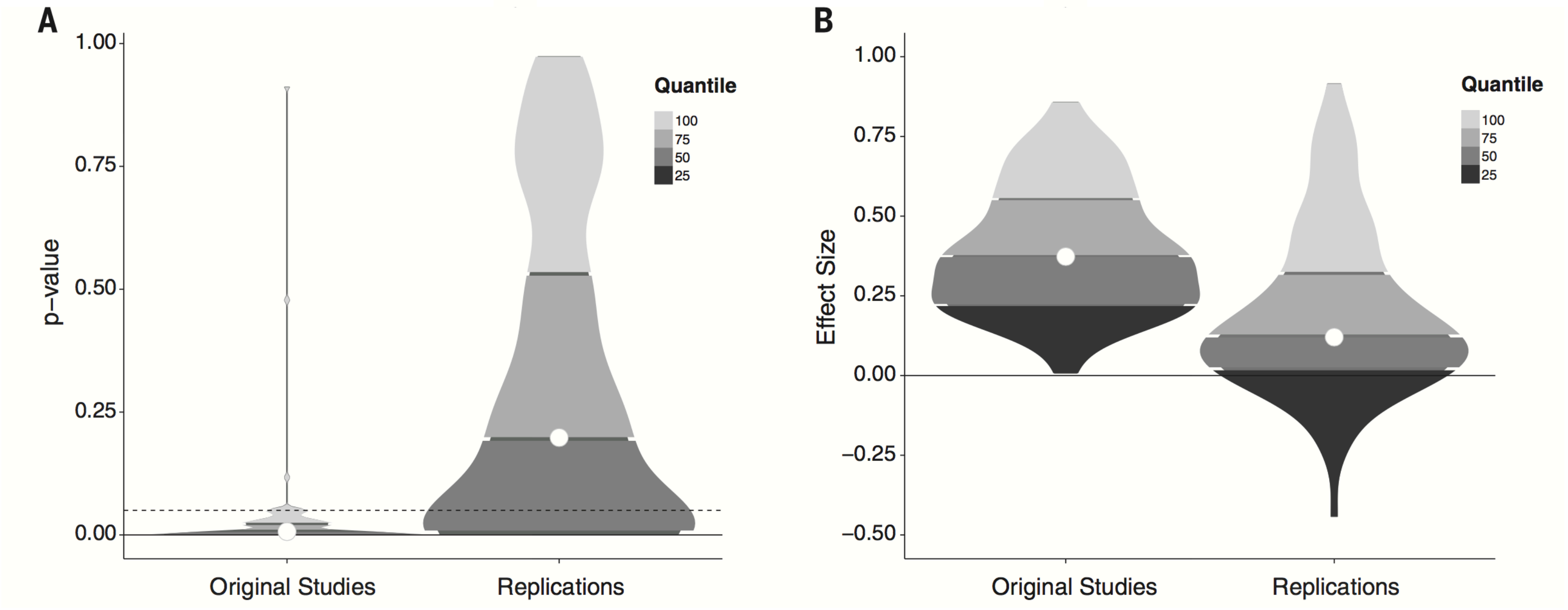


$H_0: n_1 = n_2$

Evidence of p-hacking

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

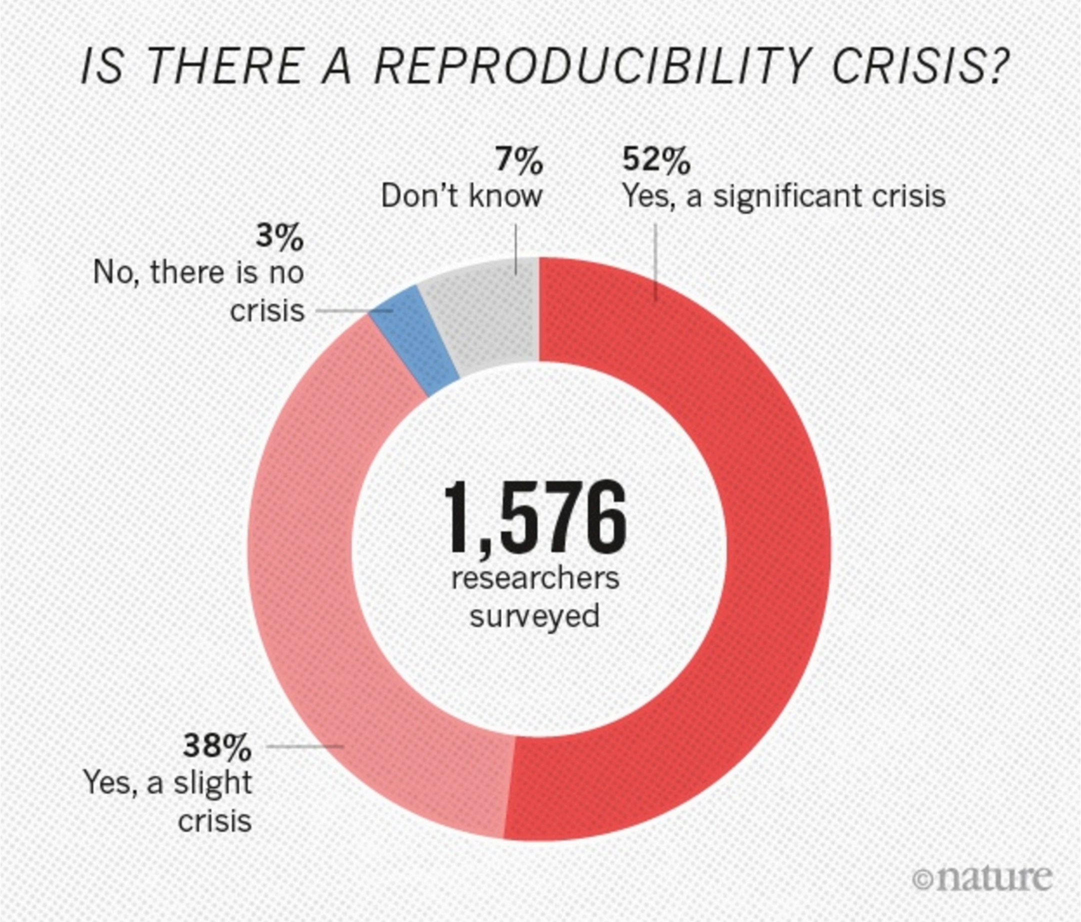
Reproducibility crisis



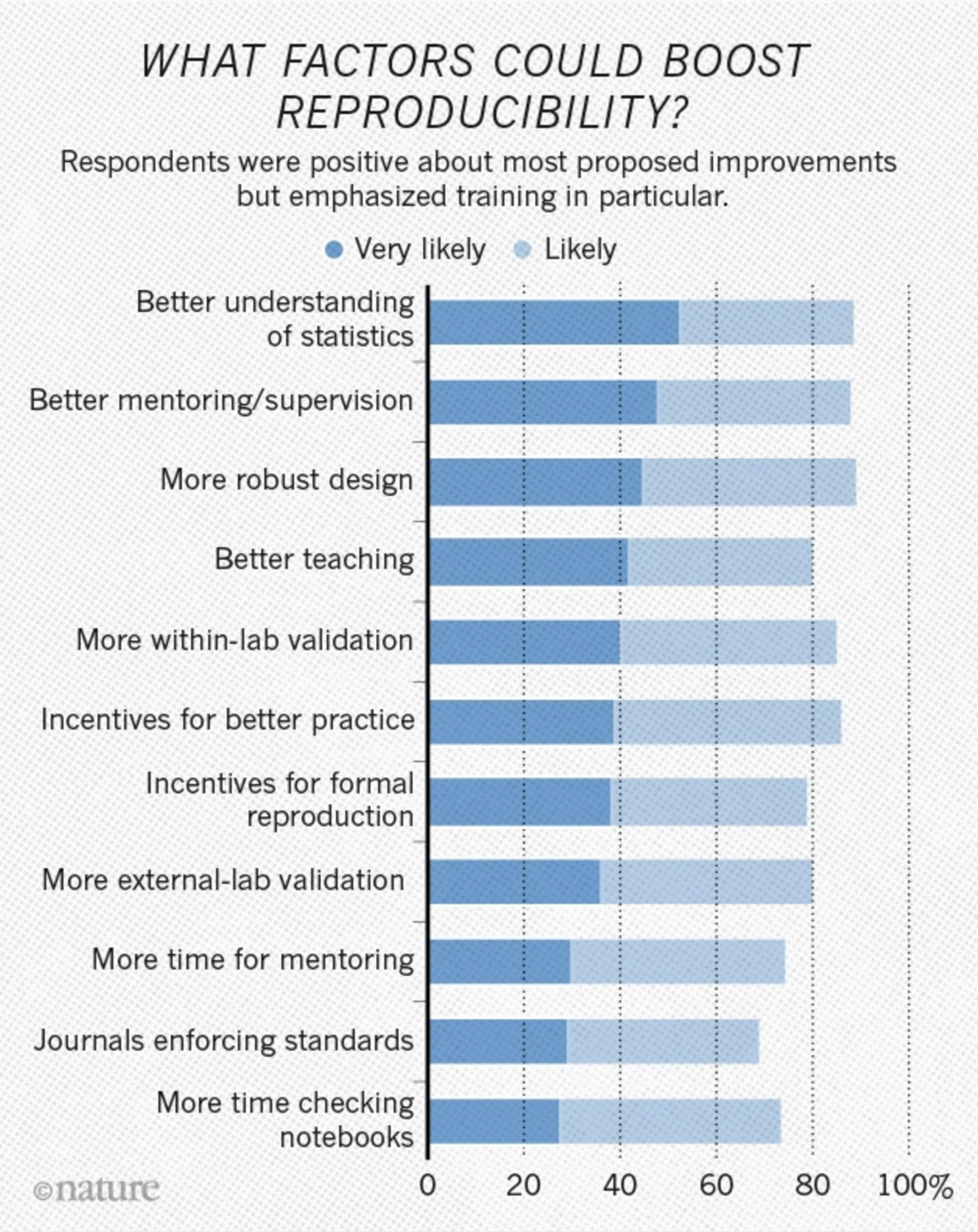
Open Science Collaboration, “Estimating the reproducibility of psychological science”, *Science*, **349** (2015)

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.

The great reproducibility experiment

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

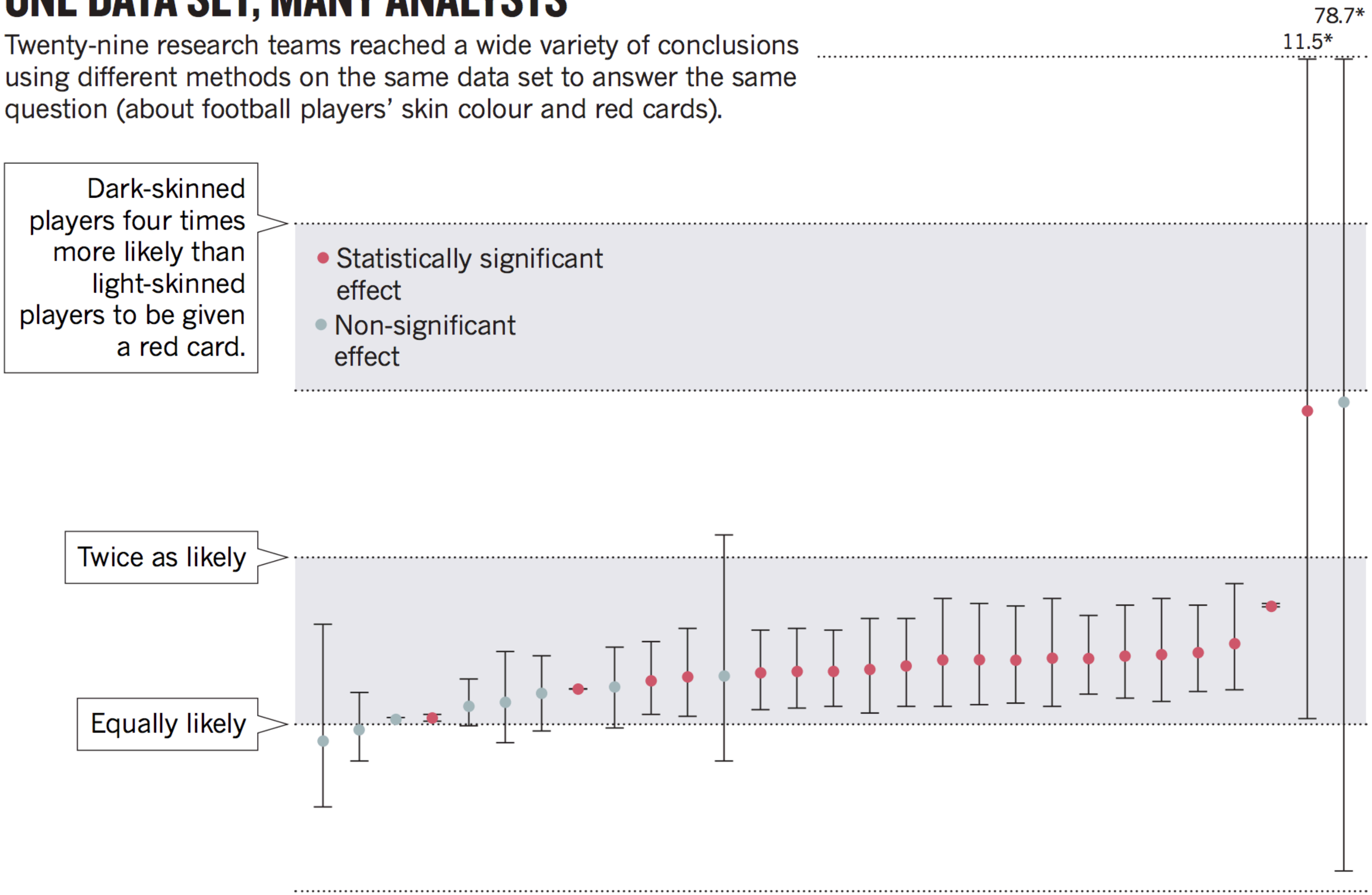
Mario Balotelli, playing for Manchester City, is shown a red card during a match against Arsenal.

Silberzahn et al., “Many analysts, one dataset: Making transparent how variations in analytical choices affect results”, https://osf.io/j5v8f

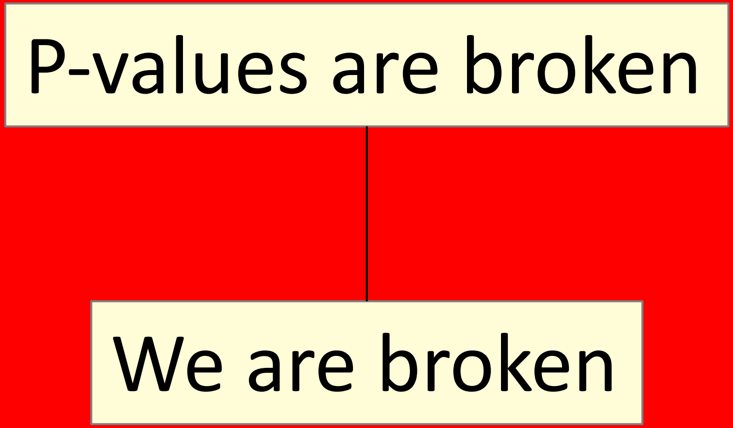
- one data set
- 29 teams
- 61 scientists
- task: find odds ratio

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?

What the hell 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

UNIVERSITY OF DUNDEE

THE BARTON GROUP

01000100010000010101010001000001

The Data Analysis Group

Hand-outs available at
http://is.gd/statlec

Centre for Gene Regulation & Expression

wellcome trust